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SUMARIO • SUMMARY • RESUMO

INVESTIGACIONES

Editorial

From the Editorial Board of the journal MLS Health and Nutritional Research in the transfer of scientific knowledge in the field of health, nutrition and food. We thank the authors who have sent their manuscripts and encourage them to continue sending their articles in order to contribute to the advancement of knowledge.

The first article deals with the "Sensory evaluation and physicochemical properties of set type yogurt enriched with Andean lupin (Lupinus mutabilis) proteins" with formulations containing 0.5, 1 and 1.5% protein concentrate (69% protein, 4% fat and 21% carbohydrates) using a commercial starter culture and cow's milk. Color, aroma, texture and taste acceptability were evaluated.

The following article analyzes the "Cultivation of orange-fleshed sweet potatoes in northern Mozambique favors dietary diversity and provitamin A intake, in rural families", the objective of the research was to know the levels of sweet potato production and dietary diversity in rural populations of Nampula and Zambézia, northern and central Mozambique.

From the field of community nutrition, the "Implication of serum vitamin d during pregnancy on obstetric and perinatal outcomes", maternal nutrition is a determining factor in the correct development of pregnancy. One of the micronutrients that becomes especially important at this stage is vitamin D. The main role of vitamin D is the regulation of calcium homeostasis, although it also plays an important role in the development of pregnancy.

The following article "Review on dietary intervention in polycystic ovary syndrome", the aim of the present study is to investigate the optimal dietary intervention in women with Polycystic Ovary Syndrome (PCOS).

Finally, "Effect of intermittent fasting on cardiometabolic health in obese persons with metabolic syndrome compared to continuous caloric restriction" analyzed different interventions such as intermittent fasting and continuous caloric restriction for the control of cardiometabolic parameters in obese adults with metabolic syndrome.

Editor in chief
Dr. Iñaki Elío Pascual

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Sensory evaluation and physicochemical properties of set-type yoghurt fortified with andean lupin (*lupinus mutabilis*) proteins

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AbstractThe aim of this study was to evaluate the sensory characteristics and the physicochemical properties of high-protein yoghurt fortified with Andean lupin (*Lupinus mutabilis*) protein concentrate. Formulations with 0.5, 1 and 1.5% of protein concentrate (containing 69% proteins, 4% fats and 21% carbohydrates) were obtained using a commercial starter culture and cow´s milk. The acceptability for colour, flavour, texture and taste was evaluated with a hedonic 9-point scale and 100 adults aged between 18-59 years. Participants selected the attributes more convenient to describe the yoghurts using the CATA (Check-All-That-Apply) test. The chemical composition, pH and acidity as well as the textural properties were evaluated. The yoghurt with 0.5% lupin protein concentrate was acceptable according to the sensory attributes. The protein concentrate, when adding at 1 and 1.5%, increased the bitterness, the residual taste and astringency of formulations. The pH values and lactic acid content in fortified products were similar to the control sample, however the syneresis was lower. The yoghurt with 0.5%. The addition of fruits, cereals or honey could be a strategy to increase the acceptability according to participants´ perceptions. The use of yoghurt as dressings in salads could also be a novel form of consumption. The set-type yoghurt fortified with Andean lupin proteins could be alternatives to increase the daily intake of proteins, however some sensory properties should be optimized.

Keywords: yoghurt; legume; proteins; sensory characteristics

Evaluación sensorial y propiedades fisicoquímicas de yogur firme fortificado con proteínas de lupino andino (lupinus mutabilis).

Resumen. El objetivo fue evaluar las características sensoriales y propiedades fisicoquímicas del yogur rico en proteínas fortificado con concentrado proteico de chocho andino (*Lupinus mutabilis*). Se obtuvieron formulaciones con 0,5; 1 y 1,5% de concentrado proteico (69% de proteínas, 4% de grasas y 21% de carbohidratos) utilizando un cultivo iniciador comercial y leche de vaca. Se evaluó aceptabilidad de color, aroma, textura y gusto con escala hedónica de 9 puntos y 100 adultos con edades entre 18-59 años. Los participantes seleccionaron los atributos más convenientes para describir los yogures utilizando la prueba CATA (Check-All-That-Apply). Se evaluó la composición química, el pH y la acidez, así como las propiedades texturales. El yogur con 0,5% de concentrado de proteína de lupino fue aceptable; al adicionarse al 1 y 1,5%, se incrementó el amargor, gusto residual y astringencia de las formulaciones. Los valores de pH y contenido de ácido láctico en los productos fortificados fueron similares a la muestra de control, sin embargo, la sinéresis fue menor. El yogur con 0,5% de concentrado de proteína de chocho mostró mayor firmeza y menor adhesividadLa adición de frutas, cereales o miel podría ser una estrategia para aumentar la aceptabilidad según la percepción de los participantes. El uso de yogur como aderezo en ensaladas también podría ser una forma novedosa de consumo. Los yogures tipo firme fortificados con proteínas de chocho andino podrían ser alternativas para aumentar la ingesta diaria de proteínas, sin embargo, se deben optimizar algunas propiedades sensoriales.

Palabras clave: yogur; legumbre; proteínas; características sensoriales

Introduction

Yoghurt is the product obtained by coagulation and fermentation through the action of proto-symbiotic microorganisms of *Lactobacillus delbrueckii subsp. bulgaricus* and *Streptococcus thermophilus* with the addition or not of other lactic acid bacteria which contribute to the determination of the characteristics of the finished product. (1). The mandatory ingredients allowed in the formulation are milk or reconstituted milk standardized in its content of fat and lactic acid bacteria cultures. Optional ingredients can also be used such as concentrated milk, cream, butter, milk powder, fruit, honey, coconut, cereals, vegetables. Non-dairy ingredients, alone or in combination, must be present in a maximum proportion of 30% (m/m) of the final product (3). In recent years, there has been a rise in consumer demand for high-protein yoghurt, namely that containing a minimum of 5.6% protein and less than 15% fat (3). The interest in high-protein yoghurt lies on the concept of weight management and maintenance of a healthy life style (3). High-protein yoghurt could be beneficial in infant, elderly, or sports nutrition due to the ability of proteins to increase plasma amino acids and trigger the synthesis of proteins (4). Furthermore, high-protein yoghurts could be beneficial in calorie-restricted diets, because the energy intake from protein seems to have a greater effect on satiety than intake of fat or carbohydrate (5).

The protein content in yoghurt can be increased prior to fermentation due to the addition of milk powder, whey powder and micellar casein concentrates or achieved after fermentation by draining, evaporation or membrane filtration (3). A plain yoghurt with a high consumer acceptance should in general have a smooth, uniform and spoonable texture. It should be free from lumps, graininess, and visual whey separation, and it has a clean and typical yoghurt flavour (6,7). The composition of the milk base and the processing parameters and conditions have an influence on the sensory and physical properties of yoghurt. High-protein yoghurt fortified with milk powder showed higher sensory acceptability compared to products added with whey powder and caseinates. However, the perception of bitterness was a limitation to consume these products. Other

sensory defects such as graininess, bitterness, too acidic flavour, and whey separation were also perceived (6).

One strategy to obtain high-protein yoghurt is the use of legume proteins. The ingredients based on legumes are a trend due to the increasing demand of vegetarian people that revolve around the care of the environment (8). The use of legume proteins in the formulation of different fermented foods could increase the intake of protein at lower costs in low-income countries (9). In addition, the research of food innovations that diversify the use of legumes may promote their cultivation in sustainable cropping systems while improving the nutritional quality of products (6).

The limitation to use legume proteins in food formulation is their off-flavour as well as the presence of anti-nutritional factors (10). The off-flavour is produced due to inadequate storage of legumes, overheating of protein extracts, among others, and it limits the use of legume ingredients in product development (10). Major anti-nutritional factors in legumes include saponins, tannins, phytic acid, gossypol, lectins, protease inhibitors, amylase inhibitor, and goitrogens. Anti-nutritional factors combine with nutrients and reduce the nutrient bioavailability. These compounds can be reduced by applying different methods and technologies, such as fermentation, germination, autoclaving, soaking etc (11). Edible legume ingredients such as flour, protein concentrates are used in the formulation of various foods to increase the nutritional value, the healthy properties and functional characteristics of products (10). In yoghurt, the addition of legume flour and protein concentrate increased the protein and fibre contents, the viscosity of formulations and the antioxidant properties of the product (12,13, 14).

Andean lupin (*Lupinus mutabilis*) is a legume native from South America which is consumed in the traditional cuisine of Peru, Bolivia and Ecuador (15).

The genus Lupinus (family Fabaceae) comprises about 267 species of lupines that grow in various regions, from sea level to the Andes (16). There are four species consumed: white lupine *(L. albus*) with wide distribution worldwide, blue (*L. angustifolius*), yellow (*L. luteus*) and Andean (*L. mutabilis*). The latter originates from the region from Ecuador to northwestern Argentina (17, 18). In 2019, 1,006,842 tons of lupines were produced in the world, Australia and New Zealand were the countries where the highest production was recorded (19).

Andean lupin has the highest protein and fat contents (40-50 g/100g and 20-30 g/100g, respectively) compared to other legumes such as pea and chickpea (20). Seeds are sources of bioactive compounds such as polyphenols and carotenoids with antioxidant and antihypertensive properties (21). Andean lupin has monounsaturated and polyunsaturated fatty acids which can promote the cardiovascular health. Proteins are represented by globulins (80%) as in other legumes and there is a small proportion of albumins and prolamins (15). The amino acids cysteine and methionine are limiting; while lysine, leucine, isoleucine, tyrosine, and glutamic acid are abundant (15, 18).

Grains contain a significant amount of dietary fiber but no starch. The shells are composed of cellulose, hemicellulose and pectin, while in the cotyledons there are polysaccharides composed of galactose, arabinose and uronic acid (22). Lupines contain bitter alkaloids from the quinolizidine family. These compounds are toxic so they must be removed (23). Most of the alkaloids are soluble in water, the traditional debittering process includes soaking the seeds for 18-20 h, followed by cooking between 0.5 and 6 h (24).

Several ingredients are obtained from Andean lupin seeds (i.e: protein concentrates, isolates, edible oil, lupin flour) (20).

The lupin protein concentrate, which has ~60% of lupin proteins, has been used in the production of bread and noodles showing good sensory characteristics and high consumer acceptability. The incorporation of lupin products such as flour into fermented foods was limited due to the persistent after-taste perceived in formulations (23). The after-taste could be attributed to the remanent of alkaloids, toxic and bitter compounds for humans and animals (15). Their presence in food represents a concern for safe consumption since their ingestion can cause intoxication. Alkaloids can be removed by soaking, cooking and washing lupin seeds, until a safe level of consumption <0.02 g/100g seeds (15). There are also improved varieties with lower alkaloid content, however these are not available in Latin America (25).

The demand for healthy products is growing every time, particularly those with new, more sustainable and lower cost ingredients (26). There is a potential to produce high-protein yoghurt with Andean lupin protein concentrate to increase the offer of healthy products (24). The use of more refined lupin ingredients such as the protein concentrate could enhance the sensory properties of the final product since it has lower alkaloid contents (24). Thus, the aim of this study was to evaluate the sensory characteristics and physicochemical properties of these products for future industrial applications

Methods

Formulation of set-type yoghurt

The procedure to obtain set-type yoghurt fortified with Andean lupin protein concentrate was previously published (27). Briefly, the lupin seeds were debittered following the traditional aqueous method. Seeds were soaked in water at 25°C for 18 h, then cooked for 1h in bowling water and washed for 5 days at 25°C. The debittered seeds were oven dried at 60°C, milled and sieved to pass through 250 µ. The debittered flour was defatted with an aqueous ethanol solution (70:30 w/v) for 24 hs by maceration, then filtered, the flour was collected and oven dried at 60°C. The defatted lupin flour was extracted at pH 7 with 1M of NaOH solution for 1h at 30°C, then centrifuged at 3300 xg to eliminate the insoluble fibres and the protein solution was spray-dried (28). The chemical composition of lupin protein concentrate corresponded to 69.4% protein, 4% fat, 5.7% ashes, 21% carbohydrates (27).

The ingredients and lactic acid starter culture used in the present study to obtained the yoghurt were different to those previously reported. The set-type yoghurts were formulated with Manfrey® skim milk powder at 13.5%, vanilla essence at 0.4%, Royal® gelatin at 0.5% and freeze-dried thermophilic culture DVS composed by *Streptococcus termophilus* and *Lactobacilus delbruecki bulgaricus* (CHR HANSEN® YF-L812 No 3381849). The Andean lupin protein concentrate was used at 0.5, 1 and 1.5% in filter water. The protein solutions were stirred at 600 *xg* for 3 min and heated at 90°C for 10 min, then skim milk powder and gelatine were added. The mix was homogenised and heated at 85°C for 4s. The yoghurt samples were added with vanilla essence and cooled at 45°C to inoculate the lactic acid bacteria culture. Bacteria were inoculated at 0.04% as recommended by the manufacturer. Each yoghurt was placed in individual plastic containers and incubated at 43-45°C. A control sample (without the addition of the

Andean lupin protein concentrate) was also obtained following the same procedure. After reaching pH 4.8, the samples were cooled and refrigerated at 5°C for 24 h (27).

Sensory evaluation

The protocol for the sensory analyses was approved by the Ethics Committee of the Faculty of Health Science of the National University of Salta (DC 714/19). Participants (n= 100) aged between 18-59 years were regular consumers of dairy products, with no food allergies or lactose intolerance and they were recruited at the University. The consumers signed an informed agreement to participate in the study. The fortified yoghurts and the control sample in their containers (40g each) were coded with random three-digit numbers. The samples were presented to the consumers in a balanced rotation order (29). Water and biscuit were also served. The participants were instructed to rinse their mouse between tasting the samples.

The yoghurt samples were evaluated according to their acceptability for colour, flavour, taste, texture and the general impression (overall acceptability) using a nine-point hedonic categorical scale rated from 1 (I dislike it extremely) to 9 (I like it extremely). The Check all that apply (CATA) test was used to evaluate the sensory characteristics of yoghurt samples (30). The participants were instructed to select the attributes that they considered convenient to described the product they were tasting. The CATA questionnaire was composed by sensory and non-sensory terms, randomly presented within the two groups of terms and between products: *bitter, astringent, milk flavour, medicine-like taste, salty, spicy, bitter aftertaste, sweet, acid, firm, thick, vanilla taste, white, whey separation*, *healthy, nutritive, I would eat it every day, snack/breakfast, dietetic food, light, ugly/nasty; tasty/pleasant.* The CATA terms were selected according to previous studies in which consumers evaluated yoghurt fortified with dairy proteins (31). At the end of the questionnaire, the consumers had to express appreciations about each product as a sentence.

Physicochemical properties

Since the yoghurts were formulated with different ingredients, the control of physicochemical properties were necessary. The pH value, lactic acid content and percentage of synaeresis were determined after 24 h of refrigerated storage. The pH values were evaluated with a HANNA® digital pHmeter and the lactic acid content was evaluated using the acid-basic titration method and phenolphthalein as indicator (32). The synaeresis was determined as the percentage of whey expulsion (33). Briefly, yoghurts in their containers were drained face down for 2h, the whey was collected in a tared glass vessel and yoghurts were weighed. The percentage of whey expulsed was calculated as the difference between the initial weight of the container and the weight after draining the yoghurt whey.

The chemical composition of fortified yoghurt and the control sample was determined according to the AOAC methods: the moisture content was evaluated by dehydration of samples in vacuum oven at 105°C, the ashes by muffle incineration of samples at 550°C, proteins were determined by the Kjeldhal method and the factor used to convert nitrogen into proteins was 6.25. The fat content was evaluated by applying the Gerber method, in which the separated fat was measured directly in a calibrated butyrometer (32). The total carbohydrate content was calculated by applying the equation= 100 - (moisture + proteins + fats + ashes).

The textural properties were analysed by uniaxial penetration of yoghurt samples using a TA-XT2 Texture Analyser (Stable Micro Systems, Godalming, UK). Each

product in the individual container was conditioned at 8°C. The penetration was done with a 25x35 mm cylindrical flat probe to 45 mm depth at 3 mm s-1 rate and a compression force of 15g. The probe was placed at 20 mm initial distance from each sample. The following parameters were evaluated: the firmness (N) defined as the maximum force to achieve a given deformation which was represented by the peak force of the penetration cycle; the firmness work done (mJ) defined as the energy required to drive the probe during the downward penetration step which was represented by the area under the positive peak. The adhesive force (N) defines as the maximum force generated during the probe upstroke, was represented by the negative peak force. These parameters were calculated by the Texture Expert Exceed software® (34).

Statistical analysis

The results of the acceptability evaluation and physicochemical properties were expressed in means ± standard deviations. The ANOVA and Tukey's tests were applied to evaluate the differences among yoghurt samples, using a significance level $p<0.05$. The frequencies of mention of each CATA term selected by the consumers were calculated for each product, and the Cochran's Q test was applied to test differences between the sensory characteristics. Statistical analyses were performed with the student version of the Infostat® software (35).

Results

Sensory evaluation

The consumers who evaluated the yoghurt samples corresponded to 33% of men, 67% women aged between 18-28 (12%), 28-38 (20%), 38-48 (25%) and 48-58 years (43%). The yoghurt with 0.5% lupin protein concentrate and the control sample were acceptable for consumers according to all the attributes evaluated (Table 1). The colour, flavour and texture attributes in yoghurts with 1 and 1.5% of the concentrate were considered indifferent to consumers. The control samples achieved the highest scores for all the attributes evaluated by participants.

Table 1.
Scores for the sensory evaluation of yoghurts fortified with 0.5, 1 and 1.5% Andean lupin protein concentrate and the control sample

Attributes	Y0.5	Y1	Y1.5	Control
Overall acceptability	6.8±0.7c	3.9±2.5a	4.7±2.6b	7.3 ± 1.7c
Colour	6.9±0.9c	5.7±1.3b	5.1±2.3a	7.1 ± 1.6c
Flavour	6.9±0.9c	5.9±1.5b	4.9±2.6a	7.2 ± 1.6c
Texture	7.1±1.0c	5.9±1.4b	4.5±2.3a	7.4 ± 1.7c
Taste	7.0±0.5c	3.3±1.4b	2.7±2.1a	7.5 ± 1.7d

Values followed by different letters between columns indicate significant differences ($p<0.05$).

The CATA test revealed that yoghurt samples achieved significant differences in almost all the attributes, except for the term *firm* (Table 2). The participants indicated that products with greater proportions of lupin concentrate (1 and 1.5%) were less thick and had less superficial whey/liquid (Table 2). The fortified products were described as astringent, pungent, with medicine-like flavour and bitter (Table 2). The residual taste was also perceived in those products. The yoghurt with 1% of protein concentrate was perceived as salty. The fortified yoghurts were also perceived as spicy and less sweet than the control sample. Yoghurts with 1 and 1.5% of protein concentrate were perceived by consumers as products with less milky and vanilla flavour (Table 2). The yoghurts fortified with Andean lupin protein concentrate were perceived as more acidic and with less white colour than the control sample (Table 2).

The product with 0.5% of the protein concentrate and the control sample were considered pleasant according to consumers. The fortified yoghurts with 1 and 1.5% were perceived as less nutritious, healthy, and light than the rest formulations evaluated (Table 2). They were not perceived as dietetic foods, for daily consumption or as a breakfast (Table 2). Some appreciations evoked by participants about these yoghurts were: "*I liked it at the beginning but in the end, I had a bitter and astringent taste*", "*It left in my mouth a medicinal-like taste*". The forms of consumption evoked were: "*If I put fruits, cereal and honey I would eat it as breakfast*", "*If it was accompanied with some fruit, it would be better*". The occasions of consumption these products were in salads or as a dressing as it was expressed by participants: "*in salads would be a good alternative*" or "*as a salad dressing*".

Table 2.
Frequency of mention of sensory characteristics evaluated thorough the CATA test in fortified yoghurts with 0.5, 1 and 1.5% Andean lupin protein concentrate and the control sample

CATA terms	Y0.5	Y1	Y1.5	Control
Bitter	4a	74b	94b	0a
Astringent	15b	22b	18b	6a
Milk flavour	29b	16b	0a	24b
Medicine-like flavour	21b	40b	51b	0a
Salty	0a	6b	0a	0a
Spicy	10b	12b	8b	1a
Bitter aftertaste	38b	32b	61b	3a
Sweet	23b	9a	10a	55c
Firm	61a	64a	64a	53a
Acid	12ab	22ab	37b	0a
White colour	45ab	30ab	23a	61b
Tasty/pleasant	13a	9a	2a	49b
Ugly/nasty	0a	26b	24b	0a
Vanilla taste	24a	33ab	20a	46b
Nutritive	14b	4a	2a	16b
Eat it every day	6a	4a	2a	22b
Snack	2a	0a	8b	35c
Breakfast	6a	2a	0a	19b

Residual taste	39b	32b	39b	10a
Healthy	14a	8a	6a	33b
Light	8a	16a	6a	41b
Dietetic food	20b	28b	10a	31b
Thick	26b	12a	15a	17a
Whey separation	17a	8a	22ab	44b

Values followed by different letters between columns indicate significant differences ($p<0.05$).

Physicochemical properties

The pH values after 24 h of refrigerate storage corresponded to 4.8 ± 0.0^{a} in Y0.5; Y1 and Y1.5, while in the control sample it was 4.7 ± 0.0^{b}. The pH was higher in fortified yoghurts as it was previously observed in yoghurts fortified with legume proteins (25). At day 1, the lactic acid content was 1.2; 1.1 and 1.1 g/100 g in yoghurts fortified with 0.5, 1 and 1.5% protein concentrate and 1.1 g/100g in the control sample. No significant differences were observed in the lactic acid content between samples. The syneresis values corresponded to 0.2 ± 0.0^{c}; 0.4 ± 0.1^{c} and 0.5± 0.2(b) in fortified yoghurts, whereas in the control sample it was 2.1 ± 0.0^{a}.

Table 3 shows the chemical composition of yoghurts. The fortified yoghurts showed lower moisture content than the control sample. The fortified yoghurts also showed higher protein and fat contents, but lower carbohydrate content compared to the control. The content of ashes were similar among fortified and non-fortified yoghurts.

Table 3. Chemical composition (g/100g) of fortified yoghurts with 0.5, 1 and 1.5% Andean lupin protein concentrate and the control sample

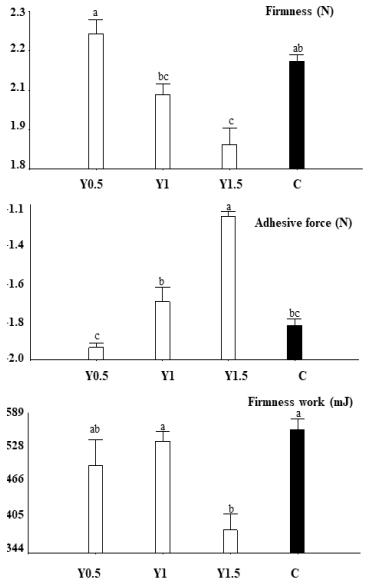
	Y0.5	Y1	Y1.5	Control
Moisture	80,8±0,3bc	80,4±0,2b	80,0±0,1c	82,6 ± 0,2a
Proteins	6,9 ± 0,3b	6,8 ± 0,1b	7,9 ± 0,2a	5,8 ± 0,1c
Fats	8,1 ± 0,2b	8,5 ± 0,1b	9,0 ± 0,2c	4,2 ± 0,2a
Ashes	1,2 ± 0,1a	1,2 ± 0,2a	1,3 ± 0,2a	1,4 ± 0,2a
Carbohydrates	3,0 ± 0,2b	3,1 ± 0,2b	1,8 ± 0,2c	6,0 ± 0,0a

Values followed by different letters between columns indicate significant differences ($p<0.05$).

Fig. 1 shows the textural properties of yoghurts. The product with 0.5% lupin protein concentrate showed higher firmness but lower adhesiveness compared to the rest of the formulations. Yoghurt with 1.5% showed the highest value for adhesive force. The values for firmness work were similar in fortified yoghurt with 0.5% and 1% protein concentrate and the control sample.

Figure 1

Textural properties (firmness value, adhesiveness and adhesive force value) evaluated in fortified yoghurts with 0.5, 1 and 1.5% Andean lupin protein concentrate and the control sample. Values followed by different letters between bars indicate significant differences ($p<0.05$).



Discussion and conclusion

Set-type yoghurts fortified with Andean lupin proteins could represent alternatives for consumption in the daily diet. The chemical composition of these products revealed a high protein content (>5.6%), so they could be classified as high-protein foods (3). The fat content was less than 15%, which is an advantage for the protection of cardiovascular health. Food with less content of fats can reduce the blood pressure and cholesterol levels (9). In addition, fortified yoghurt containing live cultures can provide beneficial bacteria which when eaten regularly may support gut health. This is because regular inclusion of fermented foods in diet, including yogurt, increase the microbial diversity of the gut (9). The fermentation also has beneficial effects in the legume ingredient added in the formulation. The process improves the nutritional value of legumes (10,36), such as the protein digestibility and mineral availability. It also reduced the content of antinutritional factors as well as it increases the biological availability of the remanent of total fibre and phenols. The fermentation also improves the viscosity of the products (36) as it was observed in yoghurt with 0.5% protein concentrate (Fig. 1).

To promote the consumption of these promising food, some sensory characteristics should be optimized. The participants perceived the attributes of aroma, colour and texture as indifferent, whereas the flavour and overall acceptability were the properties that they defined as more outstanding and that could limit the consumption (Table 1). An study in which consumers had to express their opinions and perceptions about yoghurts fortified with dairy proteins also found that the addition of whey protein concentrate and caseinates decreased the acceptability and the scores for taste compared to the products supplemented with milk powder (31). The decrease in the acceptability of flavour was explained by the greater perception of the bitter and astringent taste in those products (31). The similar impression could have caused the yoghurt with lupin proteins. In addition, the perception of the bitter taste also influenced the overall acceptability of yoghurt (Table 1 and 2).

The perception of the residual taste and medicine-like flavour in yoghurts could be explained by the interaction between the sweetener and lupin proteins, as well as their binding with the flavour receptors in mouth (37). One strategy raised in a previous study to increase the sensory acceptability was the inclusion of a higher refined product to reduce the perception of bitterness (37). Results of this study showed that the utilization of spray-dried protein extracts of lupins, as a refined product, did not positively impact on the perception of flavour. The bitterness in fortified yoghurts could also be explained due to the presence of plasmin. Plasmin can cause hydrolysis of caseins in yoghurt, leading to the formation of bitter peptides. The bitter taste in yoghurt was positively correlate with astringent mouthfeel. Astringency in milk products can be caused by different compounds, including γ-casein from plasmin-induced degradation of β-CN (3). The combination of lupin proteins with dairy protein powders which have bland flavour as well as the concentration of milk previous to fermentation could provide a high-protein, non-fat yoghurt with good sensory properties (3).

Despite the fortified yoghurts showed similar pH and acidity values measured instrumentally, consumers perceived them as more acidic, which could be explained by two facts. One was that the perception of bitterness could have influenced the perception of acidity or two, the Maillard reaction that may have occurred during the heating in the production of yogurt could have turn lupin proteins more acidic to taste (38). The Maillard reaction is a non-enzymatic reaction that occurs when the carbonyl group of reducing sugars reacts with the amino group of amino acids, polypeptides, or proteins, resulting in the natural production of Maillard reaction products (MRPs), a class of compounds with a wide range of sensory properties (38). Overreactions often turn the food bitter and accumulate burnt flavour. The control of temperature and time of heating of lupin proteins could be an alternative to reduce the Maillard reaction and thus the perception of the acidity in yoghurts.

The rejection of the bitter taste played an important role against the perception of healthy properties. In a previous study, the authors expressed that some consumers are more likely to choose a product perceived as healthier, even if it presents some sensory defect (39). The results of the present research showed that the perception of the healthy attributes was influenced by the taste of yoghurts. According to participants, fortified yoghurts were less dietetic and light than the control (Table 2). Moreover, the fortified yoghurts were perceived as less white than the control sample (Table 2), which could be attributed to the colour of the protein concentrate. Andean lupin concentrate showed a yellow colour tendency, thus, the colour parameters of fortified yoghurts should be measured instrumentally to determine specific differences among products.

The CATA test revealed that yoghurt samples achieved significant differences in almost all the attributes, except for the term *firm* (Table 2). Yoghurts were perceived as similar according to this characteristic, however there were differences in the textural properties of yoghurts (Fig. 1). Previous studies reported an increase in the viscosity of yoghurts due to the addition of lentil and chickpea flours (14, 40) which was explained by the increase in the total solids, as well as the protein and fibre contents of these ingredients. The inclusion of lupin flour in the production of yoghurt turned them less fluid and firmer (25). The lower firmness values and the higher adhesiveness showed in yogurts supplemented with 1.5% Andean lupin protein concentrate could be indicative of a weaker gel network, probably due to a poor interaction between lupin proteins and those of cow´s milk (6). The weaker gel could also be attributed to the higher pH values at the end of the fermentation process (4.8). It has been reported that a higher final fermentation pH (~4.8) produced lower apparent viscosity in yoghurts (3). On the other hand, the addition of the lupin protein concentrate was beneficial to reduce the synaeresis in

yoghurts, which could be attributed to the ability of legume proteins to absorb the whey expelled by the casein network (6).

The participants evoked new forms of consumption of fortified yoghurts. Although, they would not eat these products in breakfast (Table 2), the combination with fruits, cereal or honey could turn them more acceptable for consumption. The suggestions should be explored in future studies, in terms of sensory and physicochemical properties since it is necessary to determine the shelf life of products with more ingredients. The addition of fruits, cereal or honey in yoghurt can modify the microbiological and physicochemical characteristics (such as pH, acidity and syneresis), which play an important role in consumer acceptability (3). Another tool to increase the consumer acceptability could be the use of other flavouring such as strawberry or peach to mask the bitter taste or the combination of sweeteners of different nature. The bitterness and medicine-like flavour of products (Table 2) may also be perceived due to the interaction of the sweetener with lupin proteins (37), thus, the use of different sweetener could reduce this reaction. The utilization of fortified yoghurts as dressing in salads could also be novel for gastronomy, especially for the elaboration of vegetarian recipes. Work will be done on the development of other products that are more acceptable to the population and that are frequently consumed, such as legume-based snacks or cookies along with other crops of regional interest.

High-protein yoghurts fortified with Andean lupin protein concentrate at 0.5, 1 and 1.5% were obtained. The sensory evaluation with 100 regular yoghurt consumers revealed that only the product with 0.5% protein concentrate was acceptable according to all the attributes evaluated. Fortified yoghurt with Andean lupin proteins were perceived as more acidic, with bitter and residual taste. As the percentage of Andean lupin protein concentrate increased in products, the higher was the bitterness, after-taste, and astringency. In addition, the perception of the healthy properties decreased due to the perception of those sensory defects. The pH values and lactic acid contents were similar in fortified yoghurts compared to the control sample after 1 day of storage. The synaeresis was lower in fortified yoghurts than in the control sample. The addition of Andean lupin proteins at 0.5% increase the firmness and decreased the adhesiveness of the product. The addition of fruits, cereals or honey could increase the acceptability of the products as it was evoked by participants. The use of fortified yoghurt as dressings in salads should also be explored.

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GROWING ORANGE-FLESHED SWEET POTATOES IN MORTHERN MOZAMBIQUE FOR DIETARY DIVERSITY AND PRO-VITAMIN A INTAKE IN RURAL HOUSEHOLDS.

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Abstract. Dietary diversity is a measure to determine food access and consumption in a household, and when triangulated with other information it gives a holistic picture of the state of food security and nutrition in the community or over a wide area. The study aimed to know the sweet potato production level and dietary diversity of the rural populations of Nampula and Zambezia provinces, northern and central Mozambique. In general, data from the study showed that 17% of farmers grow white and orange-fleshed sweet potatoes. From a nutritional perspective, the study revealed that about 65% of rural households in Nampula and Zambezia consume sweet potatoes in their daily meals. Data to assess the knowledge and perception of rural households about the importance of sweet potatoes in the diet indicates that 66% of respondents consider it as a healthier food, especially the orange-fleshed varieties, due to the presence of pro-vitamin A content. Data analysis per district to determine the diet adequacy for children under five years of age indicated that, on average, 68% of children in Alto Molocuè, Gurué and Murrupula have poor dietary diversity.

Key words: dietary diversity, growing, nutrition, orange-fleshed sweetpotato, rural households.

CULTIVO DE BATATA DOCE DE POLPA ALARANJDA NO NORTE DE MOÇAMBIQUE EM PROL DA DIVERSIDADE

ALIMENTAR E INGESTÃO DE PRO-VITAMINA A EM FAMÍLIAS RURAIS

Resumo. Diversidade alimentar é uma medida que determina o consumo e acesso de alimentos em um agregado familiar, podendo esta, ser triangulada com outras informações. Esta, fornece de forma holística, uma imagem de segurança alimentar e nutricional comunitária ou área territorial mais extensa. A pesquisa tinha como objectivo, conhecer os níveis de produção da batata doce e da diversidade alimentar em populações rurais de Nampula e Zambézia, norte e centro de Moçambique. No geral, apenas 17% da população da área de estudo produz batata doce de polpas alaranjada e branca. Em termos de consumo, o estudo encontrou nos seis distritos de Nampula e Zambézia 65% de consumidores de batata doce. Dados de avaliação do conhecimento e a percepção sobre a importância da batata doce na dieta indicam que, 66% de entrevistados consideram-na um alimento saudável, especialmente, variedades de polpa alaranja, pois ela é rica em pró-vitamina A. A análise de dados por distrito para determinar a adequação da dieta em crianças menores de cinco anos indicou que, em média, 68% das crianças de Alto Molocuè, Gurué e Murrupula têm uma diversidade de dieta deficiente.

Palavras-Chave: cultivo, batata-doce de polpa alaranjada, diversidade alimentar, famílias rurais, pro-vitamina A.

Introduction

Dietary diversity is known as an indicator of a household's food consumption and access, which can be triangulated with other information. This provides a holistic picture of food and nutrition security in a community or wider territorial area. In Mozambique, diet quality is still a problem, especially in the central and northern regions of the country, where micronutrient intake is quite poor. The levels of vitamin A and iron deficiency are quite high.

The provinces of Cabo Delgado, Nampula and Zambézia have anemia rates in children above the national average, with the latter having the highest prevalence (79%). The national average for chronic malnutrition in Mozambique has fallen in the last ten years, from 43% to 38%, but the provinces of Nampula and Zambézia still have higher levels, between 46.7% and 44.6% respectively [(3)]. The prevalence of vitamin A deficiency in children under five also remains high in the country, with Nampula being the index province (55%) [(1)].

Food consumption at household level (FA) is poorest in the northern region of Mozambique (Cabo Delgado, Nampula and Niassa and Zambézia) and even better in the central and southern provinces of the country [(3)], which reinforces the need to invest in nutrition in the northern provinces of the country.

Nutrition is a key indicator of an individual's development and refers to how the body processes and uses food [(3)]. It also relates to health, habits, customs and healthy eating practices. The alteration of an individual's nutritional status, whether due to food deprivation or micronutrient deficiency, is generally known as malnutrition. In nutritional terms, pregnant and breastfeeding women and children under the age of five should be the groups that receive the most attention [(4)].

A mother who is not well-nourished during pregnancy may give birth to a child with a low birth weight (<2.5 kg), which could have major repercussions for the newborn, as this will be reflected in infant mortality, since children who are born undernourished have a high risk of morbidity and mortality due to greater exposure to common childhood diseases. Those that survive become ill and may grow poorly.

Children without access to adequate nutrition are not always sick, but they may not reach their potential for physical and mental growth [5]. Climate change contributes to changes in the nutritional status and diet of a population, as it has a negative impact on food security. Generally speaking, the negative impact is limited to the outbreak of diseases, water insecurity, poor environmental sanitation, poor livelihoods, parents' attention to children, handicapping people's ability to adapt or mitigate them [6]. The sweet potato has shown itself to be an appropriate crop in the face of climate change, because in cases of drought, it easily adapts due to its low water demand and this makes it play an important role, acting as a source of subsistence during periods of hunger and food shortages [7].

This crop is one of the staple foods in Mozambique, and can be found in practically every farming system in the country. Along with cereals and legumes (peanuts and beans), sweet potatoes are among the main products that make up the basic diet of Mozambicans [8]. In addition to its greater acceptance due to its taste, it is used almost in its entirety, boiled, roasted, stewed, fried, in puree, porridge or even desserts. [9].

Its leaves are rich in folic acid and iron (non-heme) and are used as a curry. A daily intake of 400g of greens combined with fruit and vegetables can help alleviate micronutrient deficiencies and prevent chronic diseases associated with unhealthy food consumption and lifestyle [10]. Sweet potatoes belong to the group of foods that can alleviate micronutrient deficiencies and prevent chronic diseases associated with dietary deficiencies, as they are very rich in nutrients such as high levels of carbohydrates, high concentrations of vitamin A (especially orange-fleshed cultivars), B-complex and some minerals such as calcium, iron, phosphorus, potassium, sulphur and magnesium.

Its nutritional richness makes it great for regulating blood pressure and preventing certain types of cancer. It is especially valuable because it is a food security crop for vulnerable people and can provide the population with a significant portion of dietary carbohydrates [11].

The importance of sweet potatoes goes beyond food, often serving as a means of generating income for rural and urban families in Mozambique. In 1997, the Instituto de Investigação Agrária de Moçambique (IIAM) introduced varieties of orange-fleshed sweet potato (BDPA), but its cultivation and consumption is still very insignificant in the country. Weekly rates of BDPA consumption in AFs stand at 17 percent. Analysis by province shows that consumption is highest in Maputo province and Maputo City, followed by Sofala, Tete and Zambézia. On a weekly basis, families in the provinces of Cabo Delgado and Nampula consume the least BDPA [3].

The inclusion of sweet potatoes, especially orange-fleshed ones, in the family diet can help diversify food consumption and therefore increase nutrient intake. Diet diversification is a change and choice of dietary patterns and families' traditional methods of preparing and processing local foods [12].

For some, dietary diversification means dietary diversity, and this refers to a substitute for a qualitative measurement of food consumption by assessing families' access to different food groups, called the family dietary diversity index. For others, food diversification is a snapshot of the economic well-being of a PA in relation to access to a variety of foods and serves as a reference for the adequacy of nutrient intake at an individual level [13, 14]. Whether or not the diet is appropriate is based on *scores,* adding up the number of food groups consumed at home or by the interviewee over a 24-hour period [13].

Family and individual dietary diversity is measured by establishing scores for the adequacy of intake. A score of less than four (<4) represents poor dietary diversity, a score of 4-5 represents average dietary diversity, and a score of six (6) or more indicates adequate nutrient intake [(15)].

The increase in family food diversity is associated with the family's socio-economic status and food security. At an individual level, an increase in the dietary diversity score is associated with nutritional adequacy, i.e. food security [(16)]. Food security is defined as ensuring that everyone has access to quality basic food, in sufficient quantity, on a permanent basis and without compromising access to other basic needs, based on dietary practices that allow the human body to reproduce properly, thus contributing to a dignified existence [(17).]

In Mozambique, food security is still a challenge and the adequacy of the diet varies from region to region, with better quality in families in the south of the country and part of the central region. However, in the northern region, dietary adequacy is still poor [(3)]. As is well known, a poor to moderate diet results in high rates of chronic malnutrition (short stature for age), with chronic malnutrition in Mozambique affecting around 43% of the country's children. The prevalence of chronic malnutrition is highest in the central and northern provinces, ranging from 41% to 52% respectively, and is lowest in the south; Inhambane, Gaza, Maputo Province and Maputo City, at between 26% and 39%. In rural areas of Mozambique, more children suffer from chronic malnutrition (45%) than in urban areas (39%). The prevalence of acute malnutrition (low weight for height) is 7%, but there are significant differences between the country's provinces [(3)].

Around 14% to 16% of FAs in Zambézia and Nampula, respectively, have a poor diet. These families have a low frequency of consumption of foods with a high protein content, such as meat, poultry, eggs, rats, offal, varying from 2 to 3 days a week. People in these provinces usually consume cereals, vegetables, milk, fruit, sugar and oil an average of 4 days a week [(3)].

The Mozambican government has public policies aimed at improving the food and nutritional security of its population. These policies comprise two government instruments: (i) food and nutrition security strategy and (ii) multisectoral action plan to reduce chronic malnutrition (PAMRDC). The Ministry of Agriculture and Rural Development (MADER) guarantees the availability of and access to food for families. This sector has been promoting the production of more nutritious food through the implementation of several key national programs. MADER promotes the cultivation of food crops such as corn, rice, cassava, peanuts, potatoes, soybeans and beans, as well as poultry and fish farming.

The use of improved production technologies such as animal traction, irrigation, fertilizers, certified seeds, agricultural extension and animal health monitoring guarantees the production of these crops. With regard to the promotion of nutritious food, MADER is implementing the extension program known as SUSTENTA, which aims to educate small farmers to produce crops with a high nutritional value, such as orange-fleshed sweet potatoes.

BDPA is seen as an essential food for combating malnutrition, as it is a good source of energy and pro-vitamin A. It is a food security crop, as it is less labor-intensive than other crops and is even considered suitable for women to manage. It requires less water and can be grown over a long period of time without any loss of yield [(18)].

In the country, the introduction of BDPA into the production system has brought evidence of improved levels of pro-vitamin A intake in pregnant and lactating women and children under five [(19)]. Vitamin A levels in this target group were determined on the basis of laboratory analyses of consumers' serum retinol.

The results of the laboratory analysis showed that there was an increase in vitamin A in the blood of around 89% of children, pregnant and breastfeeding women who frequently consumed BDPA over a certain period. Therefore, expanding the cultivation and consumption of BDPA by children under five, pregnant and lactating women could significantly improve vitamin A intake in Mozambique in general, and in the provinces of Nampula and Zambézia, the geographical areas with the most deficient populations [(19)].

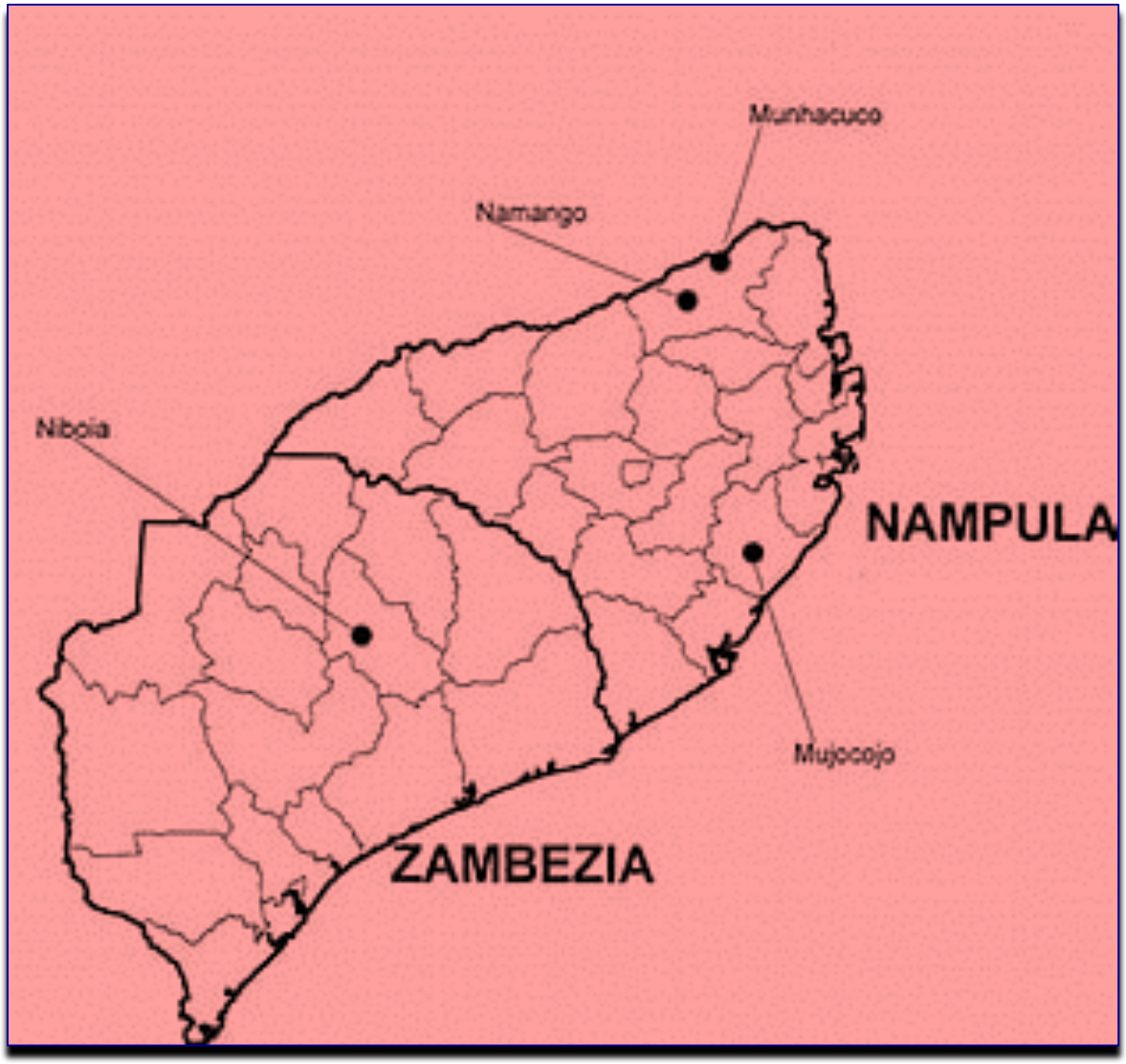
In Mozambique, around 41% of farmers grow white-fleshed sweet potatoes (BDPB) and this is an opportunity for them to make a marginal change and start growing BDPA as well, thus contributing to a higher intake of provitamin A [(20)].

Methodology

A descriptive methodology was used, covering four districts in the province of Nampula (Meconta, Monapo, Murrupula and Rapale) and two in the province of Zambézia (Alto Molocue and Gurué). Figure 1 shows the map of the two provinces in the study.

Figure 1.

Map of the provinces of Nampula and Zambézia [21].



The localities were considered primary sampling units and, for each district, 7 localities were selected from the North, Center and South. Groups of three villages were randomly selected from the northern, central and southern parts of the towns. In total, 42 towns and 168 villages made up the research area.

The sample design was based on sweet potato producers, as this was a baseline study of a project to promote the cultivation and consumption of orange-fleshed sweet potatoes. In Mozambique, there are around 3,5000,000 sweet potato growers, of which 5.3% are in Nampula, and 29% in Zambézia. It is estimated that there are around 1,200,500 potential sweet potato producers in Nampula and Zambézia [3]. On average, each AF in Mozambique is made up of 5 people, and around 240,100 Mozambicans grow sweet potatoes [22]. A minimum overall sample size of 526 beneficiaries is considered ideal for the study [23].

Thus, using a general principle of 0.7 standard deviations, a margin of error of 10% and setting the critical value of the normal probability distribution (z) at 1.96, corresponding to a 95% confidence level, data was collected from 640 heads of PAs living in 168 villages of the 42 previously selected localities in the six districts.

A household is a group of people, whether they are related or not, who usually live under the same roof and maintain the same budget to meet essential needs. Head of household is the person responsible for the household, considered as such by the other members, who normally supports the family budget and lives with the household, and may or may not be present at the time of the survey, as long as their absence is less than two months [(24)]. The formula used to calculate the sample was as follows:

Initial sampling size: n= (N2*z2*s2/MDE2)

Where:

N = total number of respondents

z=critical value of the normal probability distribution

s=standard deviation of the distribution of beneficiary data

MDE = margin of error

Based on this formula, the initial sample was 138 FAs, but it had to be adjusted for three levels of randomization, which allowed it to be increased to 564 (3*188). A non-response rate of 10% was then adjusted to reach a final size of 627 AF. However, due to a probable loss (handling error), there was a final adjustment to 640 AFs. Each FA head answered questions in a semi-structured interview based on the standard questionnaire to find out about food consumption and the agricultural situation. The food consumption frequency questionnaire (24-hour recall) was used to collect data on food consumption.

A 24-hour recall is a method used in dietary surveys to obtain complete information on an individual's food intake over a 24-hour period, corresponding to the previous day. This is carried out by a trained interviewer who asks questions about the food and drink consumed in the 24 hours prior to the interview. The 24-hour recall also makes it possible to collect information on intake over 48 hours [(25)].

Once collected, the data was checked and cleaned before being tabulated. Using the CSPro software, previously trained typists tabulated the data and during this process also checked for consistency.

Dietary diversity was determined based on the FAO criteria and its classification (scores) to determine dietary adequacy, based on the sum of the number of food groups consumed in the last 24 hours in that household or by the interviewee [(15)]. Thus, food groups were formed that corresponded to the basic needs of the PA and individual dietary diversity scores.

There are different criteria for establishing food groups, depending on the author and the country. Foods can be grouped or classified according to their origin, nutritional composition and state of processing, but the most practical classification from a dietary point of view may be the one that uses the nutritional composition criterion, i.e. according to their significant nutrients [(15)].

The estimation of the individual dietary diversity score considers nine food groups and these include (1) roots and tubers, cereals; (2) legumes and nuts; (3) dairy products; (4) meat-

based foods; (5) eggs; (6) vitamin A; (7) fruits and vegetables rich in vitamin A; (8) and other fruits and (9) vegetables [15].

In this study, the scores, whether at PA or individual level, were determined by grouping foods into nine categories, according to the nutritional needs that each one covers, and then the interviewees listed the foods consumed in the last 24 hours. To determine nutritional adequacy, each interviewer recorded the corresponding scores.

In the assessment of dietary diversity, a high score (≥6) is related to increased nutritional adequacy. A score below four (<4) represents low dietary diversity and a score of 4-5 represents medium dietary diversity [13]. The PA's dietary diversity score indicates their economic access to food, since items that require resources from the PA, such as condiments, sugar and sugary foods and drinks, are included in the score. The individual results reflect the nutritional quality of the diet [15].

It's worth noting that family food consumption doesn't always give the best interpretation of the nutritional situation of the PA or the malnutrition of children, as consumption data is often inaccurate. Nutritional outcomes are caused by meal frequency, waste, dietary diversity, feeding practices, childcare, intra-household food distribution and access to health services. One of the indicators with a strong correlation with malnutrition has been *per capita* consumption.

Therefore, individual dietary diversity was determined using children under five years of age (6-59 months) as a reference. Thus, children with an individual dietary diversity index lower than four (0-3) were associated with low dietary diversity, and those with an individual dietary diversity index greater than or equal to four (≥4) were associated with high dietary diversity. For statistical analysis, the survey used the *Census and Survey Processing System* (CSPro 7.7.2)

The aim of the baseline study was to learn about the contribution of sweet potatoes to the dietary diversity of rural populations in Nampula and Zambézia, northern and central Mozambique, through the introduction of this crop into their production system.

Ethical considerations

The study protocol was designed and reviewed by the donor to capture relevant information on agriculture and food use.

Results and discussion

Household characteristics

Rural families in Nampula and Zambézia have an average of five members. Women accounted for around 51% of the entire sample, and all the FAs in the sample had at least one child under the age of five. Among children under five, around 54% were female. Table 1 provides detailed information on the characteristics of the PAs in the area studied**.**

Table 1.

Characteristics of households in the districts of Nampula and Zambézia, north and center of Mozambique. Own elaboration.

District	AF size					No. Children <5 years		
	% women	No.	Average	95 % CI	Median	% women	Average	Median
Gurué	51,4	106	5.1	4,7-5,6	5.0	59.6	1.5	1.0
Alto Alto Molocuè	50.0	101	5.4	5,0-5,7	5.0	52.1	1.3	1.0
Murrupula	48.8	107	5.0	4,6-5,3	5.0	51.4	1.5	1.0
Monapo	52.4	107	5.5	5,1-5,8	5.0	53.2	1.4	1.0
Meconta	51.2	108	5.1	4,8-5,5	5.0	48.8	1.2	1.0
Rapale	49.8	111	5.4	5,1-5,8	5.0	58.7	1.3	1.0
Total	50.6	640	5.3	5,1-5,4	5.0	53.9	1.4	1.0

Production system

Sweet potatoes are the fifth most important crop in Nampula and Zambézia, after maize (34.9%), peanuts (16.3%), cassava (19.7%) and beans (12.9%). It represents 8.9% of all respondents, ahead of rice (7.3%). This confirms the information that MADER promotes the cultivation of food crops such as corn, rice, cassava, peanuts, potatoes, soybeans and beans [(3)]. Table 2 illustrates the classification of food crops according to their order of importance.

Table 2.

The most important food crops in the districts of Nampula and Zambézia, north and central Mozambique. Own elaboration.

Cultures	No. of respondents (n=640)	Percentage (%)	Classification
Corn	223	34.9	1ª
Cassava	126	19.7	2 ª
Peanuts	104	16.3	3 ª
Beans	83	12.9	4 ª
Sweet potatoes	57	8.9	5 ª
Rice	47	7.3	6 ª
Total	640	100.0	

The proportion of sweet potatoes in the production system

The analysis to determine the proportion of plots planted with sweet potatoes showed that the districts of Meconta and Nampula, in Nampula province, and Gurué, in Zambézia, grow the sweetest potatoes. In the Meconta district, sweet potatoes occupy around 19.2% of the cultivated area and in Murrupula, the crop represents 17.6% of the cultivated area. In Gurué, Zambezia, the area occupied by sweet potatoes is 18 percent. On average, sweet potatoes occupy 17% of smallholder farms in Nampula and Zambézia.

Overall, the average size of these farms varies between 0.5 hectares and 1.5 hectares [(26)]. Based on this data and translating the proportions found in the study into hectares, it can be seen that farmers in Gurué, Meconta and Murrupula have plots ranging from 0.09-0.29 hectares, while farmers in Alto Alto Molocuè, Monapo and Rapale have plots averaging less than 0.09 hectares each. Table 3 shows the proportion of plots with sweet potatoes in each study district.

Table 3.

Number of plots with sweet potatoes and other crops at household level in the districts of Nampula and Zambézia, northern and central Mozambique. Own elaboration.

Provinces	Districts (N=509)	Total number of plots with crops			No. of plots with sweet potatoes		% of plots with sweet potatoes
		Average	95% CI	Median	Average	Median	
Zambezia	Gurué (n=91)	3.3	3,1-3,6	3	0.6	0.0	18.0
	Upper Molocuè (n=80)	2.8	2,5-3,0	3	0.4	0.0	14.5
	Murrupula (n=77)	2.8	2,6-3,1	3	0.5	0.0	17.6
	Monapo (n=90)	3.1	2,7-3,4	3	0.4	0.0	13.1
Nampula	Meconta (n=81)	2.6	2,3-2,9	2	0.5	0.0	19.2
	Rapale (n=90)	2.6	2,4-2,8	2	0.4	0.0	15.5
Total		2.9	2,7-3,0	3.0	0.5	0.0	17.4

Sweet potatoes are one of Mozambique's main food crops and can be found in almost all of the country's production systems. [(7)]. Betting on sweet potatoes in the production system has multiple advantages because it is a food that is very rich in carbohydrates, pro-vitamin A (especially orange-fleshed varieties), B-complex and some minerals such as calcium, iron, phosphorus, potassium, sulphur and magnesium. Its nutritional richness makes it a blood pressure regulator as well as preventing certain types of cancer. It is also a culture of food security and

income generation for vulnerable families [11]. For consumption, sweet potatoes can be used almost in their entirety: the roots are eaten boiled, roasted, stewed, fried, pureed, as porridge, or even as dessert. The leaves are used to make curry [9].

Household food diversity

The overall average score for dietary diversity at the PA level was four (4), but the classification by district showed scores below four in Alto Molocuè (3.6) and Murrupula (3.7), which translates as families with an inadequate diet. The districts of Rapale and Meconta scored 5.1 and 4.7 respectively, which is above the average of four (4) and shows that these families have an adequate diet. Table 4 shows the results of the dietary diversity score for rural families in six districts in the provinces of Nampula and Zambézia, northern Mozambique.

Table 4.

Estimated mean, confidence interval and median of the dietary diversity index in families from the districts of Nampula and Zambézia, northern and central Mozambique. Own elaboration

Province	Districts	N	Average	95% CI	Median
Zambezia	Gurué	106	4.0	3,6-4,4	4.0
	Alto Molocuè	101	3.6	3,3-3,9	4.0
	Murrupula	107	3.7	3,4-4,1	4.0
Nampula	Monapo	107	4.3	3,9-4,6	4.0
	Meconta	108	4.7	4,3-5,2	4.0
	Rapale	111	5.1	4,5-5,6	5.0
Total		640	4.2	4,1-4,4	4.0

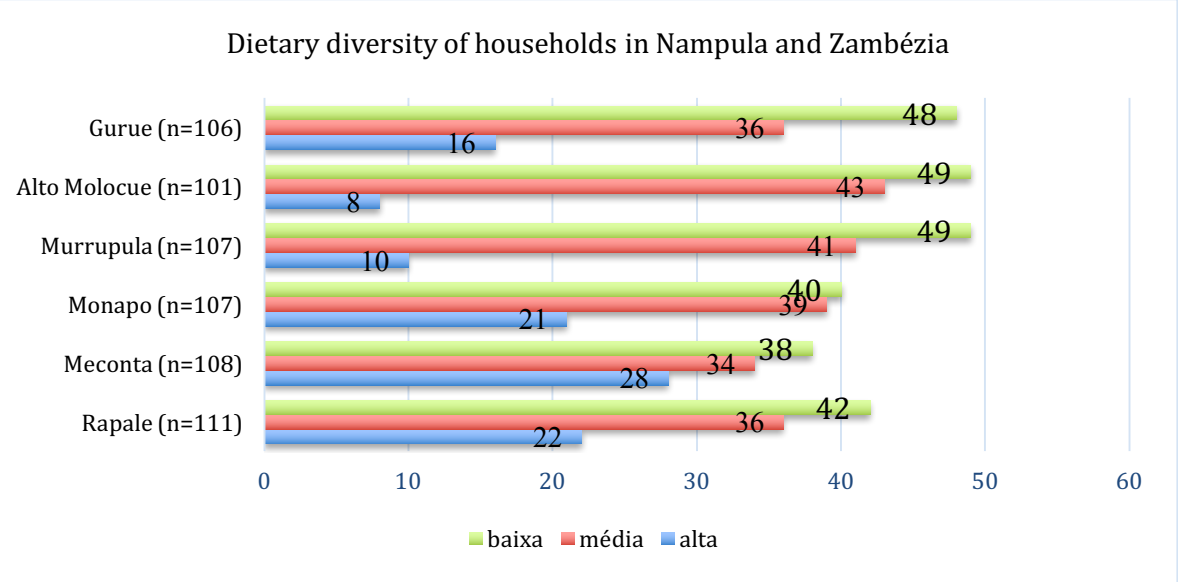
Dietary diversity is a measure that determines food consumption and access in a household, which can be triangulated with other information. This provides a holistic picture of food and nutrition security in a community or wider territorial area. The study made an additional analysis of the family situation to determine its dietary diversity. The results of the analysis showed that around 43% of families are in the poor dietary diversity category (<4) and nearly 35% are in the medium category (4) and only 22% have adequate dietary diversity (≥4).

The percentage analysis of dietary diversity by district shows a significant proportion of PAs in Alto Molocuè with poor dietary diversity (49%), followed by Murrupula (48%). The districts of Meconta and Rapale are in the lowest position (38%).

Figure 2 shows the levels of dietary diversity in the six study districts.

Figure 2.

Proportion of households with low, medium or high dietary diversity in each district of Nampula and Zambézia, northern and central Mozambique. Own elaboration.



Individual dietary diversity

At the household level, consumption is not always related to malnutrition in children, because data on consumption is often inaccurate and because nutritional outcomes have causes related to food frequency, waste, diversified diet, feeding practices, childcare, intra-household food distribution and access to health services. In this case, only *per capita* food consumption can be correlated with malnutrition. The determination of individual dietary diversity was only carried out with children under the age of five. To do this, the nine categories of food products were grouped together and the number of food items consumed by children in both provinces was determined [(15)].

Overall, individual scores ranged from 3.3 to 3.6 points, with an average of 3.5 points, which translates into poor dietary intake among children under five years of age. The median individual consumption was 3, suggesting a prevalence of inadequate dietary diversity among children under five at the family level.

This result contrasts with the SETSAN findings, which indicate that there are better infant feeding practices in the northern region of Mozambique, even though there is still a high prevalence of chronic malnutrition in this region [(3)]. The causes of this discrepancy are unclear, but it may have to do with poor access to food, or poor hygiene conditions (water and sanitation), which could contribute significantly to the high levels of malnourished children currently observed. Malnutrition doesn't just affect children under the age of five; pregnant women are another group most affected by the disease [(4)]. Etiologically, malnutrition can be associated with acute illnesses or injuries, chronic conditions or starvation. Malnutrition can also be caused by food deprivation, either isolated or associated, and can be acute (low weight for height, bilateral oedema or chronic (low height for age) or due to a lack of micronutrients such as iron, iodine, vitamin A and B vitamins.

Malnourished children are at greater risk of dying from common childhood diseases, and those who survive become ill and may have poor growth. Around a third of children under the age of five die from malnutrition worldwide. Proper infant nutrition prevents children from being exposed to frequent illnesses, allowing them to reach their physical and mental growth

potential [5]. Table 5 shows the average values of the individual dietary diversity of the rural population of Nampula and Zambézia, in northern and central Mozambique.

Table 5.

Estimation of the mean, confidence interval and median of individual dietary diversity scores in the districts of Nampula and Zambézia, northern and central Mozambique. Own elaboration.

Province	Districts	N	Average	95% CI	Median
Zambezia	Gurué	106	3.2	3,0-3,5	3.0
	Alto Molocuè	101	3.1	2,8-3,3	3.0
	Murrupula	107	3.1	2,9-3,4	3.0
Nampula	Monapo	107	3.5	3,2-3,7	3.0
	Meconta	108	3.8	3,5-4,2	4.0
	Rapale	111	3.9	3,5-4,3	4.0
Total		64(	3.5	3,3-3,6	3,0

In all districts, there is a prevalence of inadequate dietary diversity among children under five years of age. However, the scenario was more severe in Alto Molocuè (3.1), Murrupula (3.1) and Gurué (3.2) compared to Rapale (3.9) and Meconta (3.8), as illustrated in Table 5. Overall, around 58% of children consume less than three food groups a day, a clear indication of the prevalence of poor dietary intake. In Molocue, more than two thirds of children under the age of five had a low dietary diversity.

The study aimed to learn about the contribution of sweet potatoes to the dietary diversity of PA. The interviewees were asked if they usually incorporated sweet potatoes into their diet. The results indicate that all the FAs interviewed consume sweet potatoes. Table 6 shows the frequency of sweet potato consumption at household level.

Table 6.

Number of days per week that households in the districts of Nampula and Zambézia, north and central Mozambique, consumed sweet potatoes during the high and low peaks of the harvest. Own elaboration.

Province	District	No.	No. of days per week on which the FA consumed BD at the peak of collection			No. of days per week on which the FA consumed BD outside the harvest season		
			Average	95% CI	Median	Average	95 % CI	Median
Zambezia	Gurué	106	3.1	2,7-3,4	2	2.1	1,8-2,5	1
	Alto Molocuè	101	2.7	2,4-3,0	2	1.6	1,3-1,9	1
	Murrupula	107	3.1	2,8-3,5	2	1.8	1,6-2,1	1
Nampula	Monapo	107	2.3	2,0.2,5	2	1.3	1,1-1,4	1
	Meconta	108	2.5	2,2-2,8	2	1.5	1,3-1,6	1

	Rapale	11	2.2	2,0-2,5	2	1.6	1,3-1,8	1
Total		640	2.7	2,5-2,8	2	1.7	1,5-1,8	1

Respondents were asked if they would continue to eat sweet potatoes even if their family income increased one day. Data from the study revealed a downward trend in the number of consumers associated with rising incomes (36%). However, around 26% said they could increase their consumption and around 33% said they would not change their consumption pattern.

The hypothesis that sweet potatoes are the crop of vulnerable people is not proven in this study, as the percentage of respondents who will continue to eat sweet potatoes, even if their wealth status improves, was even higher (59%). A very fascinating finding of this study is the fact that, even though BDPA varieties have not yet been introduced in those areas, all the respondents declared that they had already consumed BDPA bought at the local market and other BDPA offered by friends and family. Table 7 below shows the number of days that families consumed BDPA during the week.

Table 7

Number of days per week throughout the year that households in the districts of Nampula and Zambézia, north and central Mozambique consumed BDPA. Own elaboration

Province	District	No.	No. of days per week throughout the year that the PA consumed BD		
			Average	95% CI	Median
Zambezia	Gurué	106	2.1	1,6-2,5	2
	Alto Molocuè	101	1.3	1,0-1,5	1
	Murrupula	107	2.1	1,7-2,4	2
Nampula	Monapo	107	1.5	1,3-1,8	1
	Meconta	108	1.4	1,2-1,6	1
	Rapale	111	1.9	1,6-1,2	1
Total		640	1.7	1,6-1,9	1

The consumption of BDPA is still insignificant in the country. On average, rural families consume BDPA twice a year, unlike BDPB, which is consumed twice a week (Table 6). The integration of BDPA into the production system of rural families in Zambezia improved the intake of pro-vitamin A in 89% of children aged 6-59 months and their mothers, while another group in the control area did not register this increase. Sweet potatoes can be eaten boiled, fried or mixed with wheat (known as golden bread). A loaf of bread made from BDPA puree, weighing around 250g, can provide 45% of pro-vitamin A in children under five [(19)].

The study also assessed the knowledge of heads of FAs about the nutritional importance of sweet potatoes (orange and white flesh). In this approach, 34% of respondents mentioned that they had heard of pro-vitamin A in BDPA and 58% said that BDPB also contains pro-vitamin A. Around 8% of respondents said that not all sweet potato cultivars are rich in provitamin A. The main sources of this knowledge were health facilities (79%) and local health activists (46%).

Regarding the nutritional benefits of BDPA, more than two thirds of those surveyed pointed to it as a healthier food than wheat bread. However, it is relevant to note that, although there is a notion

about the benefits of BDPA, in Murrupula and Rapale there is still a significant number of people who prefer bread to BDPA, 30% and 28% respectively.

This finding confirms the results of other studies which indicate that BDPA consumption is still low in the country, accounting for only 17% of PAs. The consumption rate is highest in Maputo, Sofala, Tete, Zambézia and Maputo City. The provinces of Cabo Delgado and Nampula have lower proportions of households incorporating BDPA into their diet [(3)] and this low consumption is due to low production. In two study areas (Nampula and Zambézia), an average of 22% of respondents declared BDPA.

Conclusions

In Mozambique, sweet potatoes are one of the main food crops and can be found in all the country's production systems. In Nampula and Zambézia, around 17% of the production area is occupied by sweet potatoes. The districts of Meconta and Murrupula, in Nampula, have larger production areas than Rapale with 19.2 percent and 17.6 percent, respectively, and in Zambézia, the two districts (Gurué surpasses Alto Molocuè) have production areas of 18 percent. Around 20% of families in Nampula and Zambézia produce sweet potatoes (white and orange flesh) and this crop ranks fifth in the entire production system, after maize, peanuts, cassava, beans and rice.

More than 2/3 of households prefer to eat sweet potatoes because they consider them healthier than wheat bread, but studies indicate that BDPA consumption is still poor in the country, accounting for only 17% of FAs. The consumption rate is highest in Maputo, Sofala, Tete, Zambézia and Maputo City. The provinces of Cabo Delgado and Nampula have the lowest proportion of FAs who incorporate BDPA into their diet.

In Nampula and Zambezia, 27% of families consume BDPA only twice, but even so, they consider it to be a low-income food. 36% of current consumers have shown a tendency to reduce consumption as their income rises. An important fact is that a significant proportion of the families interviewed said they knew about the importance of the BDPA through the health units and community health agents.

It's important to note that although there is some awareness of the benefits of BDPA in Murrupula and Rapale, there are still a significant number of people who prefer bread to orange-fleshed sweet potatoes for breakfast. Overall, BDPA consumption is still insignificant in Mozambique. This is due to low production, as these varieties were first introduced to Mozambique in 1997, but have experienced serious adaptability problems.

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BIBLIOGRAPHIC REVIEW ON THE INVOLVEMENT OF SERUM VITAMIN D IN PROPER PREGNANCY DEVELOPMENT

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Abstract. Maternal nutrition is a determining factor in the proper development of pregnancy. One of the micronutrients that becomes especially important during this stage is vitamin D. The primary role of vitamin D is the regulation of calcium homeostasis, although it also plays a significant role in pregnancy development. It has been reported that vitamin D deficiency during this stage is associated with adverse outcomes such as preterm birth, fetal problems, or preeclampsia. The aim of this bibliographic review is to analyze the implication of vitamin D in the proper development of pregnancy. Articles from scientific journals indexed with an impact factor ≥1.5, published in English or Spanish in the last 5 years, were selected. PubMed, Sciencedirect, and Cochrane were consulted. Low concentrations of serum vitamin D were associated with adverse outcomes such as gestational diabetes or preeclampsia. Adequate levels showed beneficial effects on offspring development, improving the immune system or preventing bone fractures; however, they did not show benefits in neonatal growth. High doses of vitamin D supplementation were found to be safe. It was also concluded that vitamin D supplementation with doses of up to 4000 IU/day would be safe for both the mother and the fetus.

Keywords: Vitamin D. Pregnancy. Preeclampsia. Supplementation.

IMPLICACIÓN DE LA VITAMINA D SÉRICA CON EL CORRECTO DESARROLLO DEL EMBARAZO: REVISIÓN BIBLIOGRÁFICA

Resumen. La nutrición materna es un factor determinante en el correcto desarrollo del embarazo. Uno de los micronutrientes que cobran especial importancia en esta etapa es la vitamina D. El papel principal de la Vitamina D es la regulación del homeostasis del calcio, aunque, también ejerce un papel importante en el desarrollo del embarazo. Se ha descrito que la deficiencia de Vitamina D durante esta etapa está asociada con resultados adversos como parto prematuro, problemas en el feto o preeclampsia. El objetivo de esta revisión bibliográfica es analizar la implicación de la vitamina D en el correcto desarrollo del embarazo. Se seleccionaron artículos pertenecientes a revistas científicas, indexadas y con un factor de impacto ≥1,5, en inglés o en español y publicados en los últimos 5 años. Se consultó en Pubmed, Sciencedirect y Cochrane. Se asociaron las bajas concentraciones de vitamina D sérica con resultados adversos como diabetes gestacional o preeclampsia. Niveles adecuados mostraron efectos beneficiosos en el desarrollo de la descendencia, mejorando el sistema inmune o previniendo fracturas óseas, sin embargo, no han mostrado beneficios en el crecimiento del neonato. Dosis altas de suplementación con esta vitamina mostraron ser seguras. También se concluyó que la suplementación con vitamina D con dosis de hasta 4000 UI/día resultaría seguro tanto para la madre como para el feto.

Palabras clave: Vitamina D. Embarazo. Preeclampsia. Suplementación.

Introduction

Numerous factors determine the appearance of complications during this stage, such as maternal stress (1), existing health problems (HTN, diabetes, renal disease, etc.), age, and lifestyle-related problems such as alcohol and tobacco consumption (2) and maternal nutrition (1), the latter being of particular importance.

Women's nutritional needs change during pregnancy and lactation (3). In particular, nutritional needs vary for some micronutrients, which are vital for improving pregnancy outcomes (4).

The role of vitamin D as a regulator of calcium and phosphorus homeostasis is well known (5), however, there is increasing evidence of the role of this vitamin in the development of pregnancy, preventing the onset of complications typical of this stage, such as preeclampsia. (6, 7)

There is a high prevalence of vitamin D deficiency in the world (8, 9), including in pregnant women, which opens the door to further research on the effects of this vitamin in pregnancy, as well as the benefits and safe doses of supplementation.

Vitamin D in pregnancy:

Pregnancy is a time of physical, metabolic and hormonal changes. To ensure that all these changes take place properly, the nutritional needs of women vary, especially the micronutrient requirements. The one to be highlighted in this article is vitamin D.

Vitamin D is fat-soluble and is obtained mainly after skin exposure to ultraviolet radiation from the sun. It can also be obtained through diet or by taking supplements. Some of the foods rich in vitamin D are egg yolks, oily fish, liver and fortified foods (10).

Its main function, as mentioned above, is to maintain calcium and phosphorus homeostasis, in addition to preserving bone integrity (11). However, it also plays a crucial role in the modulation of the immune system (12) and in the regulation of female reproductive function (13). This is because the vitamin D receptor (VDR) is present on monocytes/macrophages, T cells, B cells, natural killer (NK) cells and dendritic cells (12, 14, 15), as well as on all cells of the female reproductive tract. (13) Effects on the immune system are especially relevant during pregnancy, particularly during embryo implantation. By modulating the immune response, vitamin D helps prevent a reaction by the mother's body to the embryo, which contains paternal genes. (12, 16)

This vitamin also plays other roles, such as the regulation of gene transcription and expression, participation in glucose metabolism, as well as in the nervous and muscular systems (17-19). During pregnancy, it helps the formation of the baby's bones and teeth by facilitating the absorption of calcium (20).

Deficiency of this micronutrient during gestation has been associated with various problems of fetal development such as intrauterine growth retardation, neonatal rickets, and alterations in dental enamel (21, 22). In addition, it has been observed that this deficiency could be associated with adverse pregnancy outcomes such as gestational diabetes, preeclampsia (10), preterm delivery or low birth weight (23).

In the systematic review with meta-analysis by Akbari S et al. (24), which included 23 articles, showed a significant correlation between low vitamin D levels (<20 ng/ml) during pregnancy and the risk of preeclampsia.

Similar result was obtained in the open-label trial by Xiaomang J et al. (25) whose objective was to demonstrate that high-dose vitamin D supplementation in vitamin D-deficient pregnant women reduces the prevalence of preeclampsia. This study divided 450 pregnant women into 3 vitamin D supplementation groups; a low dose group (400 IU/day); a medium dose group (1500 IU/day) and a high dose group (4000 IU/day). Supplementation was administered from week 12 of pregnancy, and was followed up until week 12 postpartum. As a result, the prevalence of preeclampsia cases was significantly lower in the high-dose vitamin D supplementation group.

In the cohort study by Raia-Barjat T et al. (26) aimed to evaluate the relationship between vitamin D status and the occurrence of placenta-mediated complications in a high-risk population. To do so, they recruited 182 women at risk for placenta-mediated complications. At the end of the study it was concluded that patients with vitamin D deficiency at 32 weeks of pregnancy have a higher risk of developing placenta-mediated complications, which include preeclampsia, eclampsia, placental abruption, hemolysis, elevated liver enzymes, low platelet syndrome, intrauterine growth retardation, intrauterine fetal death or recurrent miscarriages.

Hornsby E et al. (27) conducted a double-blind, randomized, controlled clinical trial to evaluate the efficacy of daily vitamin D supplementation in pregnant women on the immune system of the newborn, in relation to the development of asthma. For this purpose, they recruited umbilical cord blood from 51 pregnant women who were taking vitamin D supplements (26 of them with 4400 IU/day and 25 with 400 IU/day). As a result, it was found that newborns born to mothers supplemented with 4400 IU/day of vitamin D had higher innate cytokine responses. Thus, by improving the immune

response, there is a lower probability of developing asthma.

In general, the prevalence of vitamin D deficiency in Europe is estimated to be approximately 40% (28); it ranges from 40% to 98% among pregnant women worldwide (4).

However, despite the importance of this vitamin, especially during the gestation phase, there is currently no consensus on its supplementation.

Although several studies (28-32) have shown that doses of up to 4000 IU per day are safe during pregnancy.

The objective of this review is to analyze the available literature to determine the role of vitamin D in the pregnancy period.

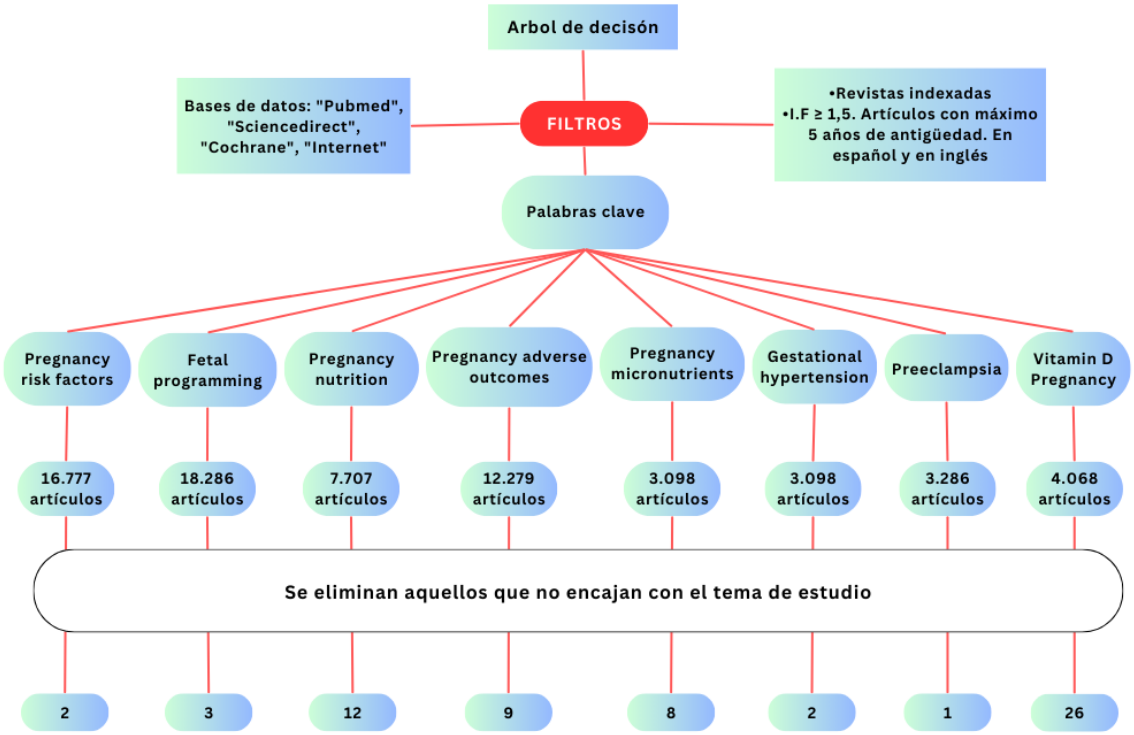
¶ (12 points)

¶ (12 points)

Method

The article presented here consists of a bibliographic review in which the available scientific literature is brought together in order to determine the role of vitamin D in the correct development of pregnancy, as well as to try to establish the need or not of supplementation of this vitamin during the gestational stage. For this purpose, clinical trials, systematic reviews and meta-analyses, online books, guidelines and dictionaries were included. It was taken into account that these articles had been published in the last 5 years. They should be in English or Spanish, and belong to indexed journals with an impact factor of 1.5 ≥1,5. This literature search for the elaboration of the state of the art began in November 2022 and ended in April 2023. The following is a detailed explanation of the different databases that have been used for this purpose:

Figure 1.
Decision tree for conducting the literature review



Eleven experimental articles were used for the discussion section.

Results

Table 1 below shows in detail the characteristics of the studies used.

Table 1. *Table summarizing the characteristics of the studies included in this discussion*

AUTHORS	TYPE OF STUDY	POPULATION	METHODOLOGY	OBJECTIVE	RESULTS
Xiaomang J et al 2021. (25)	Open randomized trial	450 pregnant women between 20 and 40 years of age, with maternal treatment and a diagnosis of vitamin D deficiency.	Women were divided into 3 vitamin D supplementation groups: low dose (400 IU/day), medium dose (1500 IU/day) and high dose (4000 IU/day). Supplements were administered from week 13 of pregnancy and followed up to 12 weeks postpartum. Serum vitamin D levels were measured before and after supplementation.	The hypothesis was that high-dose vitamin D supplementation reduces the incidence of preeclampsia.	The incidence of preeclampsia was significantly lower in the high-dose vitamin D supplementation group. In addition, high-dose supplementation did not demonstrate any adverse effects.
Raia-Barjat T et al. 2021. (26)	Prospective multicenter cohort study	182 pregnant women at risk for PMC. With diabetes, chronic hypertension, obesity, <18 years or >38 years, among	A total of 5 blood samples were collected per patient, at 20, 24, 28, 32 and 36 weeks of pregnancy. Vitamin D deficiency was defined as a 25 (OH) D level <20 ng/ml and vitamin D insufficiency <30 ng/ml.	Primary outcome: appearance of PMC. Secondary outcomes: occurrence or recurrence of preeclampsia without intrauterine growth retardation, occurrence or	At 32 weeks, the risk of occurrence of PMC (especially late PMC) was 5 times higher in patients with vitamin D deficiency than in patients with normal vitamin D levels.

		other risk factors.		recurrence of early (before 34 weeks) or late (after 34 weeks) PMC.	
Díaz-López A et al. 2020 (33)	Cross-sectional analysis	793 healthy pregnant women before the 12th week of pregnancy, over 18 years of age.	Blood was drawn from all participants before 12 weeks of pregnancy and total serum vitamin D concentrations were determined.	Objective: to determine the prevalence of vitamin D deficiency in pregnant women from the Mediterranean coast.	High prevalence of vitamin D deficiency in pregnant women on the eastern Mediterranean coast, especially in overweight women, Arab ethnic group and dark skin, low social class, low exposure to sunlight and less efficient dermal synthesis of vitamin D during winter and spring, low consumption of dairy products and low physical activity.
Vestergaard AL et al. 2021. (34)	Prospective cohort study	225 Danish pregnant women, ≥ 18 years.	Blood samples were taken from all patients to determine serum vitamin D levels and placentas were sampled for genetic analysis.	To characterize vitamin D status in women in the 1st trimester of gestation and correlate it with pregnancy outcomes and placental biology.	Forty-two percent did not reach the vit level. D ≥75 nmol/L, 10 % showed a concentration <50 nmol/L and 2 % suffered from severe vitamin D deficiency (<25 nmol/L). Women with a higher BMI are at increased risk

					for vitamin deficiency. Vitamin D insufficiency in the first trimester was associated with lower placental growth factor expression
Hornsby E et al. 2018. (35)	Randomized, double-blind, placebo-controlled trial	51 pregnant women between 10 and 18 weeks of gestation. Vitamin D deficient.	Subjects were divided into 2 vitamin D supplementation groups: low dose (400 IU/day) and high dose (4400 IU/day). Cord blood was collected and cultures were performed.	The main hypothesis was that supplementation with high doses of vitamin D in pregnancy would stimulate the innate immune system of the newborn, through the production of proinflammatory cytokines, preventing the onset of asthma.	In the high-dose vitamin D supplementation group, blood levels of vitamin D returned to normal, and the neonates of these women demonstrated increased innate cytokine responses. Doses up to 4000 IU/day appear safe for both the pregnant woman and the baby.
Roth DE et al. 2018. (36)	Randomized, double-blind, placebo-controlled trial	1,300 pregnant women, 18 years of age or older and between 17 and 24 weeks of gestation. Residents in Bangladesh.	Five groups were made and each woman was randomly assigned to one of them. A different dose of vitamin D was administered in each group: 0 IU/week postpartum ("placebo"); 4200 IU/week prenatal and 0 IU/week	The primary outcome was length-for-age z-score (LAZ) at 1 year (364-420 days) of age. As a secondary outcome, weight-for-age z-score was measured.	Vitamin D supplementation from mid-pregnancy to delivery or 6 months after delivery did not show significant effects on offspring growth. However, it proved that its supplementation is safe.

			postpartum; 16800 IU/week prenatal and 0 IU/week postpartum; 28000 IU/prenatal and 0 IU/week postpartum; or, 28000 IU/week prenatal and postpartum.		
Brustad N et al. 2022 (37)	Randomized clinical trial	623 pregnant women with 26 or less weeks of gestation, a daily intake of vitamin D <600 IU/day and no endocrine, cardiac or renal disorders.	The sample was randomly divided into two vitamin D administration groups: high dose 2400 IU/day or placebo group (0 IU/day); from week 24 of pregnancy until week 1 postpartum.	Relationship of prenatal vitamin D supplementation and fracture risk, as well as bone mineralization of the offspring.	Significantly lower incidence of 60% of fractures in children born to mothers who had received high-dose vitamin D during pregnancy, compared to those whose mothers belonged to the placebo group.
Yin W-J et al. 2020. (38)	Prospective cohort study	6821 pregnant women aged ≥18 years, residents of Hefei, singleton pregnancy and no assisted conception. Who were in the second trimester of pregnancy.	Serum vitamin D concentration was measured and at 24-28 weeks of gestation, diagnostic tests for gestational diabetes mellitus were performed.	In this study we sought to estimate the relationship of vitamin D with gestational diabetes mellitus.	Low vitamin D concentrations were significantly associated with an increased risk of gestational diabetes mellitus. The risk was significantly reduced only in those women taking supplementation and whose serum vit.D levels approached 50 nmol/L.

Bakleicheva M et al. 2021. (39)	Prospective randomized multicenter study	88 pregnant women in the first trimester of gestation, aged 20-44 years, singleton pregnancy, BMI ≤30 kg/m2 and known serum vitamin D level.	Patients were divided into 3 groups depending on the initial serum vitamin D level (group 1: < 10 ng/ml, group 2: 10-30 ng/ml, group 3: >30 ng/ml).	Objective: to evaluate the characteristics of the course of pregnancy in women with different serum vitamin D levels in the first trimester.	In the group with pronounced vitamin D deficiency (< 10 ng/ml) the risk of miscarriage was 2 times higher than in the group with normal vitamin D levels (>30 ng/ml).
Liu C-C et al. 2023. (40)	Retrospective observational study	1048 women with known vitamin D levels with a delivery ≥ 20 weeks gestation; 746 women who were vitamin D deficient (<20 ng / ml) and received the same vitamin D supplementation; and 3654 women with unknown vitamin D levels and delivery ≥	Vitamin D supplementation with 2000 IU/day was initiated at 12-16 weeks of pregnancy if vitamin D was present. If the level exceeded ≥20 ng/ml, maintenance doses were administered at 800 IU/day until birth. If vitamin D level remained <20 ng/ml, supplementation of 2000 IU/day was continued until levels were ≥20 ng/ml or delivery.	We sought to study the correlation between serum vitamin D levels during gestation and the occurrence of adverse pregnancy outcomes.	Inverse correlation between initial vitamin D level and maternal BMI. Doses of up to 4000 IU/day of vitamin D are safe. And high serum vitamin D levels may protect against preterm delivery, low birth weight and postpartum hemorrhage.

		20 weeks gestation			
Ogiji J et al. 2022 (41)	Retrospective observational study	161 pregnant women.	During the first trimester of pregnancy, blood samples were collected to determine serum vit.D concentrations. Vitamin D levels of women who developed postpartum depression (PPD) were compared with those who did not.	We sought to study the relationship between serum vitamin D levels during pregnancy and the occurrence of postpartum depression.	The occurrence of postpartum depression was significantly negatively correlated with prenatal vitamin D levels.

Discussion and conclusions

Vitamin D deficiency is considered a very common condition or pathology among pregnant women, as seen in the studies of Diaz-Lopez A et al. (33) and Vestergaard AL et al. (34); in some areas of the world, it can reach 100% of the population.

Of the 11 studies, 3 of them studied the implication of vitamin D supplementation on different offspring developmental outcomes. All three were randomized, double-blind, controlled trials. The first of them (35) related it to the stimulation of the neonate's immune system development, decreasing the risk of asthma. Another (36) proposed the relationship of vitamin D with the growth of the newborn; and the third (37) proposed that supplementation with this vitamin during gestation decreases the risk of fractures in the offspring. Two of them concluded that vitamin D favorably influences newborn development.

As mentioned above, two of the studies used looked at the prevalence of hypovitaminosis D in a population of women from the Mediterranean coast (33) and in a population of Danish women (34), a cross-sectional study and a prospective cohort study, respectively. Both concluded that there was a significant vitamin D deficiency among pregnant women.

Four other studies used analyzed the relationship of vitamin D deficiency with different pregnancy outcomes. A 25 (OH) D level of less than 20 ng/ml was taken as the reference value for vitamin D deficiency. These were prospective multicenter cohort studies. The first analyzed this relationship with the risk of suffering placenta-mediated complications (26); the second posited this relationship with the risk of suffering gestational diabetes mellitus (39); and the third (40) studied the characteristics of the course of pregnancy according to different serum vitamin D levels. The last one (41) analyzed the relationship of serum vitamin D levels with the development of postpartum depression. All four studies concluded that the risk of adverse pregnancy outcomes was significantly higher in women with low serum vitamin D levels.

The remaining 2 studies examined the effect of vitamin D supplementation during gestation on the occurrence of adverse pregnancy outcomes. One of the studies was an open-label randomized trial (25) that proposed that high-dose vitamin D supplementation from early pregnancy reduces the incidence of preeclampsia. This one concluded that the incidence of preeclampsia was significantly lower in those women who were supplemented with high doses of vitamin D. The other article sought to study the association between serum vitamin D levels and the occurrence of adverse pregnancy outcomes (40), concluding that doses of up to 4000 IU/day of vitamin D supplementation were safe, and that high serum vitamin D levels were protective against preterm delivery, low birth weight and postpartum hemorrhage.

All the articles reviewed that studied the association of vitamin D levels with adverse pregnancy outcomes had favorable results. In the study by Yin W-J et al. (38) concluded that adequate levels ofthis micronutrient (>50 nmol/L) during pregnancy significantly reduced the risk of gestational diabetes mellitus.

Bakleicheva M et al. 2021. (39) demonstrated that women with severe vitamin D deficiency during pregnancy had a significantly increased risk of miscarriage. And the study by Ogiji J et al. (41) concluded that the occurrence of postpartum depression had a significant

inverse association with serum vitamin D levels during pregnancy.

The study by Raia-Barjat T et al. (26) concluded that there was a significant association between low serum vitamin D levels during pregnancy and the occurrence of placenta-mediated complications, preeclampsia being one of these complications.

As mentioned above, Vestergaard AL et al. (34) showed that there was a high prevalence of vitamin D deficiency among pregnant Danish women. In addition, in this study, vitamin D insufficiency during the first trimester of pregnancy was associated with low expression of placental growth factor, which is a biochemical marker predictive of risk of preeclampsia in the first trimester of pregnancy.

Thus, 3 of the articles analyzed demonstrated significant associations between low serum vitamin D levels during pregnancy and the occurrence of preeclampsia (25, 26, 35).

Of the studies analyzing the relationship of serum vitamin D concentrations during pregnancy to neonatal development, the one by Roth DE et al. (37) showed no significant differences between these concentrations and infant growth.

However, Liu C-C et al. (40) demonstrated that high serum levels of vitamin D during pregnancy protect against low birth weight.

In addition, adequate levels of this vitamin during pregnancy appear to protect offspring from health problems such as asthma by stimulating the innate immune system of the newborn, as demonstrated by Hornsby E et al. (35) in their clinical trial. They may also protect against fractures in the child, concluded Brustad N et al. (36).

Regarding supplementation with this vitamin, 4 of the studies (25, 36, 35, 40) showed that supplementation doses of up to 4000 IU/day are safe for both the mother and the fetus.

The evidence obtained so far suggests that correct serum levels of vitamin D can influence the correct development of pregnancy, both by protecting the mother against adverse pregnancy outcomes (such as diabetes mellitus, premature delivery or postpartum depression, among others), and by protecting the fetus from future bone fractures, or by reinforcing its immune system. And, in the opposite case, deficient levels of this vitamin during pregnancy may favor the appearance of problems characteristic of this stage such as preeclampsia or gestational diabetes mellitus.

Therefore, in conclusion, it can be stated that the role of vitamin D during pregnancy is not only to maintain calcium and phosphorus levels and bone health, but that its functions go beyond that. For example, by favoring the implantation of the fetus in the uterus by modulating the immune response, or by preventing the onset of preeclampsia. In addition, as mentioned above, the prevalence of vitamin D deficiency is widespread among pregnant women worldwide, so it would be very interesting to reach a consensus on the recommended vitamin D supplementation dose for all pregnant women. According to what was observed in this review, it could be stated that a dose of up to 4000 IU/day of vitamin D would be safe for both the mother and the fetus, in addition to being effective in normalizing maternal serum concentrations and preventing various pregnancy problems. Therefore, in order to prevent the occurrence of problems due to deficiency of this micronutrient, supplementation with 4000 IU/day, a dose that has been proven to be safe, should be recommended for all pregnant women. However, the evidence is still limited and much more research is needed

in this area as there is still no agreement on the optimal concentration of vitamin D, nor has its supplementation been standardized for all pregnant women, as has been done with other micronutrients such as folic acid.

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DIETARY INTERVENTION IN POLYCYSTIC OVARIAN SYNDROME – A BIBLIOGRAPHICAL REVIEW

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Abstract: The aim of the present study was to investigate which diet is the best option to treat polycystic ovarian syndrome (PCOS). A bibliographic review was carried out. Official web sites and documents were taken into consideration. Nevertheless, for the analysis of studies, just articles from indexed magazines were used. These articles were published between 2015 and 2022, and they were selected form the database PubMed. At the end, 19 articles were used. All of the discussed diets can be helpful to lose weight in case of overweight or obesity. In case of inflammation, the Mediterranean diet may be the best option because of its antioxidant value. When SOP coexists with diabetes, both the DASH diet and the ketogenic diet can be of great help. A low glicemic diet can be useful to improve the levels of sex hormones and the lipid profile in women with PCOS. More investigations and studies with bigger samples are needed to confirm the results shown in this work. However, the information exposed in this review points out that an anti-inflammatory diet, losing weight, in case it was necessary, and controlling the carbohydrates intake, is necessary to improve the symptomatology and health of women with PCOS.

Keywords: polycystic ovarian syndrome. Mediterranean diet. DASH diet. Ketogenic diet. Low glicemic diet.

REVISIÓN SOBRE LA INTERVENCIÓN DIETÉTICA EN SÍNDROME DE OVARIO POLIQUÍSTICO

Resumen: El objetivo del presente estudio es investigar cuál es la intervención dietética óptima en mujeres con Síndrome de Ovario Poliquístico (SOP). Para ello, se realizó una revisión bibliográfica. Se estudiaron documentos, páginas web oficiales y distintos artículos científicos. Para el análisis de estudios, fueron seleccionados distintos artículos que investigaban el efecto de una de las dietas de estudio en mujeres con SOP. Se tuvieron en cuenta un total de 19 artículos publicados entre 2015 y 2022, obtenidos de la base de datos PubMed. Como resultado se obtuvo que cualquiera de las dietas de estudio puede resultar de interés clínico para la pérdida de peso. La dieta mediterránea (DM) es interesante por su capacidad antioxidante. La dieta DASH y la dieta cetogénica (DC) han mostrado ser eficaces para controlar la glucemia en la población de estudio. La dieta de bajo índice glucémico (IG) puede mejorar el perfil de hormonas sexuales y otros parámetros analíticos, como el colesterol total o los triglicéridos. Son necesarios más estudios y con una mayor muestra para poder confirmar los resultados hallados. No obstante, la información expuesta en este artículo muestra que una pérdida de peso, en caso de que sea

necesario, una dieta antiinflamatoria y un control en la ingesta de hidratos de carbono son características a tener en cuenta para mejorar la sintomatología y la salud de mujeres con SOP.

Palabras clave: Síndrome de ovario poliquístico. Dieta mediterránea. Dieta DASH. Dieta cetogénica. Dieta de bajo índice glucémico

Introduction

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disease in women of childbearing age (1,2). These women usually present the following symptoms: anovulation or irregular menstrual cycles, hyperandrogenism, acne, hirsutism, ovarian follicles (fluid sacs), insulin resistance, excess visceral fat, infertility or obesity (2). In addition, about 20% of women in this population suffer from sleep apnea (3). Also, women with this condition suffer from systemic inflammation (4,5).

The syndrome is also associated with thyroid hormone malfunction (6). In the long term, this endocrine pathology may increase the risk of non-alcoholic fatty liver disease, cardiovascular disease (CVD) and endometrial cancer (2).

It is noteworthy that PCOS can significantly affect the quality of life of women who suffer from it (7,8), especially mental health (9). Depression (sometimes aggravated by hirsutism and infertility), acne and obesity are the three factors that worsen the quality of life of women with PCOS the most (7).

The etiology of the syndrome is not clear, but it is known to have a genetic and an environmental component (1). Some of the factors that can trigger this disease are hereditary factors, low birth weight, obesity, sedentary lifestyle or an unbalanced diet (1).

As for the dietary factor, some nutrients, such as sugar or saturated fats, can generate oxidative stress and inflammation, which in turn increase the risk of causing metabolic and hormonal dysfunction, for example, in the ovaries (10).

In addition to an unhealthy lifestyle, a prerequisite for PCOS is an excessive secretion of androgens by the female sex glands (11).

There is a theory that explains the origins of PCOS from an adaptive perspective. In times of food scarcity, where our ancestors lived situations with a high level of stress, there were certain genes and phenotypes that would be useful to favor survival. However, during the last century, most regions of the world have had unlimited access to food. These phenotypes, which once promoted an evolutionary advantage, are now a risk that increases the prevalence of obesity, cardiovascular disease and type II diabetes mellitus (11). As shown in Figure 1, the adaptations that have benefited our ancestors, such as insulin resistance, hyperandrogenism, increased energy reserves or less fertility, are now pathogenic (12).

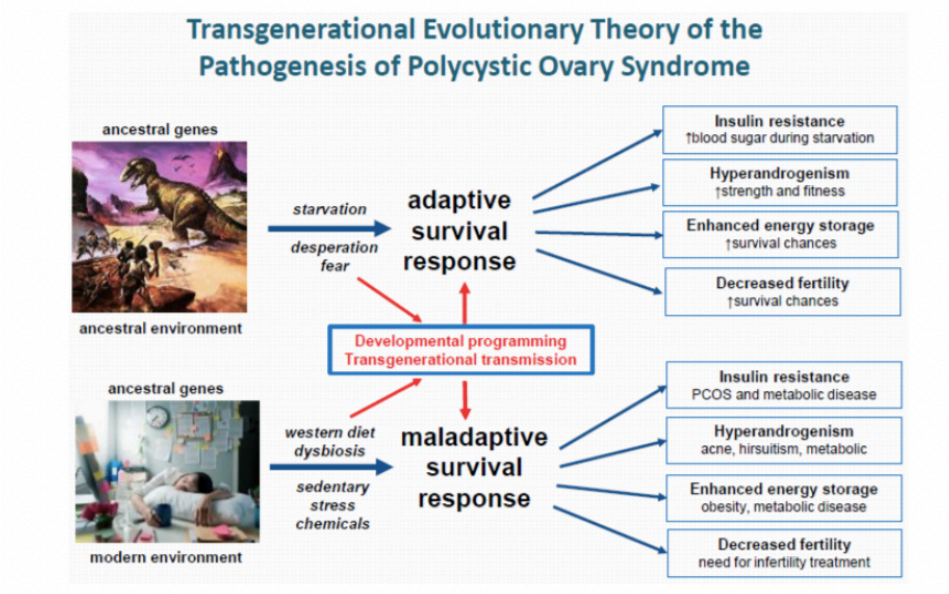

Figure 1: Theory of the pathogenesis of PCOS (13).

Diagnostic criteria

The Rotterdam criteria are mainly used to diagnose PCOS. Two of these three criteria must be met (8, 14):

- Oligo-anovulation: is the clinic of amenorrhea or oligomenorrhea. Oligoamenorrhea is the presence of less than 9 menstrual periods in a year or the presence of more than 3 menstrual periods/year of at least 38 days. That is, they are irregular menstrual periods (14). On the other hand, amenorrhea is the absence of menstruation for 3 or more menstrual periods (15).
- Hyperandrogenism: androgens are testosterone, androsterone and androstenedione. The physiological values of these sex hormones in women are: testosterone less than 0.6 ng/ml, androsterna less than 9 ng/ml and androstenedione less than 3 ng/ml. Reference values may vary depending on the laboratory. In clinical practice, the total testosterone value is the most commonly used to determine the presence or absence of hyperandrogenism (16).
- Have ovaries with a polycystic appearance: the diagnostic method for evaluating this parameter is ultrasound. To meet this third criterion, the ovaries must have a minimum of 12 follicles, between 2 and 9 millimeters each, or at least one ovary must have a volume greater than or equal to 10 ml (14).

On the other hand, there are two other methods to diagnose this disease. The Androgen Excess and PCOS Society states that hyperandrogenism and ovarian dysfunction must be present. This dysfunction may be due to alterations in ovulation and/or ovarian morphology. In contrast, the National Institute of Child Health and Human Development does not consider ovarian morphology as a diagnostic criterion, but does consider hyperandrogenism and ovulatory disorders (11).

Some experts point out that the term PCOS is not correct because it is not always necessary to have ovarian cysts to have the disease and having cysts does not indicate excessive production of androgens by the ovaries (11).

Treatment

Neither the U.S. Food and Drug Administration (FDA) nor the European Medicines Agency (EMA) has approved any specific drug to treat PCOS. For this reason, treatment should be individualized (11).

- Oral contraceptive pills: combine estrogens and progesterone. They restore the menstrual cycle and improve the symptomatology of acne and hirsutism (17). Promoting regular menstrual cycles is important for the prevention of endometrial pathologies, such as cancer (11).
- Metformin: the effects of metformin in regulating the menstrual cycle and improving signs of hyperandrogenism are mild to moderate (17). However, this drug is efficient in improving insulin resistance in women with PCOS, and is the most widely used treatment in cases of diabetes (11). Similarly, it aids in weight loss (17).
- Weight loss drugs: positive short-term effects have been seen in women with PCOS (11). Glucagon-like peptide-1 (GLP-1) is efficient in treating obesity in these women (17). However, the long-term repercussions that these drugs may cause in the study population are unknown (11).
- Bariatric surgery: Bariatric surgery is an intervention to be considered in obese patients with PCOS. Depending on the final weight after surgery, the characteristic signs and symptoms of the syndrome may reverse. This type of surgery improved the weight, menstrual cycles, and hormonal and metabolic profile of the women in the study by Hu et al. (18). According to these investigators, bariatric surgery should be a priority in obese patients with PCOS.

The criteria to be able to undergo this intervention are the same in the general obese population as in obese women with the syndrome (11). In order for a woman to be eligible for this operation, the body mass index (BMI) must be greater than 40 kg/m^2 or greater than 35 kg/m^2 and have another serious weight-related health condition (19).

- Other treatments to consider: cosmetics or retinol pills for acne or different shaving techniques for hirsutism (11). In addition, myoinositol-based supplements have been found to be effective in normalizing ovarian function in women with PCOS (20).

In conclusion, the treatment to be used will vary according to the symptomatology of each patient. The recommendation to combine several drugs such as oral contraceptives and metformin is increasingly widespread (17).

Before treating the syndrome with these drugs, it will be convenient to study possible changes in the patient's lifestyle. The first-line treatment in PCOS is lifestyle change (1,21, 22). The practice of physical exercise, a dietary treatment adapted to each patient, and reducing the percentage of fat; since up to 80% of women with PCOS are overweight or obese (23), are different alternatives that would improve the symptomatology of women with this syndrome (24).

Nutritional strategies to reduce overweight and obesity and improve insulin sensitivity will be beneficial in women with this disease (25). Some nutritional strategies that have shown some therapeutic interest in this pathology are the Mediterranean diet (MD), the Dietary Approach to Stop Hypertension (DASH), the ketogenic diet (KD) and a low glycemic index (GI) diet.

Likewise, achieving a healthy lifestyle can improve the quality of life of women with PCOS, even if weight loss is not achieved (8). Similarly, because not all women with the syndrome are overweight or obese, the impact that the diet may have beyond weight loss should be of clinical interest (26). Along the same lines, following a balanced diet is especially important in these women because, at the same BMI, women with PCOS have higher blood glucose and insulin levels than the general population (27). However, losing fat could be key to improving the metabolic and hormonal profile that leads to infertility in women with PCOS (28). Ultimately, a weight loss may be necessary to restore the menstrual cycle and thus fertility in the study population (29).

Current scientific evidence suggests that a well-adjusted and balanced diet is beneficial in improving insulin resistance, body weight and metabolic profile; and in preventing typical complications of the syndrome (26).

Mediterranean diet

DM was first defined by Ancel Keys with the 7-country study, who advocated that it was a diet high in vegetable oils and low in saturated fat (30). After its study, the diet has been defined in various ways, but some concepts that have been maintained over time are: that this style of eating provides a high consumption of olive oil, vegetables, fruit, legumes, nuts, whole grains, fish and seafood; a moderate consumption of dairy products, meat and red wine and a low consumption of sweets and saturated fats (30,31). DM is known for its effects in the prevention of CVD, type II diabetes mellitus, dementia and some types of cancer (32). This protective characteristic of DM is due in part to its ability to reduce visceral fat (31) and its anti-inflammatory role (5,27,33).

Adherence to DM is measured with the PREDIMED questionnaire, which consists of 14 simple questions that inquire about the dietary habits of the population (34). This questionnaire stems from the PREDIMED (prevention with Mediterranean diet) study (35), which was a clinical trial that sought to analyze the effect of the Mediterranean diet in the primary prevention of cardiovascular disease (36). In addition to the effects of the diet at the cardiovascular level, the results of the PREDIMED study show that good adherence to DM reduces the risk of type II diabetes, arterial hypertension, atrial fibrillation, cognitive impairment and breast cancer (36).

DASH diet

The acronym DASH stands for Dietary Approaches to Stop Hypertension (37). This diet was created by the National Institute of Health (38) at the end of the 1990s in the United States. The first time its effect was studied was with the study by Apple et al. (39), which consisted of comparing the effects of three different diets. The first was the control diet, the second a diet high in fruits and vegetables, and the third a combined diet, in which there was a high intake of fruits and vegetables and a minimal intake of fats. The conclusion of the study was that a diet high in fruits and vegetables and low in fat can significantly reduce blood pressure.

Four years later, Vollmer et al. (40) conducted a study not only to see the effects of the DASH diet on blood pressure, but also to find out the effect of sodium intake on this health parameter. The study participants were divided into two groups: control diet and DASH diet. Sodium intake was randomly assigned. As a result, it was observed that the DASH diet, together with a low sodium intake, was associated with a significant reduction in blood pressure.

The DASH diet does not include special foods, but simply makes several recommendations, including: eating fruits, vegetables and whole grains; including low-fat dairy products, chicken, fish, legumes, nuts and seeds and vegetable oils; and limiting the consumption of foods high in saturated fats, such as whole dairy products, fatty meat or palm oil, and foods high in simple sugars, such as sweets (41). This diet is intended to generate a high intake of potassium, calcium, magnesium and fiber and to reduce sodium intake to below 2.3 g/day (38).

This diet is mainly indicated for patients with hypertension (38), as it is directly related to a reduction in blood pressure (37). However, because it is a healthy dietary pattern, people without pathologies can also benefit from it. Similarly, patients suffering from diabetes, dyslipidemia or overweight can improve their health by following the DASH diet (38).

Ketogenic diet

The ketogenic diet was introduced in 1921 to treat epilepsy (42). It was thought that this high fat, adequate protein and low CH diet would be optimal for patients suffering from epileptic seizures, as it simulates the physiological situation that occurs during fasting. The ketogenic diet produces acidosis, dehydration and ketosis (as does fasting) but can be carried out for much longer (42,43).

This diet was widely used in children with epilepsy for two decades. However, with the appearance of new drugs, its therapeutic interest diminished and it was not until the beginning of the 21st century that the efficacy of this dietary intervention in the treatment of epilepsy was again emphasized (43).

The ketogenic diet consists of between 40 and 50 g of carbohydrates per day, which lowers hepatic and muscle glycogen and thus lowers blood glucose and insulin (29). This reduction of CH makes the body unable to use glucose as energy and, therefore, ketone bodies are produced from fatty acids (44). The main ketone bodies produced are acetone, acetoacetate and beta-hydroxybutyrate (BHB) (44). The latter is the most important marker of blood ketosis (21). BHB elevation occurs physiologically with fasting and with the ketogenic diet at values between 1 and 8 mmol/l (45). However, in situations of diabetic ketoacidosis, BHB can reach concentrations greater than 20 mmol/l (21).

In short, this diet can be an effective tool in people with type II diabetes mellitus, obesity and metabolic syndrome (46), as well as to treat other PCOS-related diseases, such as congenital hyperinsulinism or nonalcoholic fatty liver disease (44).

Low glycemic index diet

A low glycemic index diet is a nutritional intervention based on the elevation of blood glucose caused by food, i.e., its glycemic index (GI) (47). The glycemic index of a food can be between 0 and 100. Foods with a GI closer to 0 raise blood insulin more slowly than those with

a GI close to 100, which raise it faster. As shown in Table 1, foods can be classified into foods with a low, moderate or high GI (48).

Table 1

Classification of certain foods according to their glycemic index

Low GI foods	0-55	Barley, quinoa, pasta, carrots, apples, milk, yoghurt, pulses
Foods with moderate GI	56-69	Pita bread or rye bread, couscous, brown rice, raisins
High GI foods	70-100	Potatoes, white rice, most processed cereals, sugary drinks, sugar, watermelon, pineapple, etc

Note: taken from Mayo clinic

The GI can be affected by the stage of ripeness of vegetables and fruits or the method and point of cooking (48,49). It is also important to take into account the glycemic load (GL) of foods. This concept, which was introduced in 1997, defines the effect that a food has on blood glucose levels depending on the amount of CH it contains (50). A high GI food does not necessarily have to have a high GC. For example, fiber and water are two dietary components that will influence the GC of a food (49).

Low GI diets were born to treat diabetes (49). They reduce fasting insulin and HOMA-IR index more than high GI diets (51). Similarly, these nutritional strategies in diabetics can reduce BMI and improve lipid profile (52). However, some authors state that there is no significant difference between a high GI diet and a low GI diet in terms of fasting glucose concentrations (51).

These diets may be beneficial in helping to treat other pathologies. Increasing low GI foods and decreasing high GI foods within a healthy dietary pattern, with an appropriate distribution of macronutrients, provides benefits in cerebrovascular diseases, obesity and cancer, as well as in the control of dyslipidemia (49).

Method

The PubMed database was used mainly for the preparation of this literature review. In addition, the Google Scholar database and some official web pages were used. The search took place between December 2022 and March 2023.

The inclusion criteria for the studies analyzed were experimental and observational studies, whose population were women of childbearing age between 16 and 50 years, without associated pathologies, with or without dyslipidemia, with any BMI. Studies had to be published between 2015 and 2023 that looked for the relationship between PCOS and each of the study diets. The method used to diagnose the disease was not taken into account.

The exclusion criteria were systematic or bibliographic reviews on the subject treated, meta-analysis of data from studies and clinical trials that studied the effect of CH and PCOS in

a general way, without specifying the type of diet. We also excluded those studies whose population included animals or women with pathologies aggravated by the syndrome, such as type II diabetes mellitus or non-alcoholic fatty liver disease.

The following keywords were used: *Polycystic ovary syndrome. Mediterranean diet. DASH diet. Ketogenic diet. Low glycemic index diet.* Ultimately, 19 articles were used for the study analysis.

Results

For the reasons explained above, DM may be of interest in women with PCOS. Firstly, because of its anti-inflammatory capacity. In the study conducted by Wang et al. (10) found that a diet high in foods with a high dietary inflammatory index (DII) increased the risk of PCOS. As an example, some anti-inflammatory foods that make this diet an interesting intervention are fruits and vegetables or oily fish and nuts, rich in omega-3 fatty acids (10, 53).

Secondly, DM has great antioxidant power, as it is rich in fruits and vegetables and olive oil (54). In addition, this diet is low in sodium and high in potassium, thus promoting a good balance of these minerals and, therefore, good heart health (10).

Finally, Barrea et al. (27) observed that in women with PCOS, greater adherence to DM is associated with less clinical severity of the syndrome. Similarly, the same author and his research group conclude that adherence to this diet is one of the three most influential parameters for not aggravating cardiometabolic risk in obese women with PCOS (33).

According to M Azadi-Yazi et al. (55), the positive effect of the DASH diet in women with PCOS may be due to weight loss, as this would reduce blood testosterone levels. In line with these results, Cutillas-Tolin et al. (6) concluded that this diet could be effective in reducing BMI in women with PCOS.

On the other hand, another mechanism that explains the positive effect of the DASH diet in women with ovulation problems is that the calcium intake in this dietary pattern is high, and some metabolic problems of women with PCOS may be due to a poor metabolism of this mineral and of vitamin D. Lastly, this diet is rich in minerals such as magnesium, which increases the antioxidant capacity of the organism and, according to several authors, can improve insulin sensitivity (55,56). Likewise, the results of the study carried out by Asemi Z. et al. (56) show that the amino acid arginine, which is found in abundance in this diet, has a beneficial effect on insulin sensitivity.

In PCOS the ketogenic diet is still under study (59). The results obtained from the research carried out by Paoli et al. (58) suggest that this diet may be of interest due to the frequent glucose mismetabolization, as well as the activation of the protein compounds AMPK and SRT-1, which are responsible in some way for regulating energy metabolism (47, 48). Similarly, the results of the study by Magagnini et al. (45) show that a ketogenic diet reduced the HOMA index and insulin resistance. On the other hand, as some authors point out, CD can reduce hyperandrogenism, since it increases the transport of sex hormones by increasing sex hormone binding globulin (SHBG) and also increases circulating progesterone (44,45).

Similarly, according to Yang et al. (59), the ketogenic diet is of clinical interest in the study population because it is a method of fat loss. These results are supported by other studies, which show that after the intervention there was a reduction in BMI (29,45).

Finally, numerous investigations have concluded that a low glycemic index diet may be of therapeutic interest in women with PCOS (60,61). According to Hoover et al. (65), low-GI diets may reduce the risk and improve the signs and symptoms of PCOS. In this same study, it is stated that a low GI diet had a greater effect on satiety than a high GI diet (65). Other authors support the positive effect that this dietary pattern has on blood glucose control in the study population (62). It is worth mentioning that Szczuko (63) and his team observed that this diet had an effect on the reduction of insulin-like growth factor-1 (IGF-1). Numerous researchers have also written about the role of a low-GI diet in reducing body weight and various anthropometric values (60,61).

In short, the characteristics that can make a low GI diet beneficial in women with PCOS are that this diet provides an intake of complex carbohydrates, a high intake of fiber (especially soluble), a low intake of saturated fats and a high intake of unsaturated fats and a significant intake of vegetable proteins, reducing those of animal origin; it is rich in micronutrients (61).

Discussion

Mediterranean diet and PCOS

Part of the results of the study Barrea et al. (27) are contrary to those obtained by Moran et al. (53). The first investigator and his team suggest that those women with PCOS show lower adherence to DM than those women without the syndrome, while Moran et al. (53) state that sick women showed more adherence to a Mediterranean-style diet.

A key factor explaining the difference between the two results is the sample chosen for each study. The first study consists of Italian population, while the second one analyzes data from women in Australia. Moreover, only in the study by Barrea et al. (27) used the PREDIMED questionnaire, a tool mostly used to assess adherence to DM.

On the other hand, both studies affirm that DM can be a useful tool as a dietary treatment in women with PCOS. These results coincide with those of other studies (10,33). These studies affirm that DM can prevent an obese woman with PCOS from increasing her cardiometabolic risk associated with excess weight, as well as decreasing the inflammatory state typical of the syndrome.

However, in the case-control study by Ana Cutillas-Tolín et al. (6) no clear association was seen between a high DM adherence rate and an improvement in typical PCOS phenotypes. These results may be due to the fact that other healthy dietary patterns were also observed in this study, not comparing DM with a control diet.

DASH diet and PCOS

Of the 4 studies analyzed, 3 (55,56,57), which are experimental, support that there was a significant reduction in the body weight of those women who followed the DASH diet compared to those who followed a control diet. Similarly, in the study by Cutillas-Tolín et al. (6), which is observational, states that the DASH diet can improve BMI.

In addition to a reduction in weight, and therefore in BMI, M Azadi-Yazdi et al. (55) also observed a greater loss of fat mass in women following the DASH diet. Along the same lines, Asemi Z et al. (56) observed a significant reduction in waist and hip circumferences when following the DASH diet compared to the control diet.

As for the hyperandrogenism typical of the syndrome, it is unclear what effect the DASH diet may have. M Azadi-Yazdi et al. (55) obtained as a result of their study a reduction in androstenedione. However, in this research, no significant reduction in the free androgen index was observed, which was observed by Foroozonfard et al. (57). This difference may be due to the fact that Foroozonfard et al. (57) used the intention-to-treat principle, i.e., they included all study participants in the statistical analysis, even if they had not followed the diet correctly, whereas M Azadi-Yazdi et al. (55) did not.

None of the authors mentioned above observed a significant reduction in testosterone levels when comparing the study diet and the control diet. On the contrary, an increase in the SHBG protein complex has been observed (55,56, 57).

As for the parameters related to blood glucose levels, numerous studies show that these can be improved with the DASH diet. The group following the DASH diet showed a greater reduction in circulating insulin levels and HOMA index than the control group (55, 56, 57).

Ketogenic diet and PCOS

In the 4 experimental studies analyzed (58, 29, 45, 59) a reduction in body weight was seen in the study women. This is because all the ketogenic diets in the various studies were designed to be hypocaloric. In addition to weight loss, this diet has led to improvements in other anthropometric parameters: decrease in waist circumference, hip circumference and fat mass.

While in the study by Yang et al. (59) stated that a ketogenic diet can reduce subcutaneous and visceral fat in women with PCOS and hyperuricemia without negatively affecting muscle mass, in the study by Cincione et al. (29) observed a small but significant reduction in the amount of muscle mass after the ketogenic diet. Similarly, a difference in blood lipid lowering has been seen in these two studies. In the study by Yang et al. (59) total cholesterol, LDL and blood triglycerides did not decrease after the ketogenic diet significantly. In the Cincione et al. (29) yes. Both differences, both the loss of muscle mass and the reduction in blood lipids, may be due to the fact that in the second study a very low calorie diet was followed and in the Yang et al. study the diet was less restrictive.

The three uncontrolled trials analyzed (6,31,52) show an improvement in terms of biochemical parameters related to blood glucose after following a hypocaloric ketogenic diet. A reduction in the HOMA-IR index of insulin resistance was seen.

Regarding hormones, a decrease in antimullerian hormone has been seen, as well as an increase in progesterone and SHBG (58, 29, 45) and a decrease in testosterone in those studies in which the concentration of this hormone was analyzed (58, 29, 45).

Finally, it is worth mentioning the positive effect of this diet on women with ovulation and fertility problems. Of the 17 women participating in the study by Cincione et al. (29), 5 recovered their menstrual cycle after years of amenorrhea, 12 managed to have a regular cycle and, of these 12, 5 managed to become pregnant after having previously failed.

Low glycemic index diet and PCOS

All experimental studies in which the effect of a low-GI diet on body weight in women with PCOS has been observed (60,61,62,63) have shown significant weight loss after such an intervention. Similarly, the case-control study of Panjeshahin et al. (64) suggests that those women who followed a high GI diet had significantly higher BMI.

Regarding changes in parameters related to glucose metabolization after following a low GI diet, the evidence is inconclusive. In the studies carried out by Hoover S.E et al. (65) and Szczuko M et al. (63) in which these variables were analyzed, lower basal glucose and insulin were seen after performing the low GI diet. However, the same investigator in another study (61) saw that there was no significant difference in terms of insulin and blood glucose decrease at the end of the study weeks. It is worth mentioning that, in this study, a small improvement in insulin and blood glucose was seen.

According to Szczuko M et al. (61), it is likely that the improvement in glucose metabolization parameters was not significant in this study because the participants did not comply with the physical exercise recommendations.

On the other hand, the sex hormone profile may be improved by following a low-GI diet in women with PCOS. Szczuko M et al. (63) observed a positive correlation between IGF-1 protein (polypeptide hormone that increases with a low GI diet) and SHBG concentration. Similarly, Shishehgar F et al. (62) observed a significant increase in this protein after dietary intervention. This increase directly improves the hormonal profile of these women. This same study also observed a reduction in circulating testosterone (62), data supported by other research (63) but contrary to those provided by the results of Szczuko et al. (61).

Continuing with hormones, Hoover SE et al. (65) observed that following a low GI diet reduced ghrelin levels more than following a high GI diet (65). These results are of particular interest, as numerous investigations suggest that women with PCOS may have altered hunger and satiety mechanisms. It may be that by following a low GI diet and reducing ghrelin these women achieve better weight control.

Finally, other biochemical parameters such as total cholesterol, LDL and triglycerides are also significantly reduced after following a low GI diet (60,61,62,63). However, in the case-control study by Panjeshanin et al. (64) related good adherence to a low-GI diet to having elevated total cholesterol. As the authors themselves state, this may be due to the fact that cooking methods were not taken into account. Continuing with other blood lipids, Szucko et al. (61) did not obtain significant improvements in HDL levels in the participants; such improvement was observed by this author and his team in another investigation (63), as well as by Lagowska K and Drzymala-Czyz S in their study (60). Again, as the authors themselves

state, it may be that the increase in HDL was not significant in the first study by Szucko et al. (61) because the women did not comply with the recommendations of practicing physical exercise at least 3 times a week.

The present work has some limitations. The total samples of most studies are less than 60 women, i.e., the samples are somewhat small considering the prevalence of PCOS. On the other hand, the studies analyzed on DM and PCOS deal, for the most part, with adherence to this dietary style. Therefore, how PCOS symptomatology is influenced by following DM was not studied in depth in these investigations.

On the other hand, a strength of this review is that no other literature review comparing the 4 study diets analyzed here was found. Likewise, articles whose samples had any BMI were included in this study. That is, no study has been excluded because of the weight of the women in the sample, so that the general results can be extrapolated to any woman with PCOS who does not have any other serious health condition.

Conclusions

It has been shown that the four study diets: DM, DASH, DC and a low GI diet can be beneficial in treating PCOS, depending on the context and characteristics of each woman.

In case the woman needs to lose weight, any of the diets analyzed in this literature review, as long as they are properly designed and generate a caloric deficit, could be effective tools. However, in case of obesity or marked overweight, a very low calorie CD can be used as a first intervention. After achieving a rapid initial fat loss, it may be useful to follow a more flexible diet, such as the Mediterranean diet or DASH, as these dietary patterns allow better adherence. However, HCs should continue to be controlled, avoiding simple HCs.

Following this line, it is noteworthy that weight loss in women who need it can itself generate improvements in both cardiometabolic health and symptomatology in women with PCOS, regardless of how it has been achieved. On the other hand, due to the antioxidant power of DM, this dietary pattern may be of great help in women with chronic inflammation. For improving fertility in women with PCOS, DC has shown some efficacy. Likewise, women who suffer markedly from hyperandrogenism may benefit from a CD, as this diet has been found to be effective in improving the hormonal profile of women with PCOS. In short, more studies with more participants are needed to further investigate the effect of diet on PCOS.

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EFFECT OF INTERMITTENT FASTING ON CARDIOMETABOLIC HEALTH IN OBESE PERSONS WITH METABOLIC SYNDROME COMPARED TO CONTINUOUS CALORIC RESTRICTION

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Abstract. The prevalence of metabolic syndrome is increasing due to overeating and sedentary lifestyles. It is a risk factor for the development of diabetes mellitus II and cardiovascular disease. Effective and long-lasting weight loss involving lifestyle changes is necessary for its treatment. Continuous calorie restriction is the most commonly prescribed method of weight loss. However, people often regain the weight lost. Intermittent fasting protocols are being investigated as a safe and effective treatment for weight loss and improvement of cardiometabolic health, therefore, the aim of this research is to define the effects of intermittent fasting versus continuous calorie restriction for the control of cardiometabolic parameters in obese adults with metabolic syndrome. A literature review was carried out in which articles from scientific databases were consulted and analysed. Specifically, 10 articles published in the last 10 years belonging to PubMed were analysed. Intermittent fasting induces a weight loss equivalent to continuous calorie restriction; however, the loss of fat mass is greater when intermittent calorie restriction is performed. Changes in glucoregulatory markers are contradictory and inconclusive. Regarding the lipid profile LDL-cholesterol and triglycerides decrease equivalently with both interventions, not affecting HDL-cholesterol levels. Intermittent fasting and continuous calorie restriction protocols have similar effects on cardiometabolic health. Intermittent fasting is a safe intervention nevertheless, there is a risk of hypoglycaemia in people treated with antidiabetics.

Keywords: “obesity”, “cardiometabolic”, “health”, “periodic fasting”, “alternate day fasting”, “weight loss” and “overweight”.

EFECTO DEL AYUNO INTERMITENTE SOBRE LA SALUD CARDIOMETABÓLICA DE PERSONAS OBESAS CON

SÍNDROME METABÓLICO EN COMPARACIÓN CON UNA RESTRICCIÓN CALÓRICA CONTINUA

Resumen. La prevalencia de síndrome metabólico está aumentando debido a la sobrealimentación y sedentarismo. Es un factor de riesgo para el desarrollo de diabetes mellitus II y enfermedades cardiovasculares. Para su tratamiento es necesaria una pérdida de peso efectiva y duradera que englobe cambios en el estilo de vida. La restricción calórica continua es el método de pérdida de peso más prescrito, sin embargo, las personas suelen recuperar el peso perdido. Los protocolos de ayuno intermitente se están investigando como un tratamiento seguro y eficaz para la pérdida de peso y mejora de la salud cardiometabólica, por tanto, el objetivo de esta investigación es definir cuáles son los efectos de realizar ayuno intermitente frente a una restricción calórica continua para el control de los parámetros cardiometabólicos en adultos obesos con síndrome metabólico. Material y métodos pertenecientes a bases de datos científicas. Se analizaron concretamente 9 artículos publicados en los últimos 10 años registrados en PubMed. El ayuno intermitente induce una pérdida de peso equivalente a la restricción calórica continua, no obstante, la pérdida de masa grasa es mayor cuando se realiza restricción calórica intermitente. Los cambios en los marcadores glucoreguladores son contradictorios y poco concluyentes. Respecto a el perfil lipídico el colesterol LDL y triglicéridos disminuyen de forma equivalente con ambas intervenciones, sin modificaciones en el colesterol HDL. Los protocolos de ayuno intermitente y restricción calórica continua tienen efectos similares sobre la salud cardiometabólica. El ayuno intermitente se trata de una intervención segura, pero existe riesgo de hipoglucemia en personas tratadas con antidiabéticos.

Palabras clave: “obesity”, “cardiometabolic health”, “periodic fasting”, “alternate day fasting”y “weight loss”.

Introduction

There is currently a high and increasing prevalence of overweight and obesity worldwide. In public health, many resources are allocated to the treatment of noncommunicable diseases derived, in part, from overeating and sedentary lifestyles [1,2].

Metabolic syndrome (MS) is a group of disorders that include high blood glucose levels, arterial hypertension (AHT), obesity, hypertriglyceridemia and low levels of HDL cholesterol. Thus, MS is a key factor in the development of cardiovascular disease and type II diabetes. The etiology is widely debated, however, obesity plays an important role in the development of this set of anomalies [1,3].

The use of drugs to control hyperglycemia, dyslipidemia and hypertension is justified as a treatment, but it is crucial to implement lifestyle changes that lead to a sustained weight loss over time together with healthy hygienic and dietary habits [4]. Continuous caloric restriction of energy (CCER) is the most prescribed weight loss method in obese people. The aim is to induce a caloric deficit of approximately 500-700 Kcal/day to reduce weight. The change in body composition over time is not affected by changes in macronutrient ratios, thus subjects often gain the weight they lost through nutritional intervention [5,6].

The Adult Treatment Panel III (ATPIII) proposed a definition that takes into account as diagnostic criteria the presence of 3 of the following factors; fasting hyperglycemia, elevated waist circumference, hypertriglyceridemia, decreased HDL cholesterol and AHT [1].

On the other hand, there is a current definition coined by the International Diabetes Federation (IDF) which proposes that the person with metabolic syndrome is

characterized by central or abdominal obesity together with 2 or more of the following factors: hypertriglyceridemia, decreased HDL cholesterol, hypertension or fasting hyperglycemia. In any case, the difference between the various definitions centers on whether the common factor is insulin resistance or central obesity [(3)].

Table 1

Comparison of the different diagnostic criteria set forth by the WHO, ATPIII and FDI [(8)]

	WHO	ATPIII	FDI
Definition	Glucose intolerance or DMTII and/or insulin resistance with two or more of the following components	Have more than 3 of the following components	Central obesity plus any two of the following four components
		Components	
Central obesity	Waist/hip ratio >0.9 men and >0.85 women and/or BMI > 30kg/m2	Waist circumference ≥ 102 in men and ≥ 88 in women	Increased waist circumference according to race- and sex-specific limits
Blood pressure	≥ 140/90 mmHg o antihypertensive treatment	> 130/85 mmHg or antihypertensive therapy	> 130/85 mmHg or antihypertensive therapy

Lipid profile	Triglycerides ≥ 150 mg/dl and/or HDL cholesterol < 35 mg/dl for men and < 39 mg/dl for women	Triglycerides ≥ 150 mg/dl and/or HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for women	Triglycerides ≥ 150 mg/dl and/or HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for women
Glucose	Impaired glucose tolerance or DMTII or insulin resistance	< 11mg/dl or DMTII	≥ 100 mg/dl or DMTII
Microalbuminuria	Urinary excretion rate > 20 mg/min or albumin/creatine > 30 mg/g	-	-

1.1. Etiology

The etiology of MS is still unclear and many triggers have been proposed that may contribute to its onset, including insulin resistance, dysfunction of insulin-producing cells in the pancreas, malfunction of protein kinases and phosphatases, non-expression of IRS1 and IRS2 genes due to epigenetic factors, obesity and lipotoxicity, glucotoxicity and elevated oxidative stress, chronic inflammation, intestinal microbiome and dietary effects [(7)].

MS is also well known as insulin resistance syndrome because of the role insulin plays in its development [(1,7)]. In a properly functioning organism, the increase in blood glucose stimulates the B-pancreatic cells that release insulin. On the other hand, the release of insulin together with the increase in blood glucose stimulates the uptake of glucose by the hepatic cells that will carry out glycolysis or glycogenogenesis, or its uptake by the adipose tissue. All this suppresses the production of new glucose by the liver so that all these physiological processes contribute to maintaining glucose within its homeostatic range. The most important glucose transporter is GLUT4 expressed mainly in adipose tissue and muscle. GLUT4 is stimulated by insulin and its activation is necessary for the passage of glucose into the cell [(7)].

In the first phase of insulin resistance, there is a decrease in insulin secretion, resulting in hyperglycemia after ingestion. The second phase is a chronic

hyperinsulinemia that does not resolve the previous situation since the tissues do not respond efficiently to insulin. This situation, maintained over time, leads to apoptosis of the B-pancreatic cells, which eventually lose their functionality. Therefore, insulin resistance would largely explain the existing complications in the glycolytic pathways that generate the components contemplated in MS [7,8].

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The mechanism by which insulin resistance occurs is still unclear, but it appears that protein kinases and phosphatases may play a crucial role in its development. In addition, insulin receptor proteins -1 (IRS1) and -2 (IRS2) also play key roles in the insulin signaling cascade, therefore, a suppression in the function or gene inactivation of these proteins has also been linked to insulin resistance. Moreover, studies in animal models suggest that chronodisruption negatively influences insulin signaling pathways [7,8].

It is clear that an extra energy intake combined with a sedentary lifestyle contributes to an excess in the energy balance which results in the accumulation of excessive fat. There are differences between subcutaneous and visceral fat deposits, such that visceral fat deposits associated with MS have different gene expression mechanisms and are associated with increased insulin resistance, lower HDL cholesterol and increased LDL cholesterol. In those individuals in whom there is a deficit of insulin produced by resistance or dysfunction of the B-pancreatic cells, an increase in lipase occurs [2].

The increase in free fatty acids (FFA) in turn stimulates hepatic production of VLDL triggering hypertriglyceridemia. On the other hand, an exchange of triglycerides from VLDL proteins for cholesteryl esters from HDL-C takes place resulting in a rapid clearance of HDL-C. Excess triglycerides are also transferred to LDL which will be catabolized by hepatic lipase generating smaller and denser LDL particles. These particles are more atherogenic than large LDL, as they are more susceptible to oxidation and absorption in the arterial wall. All this explains clinical signs such as hypertriglyceridemia, increased LDL levels and low HDL levels [2].

AHT appears to have a multifactorial cause mediated by endothelial dysfunction, hyperactivation of the sympathetic nervous system, inhibition of nitric oxide synthase, and the effects of cytokines released by fat tissue. In addition, obesity is associated with an increase in the renin-angiotensin-aldosterone system [2,7].

On the other hand, fat tissue has endocrine and autocrine functions. Among the adipokines secreted is adiponectin, which is related to lower systemic inflammation and higher insulin sensitivity, thus having a positive effect. In addition, obese individuals with

metabolic complications have elevated levels of C-reactive protein, interleukin-6 (IL-6) and tumor necrosis factor a (TNF-a) that contribute to macrophage infiltration of adipose tissue causing inflammation and downstream insulin receptor resistance [2, 8].

Inflammation is not only caused by macrophage infiltration and cytokine release, but has also been linked to alterations in the intestinal microbiome. Studies using experimental models suggest that a diet high in fat and low in soluble fiber (inulin) may alter the intestinal microbiome causing inflammation, an important component in the development of MS [7].

Risk factors for the development of MS include family history of MS, smoking, advanced age, obesity, low socioeconomic status, Mexican-American ethnicity, climacteric status, lack of physical activity, inappropriate intake of sugary beverages, alcoholism and Western diet, medications used in HIV or those used as antipsychotics [1].

1.2. Metabolic syndrome and other associations

Although MS was originally defined to predict the risk of cardiovascular disease (CVD), its ability to predict the risk of IMTD has been investigated. Finally, through various investigations it was concluded that early diagnosis of MS predicts incident diabetes in individuals from numerous backgrounds. The greater the number of MS components, the greater the risk of suffering IMTD, with fasting glucose and glucose intolerance being the most important determinants. A diagnosis of MS increases the risk of developing T1DMD by a factor of 5 [2].

MS is also associated with non-alcoholic fatty liver disease so that it has sometimes been referred to as the "metabolic liver syndrome". It appears that non-alcoholic fatty liver disease is associated with the components of MS such as; elevated waist circumference, AHT, elevated fasting glucose, insulin resistance and other components. The higher the number of SM components, the higher the risk of nonalcoholic fatty liver disease [2].

On the other hand, it has also been associated with the risk of cancer, however, this association is more closely related to the obesity component. It appears that inflammation of adipose tissue, hyperglycemia, hyperinsulinemia and/or insulin-like growth factor promote the development of cancer [2].

In any case, the importance of the diagnosis of MS lies in the impact it has on the probability of suffering CVD, as well as T1DM, taking into account that the main cause of death in the world is acute myocardial infarction, the prevalence of which continues to increase according to the United Nations (UN) [4]. There are also alarming data on the prevalence of MS, such as those presented by the National Health and Nutrition Examination and Surveys (NHANES), which determine its presence in 35% of U.S. adults [1]. It seems that cases of MS will increase in parallel with obesity and overweight, a fundamental factor in its development [2].

1.3. Treatment of metabolic syndrome

Treatment of MS is applied in order to reduce CVD and T1DMD. Lifestyle change strategies should be integrated with nutritional treatment and exercise [7].

Treatment of dyslipidemia and hypertension with drugs should also be considered. Among the drugs widely used for the treatment of dyslipidemias are statins that can be used together with cholesterol absorption inhibitors or bile acid sequestrants. After lowering LDL cholesterol with the drugs mentioned above, there is still some risk of CVD due to low HDL cholesterol levels. It seems that niacin increases HDL cholesterol levels, so that the combination of both treatments could be useful in some patients; however, there are no significantly superior benefits in those patients already treated with statins [2].

A meta-analysis comparing the efficacy of various interventions for SM reversal assumed that the likelihood of reversal was higher when lifestyle changes were applied compared to pharmacological treatments [15].

Finally, we must take into account the progress of nutrigenomics, a science that studies the mediated interactions between genes and nutrition. Thus a recent study has observed how women with the IRS-1 rs2943641 TT genotype have a lower insulin resistance and thus risk of TIDD when their circulating Vitamin 25(OH)D levels were higher, however, the beneficial effect was not as strong for carriers of another allele [7]. This is an example of how gene therapies can be applied in this field, however, it is still a science of lifestyle changes should lead to a loss of 7-10% of body weight, addressed through a caloric deficit of 500-1000 kcal/day to induce such a loss over a period of 6-12 months in order to improve MS symptoms and CVD risk [5].

The Mediterranean diet can be prescribed together with caloric restriction or not to all people with MS. Olive oil is an essential component of the Mediterranean diet, and studies that have evaluated its use in the treatment of MS conclude that replacing fats used with olive oil may have a beneficial effect in the treatment of MS [14]. The lipid content of the diet should be between 25-35% of total calories, since values outside this range can worsen atherogenic dyslipidemia. Fats should come primarily from polyunsaturated and monounsaturated fatty acids (olive oil) that have cardioprotective benefits against CVD and AHT in humans [5,7].

Regarding alcohol consumption, a review study shows that people who have a moderate consumption of wine or beer are less likely to develop MS, with beer being less preventive than wine, compared to those who do not drink alcohol or drink it in large quantities [14].

There are other dietary patterns that may be beneficial in the treatment of MS such as the DASH diet that has been shown to improve the symptoms of the syndrome, also the new Nordic diet and vegetarian diets (Table 2) [14,15]. It is worth noting the benefit of accompanying the above changes with a physical exercise program that includes 30 to 60 minutes of moderate physical activity for the control and treatment of MS development that needs a research trajectory [5,14].

Table 2.

Dietary patterns and potential benefits in the control of MS (15)

Dietary pattern	Nutritional distribution	Improvements in the SM components
Mediterranean Diet	· 35.45% kcal/day of lipids (mainly monounsaturated and polyunsaturated from olive oil and nuts) · 35-45% kcal/day of carbohydrates · 15-18% kcal/day of protein	Decreases; CVD, hypertension, mortality, dyslipidemia, and IIDM
Vegetarian diet	· Restriction of foods of animal origin · High intake of plant foods · Rich in polyunsaturated fats	Decreases; HTA, body weight, CVD, mortality and DMII
Nordic diet	· High in fiber-rich whole foods · Few meat and processed foods	Decreases HTA and increases HDL cholesterol levels
DASH diet	· Low in fat (27% kcal/day), especially saturated fat (6% kcal/day) and cholesterol · Sodium reduction to 1500- 2300 mg/day · Rich in fiber (>30 g/day), potassium, magnesium and calcium	Decreases; HTA, CVD, cancer, DMII, body weight and adiposity

1.4. Continued caloric restriction (CCR)

CCR is the most prescribed weight loss method in obese adults and also in those with MS. The objective of the treatment is to induce a daily caloric deficit of about 25-30% (500 - 750 kcal) of total calories without lack of essential nutrients in order to achieve a significant weight loss that can be maintained over time. There is evidence that adherence to treatment is lost or decreases after 1 to 4 months and is inefficient when the lost weight is regained [6,17]. For this reason, it is necessary to address new nutritional treatments in the control of MS that improve follow-up and long-term success in weight loss and control of metabolic parameters [6,16].

In general, it can be said that CCR has benefits on life expectancy and health. There are four mechanisms through which CCR increases cellular longevity and lifespan; adaptations of the neuroendocrine system, prevention of inflammation, hormonal response and protection against oxidative stress [10].

The adaptations of the neuroendocrine system have their benefit in a reduction of anabolic hormones, insulin resistance and hormones that promote thermogenesis, as well as an increase in anti-inflammatory hormones. It has been demonstrated in experimental animal models that CCR is able to delay diseases such as cancer, cardiomyopathy, neurodegenerative diseases, diabetes, kidney disease and arteriosclerosis [10].

It has been established that RCC is capable of resolving errors produced in DNA and promoting the elimination of damaged proteins and lipids, as well as playing an antioxidant role by activating endogenous enzymatic and non-enzymatic mechanisms. It also triggers processes such as enhanced apoptosis, autophagy and decreased oxidative stress. It is able to reduce fasting insulin levels and some growth factors and cytokines such as tumor necrosis factor α (TNFα) which causes inflammation and is elevated in MS. Studies with primates have also observed how a 30% CCR can decrease glucose intolerance, CVD and cancer [10].

1.5. Intermittent caloric restriction (ICR)

Among the dietary strategies currently being investigated are intermittent fasting or intermittent calorie restriction (ICR) which appears to have benefits on CVD, T2DM, metabolic disorders and cancer due to the caloric restriction it entails. The main cardiometabolic benefits when ICR strategies are applied are decreases in insulin resistance, body weight, blood pressure, dyslipidemia and inflammation in general terms [9]. RCI generally refers to the intake of a very low calorie diet (VLCD) 500-700 kcal for approximately 2 to 4 days a week. These types of interventions are more commonly accepted by people, as strict caloric restriction is only done on specific days of the week. It is therefore interesting to evaluate the benefits of these regimens for obese individuals with MS [9].

A limitation in the field of intermittent fasting is the lack of clear terminology defining the different regimens of IFN. In general, dietary patterns in which prolonged periods of reduced or no intake are included with those in which the person eats normally are referred to as RCI [6]. The characteristics of the different ICR regimens known as; alternate day complete fasting (ADA) or consecutive (2:5 diet), alternate day modified fasting (AMDA) and time-restricted feeding (ART) are detailed below [12,13].

In alternate day complete fasting (ADA), fasting days in which no caloric intake is performed alternate with feeding days in which food and beverages are consumed ad libitum [18]. In the two-day-a-week (2DS) fasting, also known as the 5:2 diet, the fast is prolonged for two days and then food is consumed ad libitum for the rest of the week. [6,19].

Method

The literature review was carried out by analyzing the scientific evidence on ICR protocols in the treatment of MS, in addition to their application compared to classic CCR for the control of the syndrome.

It was carried out through the initial selection of 8577 articles, 1634 were eliminated for not being original or duplicates, 6849 for not meeting the inclusion criteria and 85 for not fitting the subject matter. The literature search was initiated in January 2022 and completed in April 2022.

The search was carried out in Pubmed, Cocharane, Google Scholar and Clinical Trials databases. The key words used were "obesity", "cardiometabolic health", "periodic fasting", "alternate day fasting", "weightloss" and "overweight". The inclusion criteria for the selection of articles were those published since 2012, indexed in scientific journals with an impact factor greater than 1.5 and dealing with topics related to ICR, SM and CCR. The exclusion criteria were articles published more than 10 years ago, in non-indexed journals and those published in journals with an impact factor of less than 1.5. In addition, articles were excluded if the sample included persons with normal weight and preserved cardiometabolic health. Finally, most of the selected articles were found in Pubmed belonging to scientific journals.

Results

In relation to the effectiveness of ICR as an alternative treatment to CCR in people with MS, 3 articles were included, 2 of which were randomized clinical trials and 1 a systematic review. Table 3.1 details the characteristics and results found in each study [18,19,22].

Regarding weight loss two of the articles [18,19] concluded that weight loss is greater when performing RCI protocols compared to RCC, however, Kunduraci et al. [22] found no significant differences, but significant weight loss in both groups. In this same study, improvements in waist/hip ratio, fat mass, total body water and BMI were observed in participants who performed ICR compared to CCR, therefore, although ICR does not offer advantages over weight loss, it does result in a greater decrease in fat mass and contributes to maintaining lean mass (20). Also Parvaresh et al. [17] reported a greater reduction in waist-to-hip ratio in the RCI group.

Various glucoregulatory markers were analyzed; two of the studies showed significant reductions in fasting glucose [19,22] when comparing both groups, whereas Wang et al. [18] did not find the same results. Regarding fasting insulin concentrations,

HbA1c and HOMA-IR there were no differences between the intervention arms in two of the articles [18,19], however, significant differences were found in HOMA-IR in the study by Kunduraci et al. [22].

Regarding the changes in the lipid profile of the participants, all the studies state that the reductions in total cholesterol, LDL and triglycerides were similar in the RCI and RCC groups. HDL cholesterol remained unchanged in both intervention arms [18,19,22].

Some caution should be exercised in interpreting the above findings since the randomized clinical trials conducted by Parvaresh et al. [19] and Kunduraci et al. [22] are of short duration (8-12 weeks) and a small sample (70 participants). In addition, it should be noted that the RCI regimens applied in each trial were different, Kunduraci et al. used ART regimens while Parvaresh et al. studied ADF regimens. Studies with a larger number of participants with MS are needed to corroborate the results and have clinical relevance to ensure that RCI is an alternative to RCC for this type of profile.

There are few studies that compare the efficacy of ICR with CCR in people with MS, since most of them use overweight and obese people as a sample. As a result of the above, 6 articles have been included that directly analyze the benefits of performing ICR with respect to CCR in overweight and obese individuals, since obesity itself is a key factor in the development of MS. Depending on the type of study, 1 literature review [6], 1 systematic review [11] and 4 randomized clinical trials [20,21,23,25]were included.

Regarding the changes produced in body composition, all articles endorse a significant and similar weight loss when performing CCR or ICR [6,11,20,21,21,23,25]. Also Cioffi et al. [17] corroborate these results in their meta-analysis. In this aspect it does not coincide with 2 of the articles whose results in people with MS approve a greater weight loss with RCI regimens [16,19].

Several glucoregulatory markers were analyzed; fasting glucose, HOMA-IR, HbA1c, fasting insulin, insulin sensitivity and insulin resistance. In the case of fasting glucose showed similar reductions in both intervention arms in 4 of the studies [6,11,20,25], Sutton et al. [23] reported that there were no reductions in fasting glucose concentrations during the study in the RCI group. On the other hand, 2 of the studies [11,21] showed that the reductions in fasting glucose and HbA1c were greater in the group that underwent ICR; however, Welton et al. warned of the risk of hypoglycemia that exists in those treated with oral antidiabetics or insulin, for which reason caution should be exercised when implementing this type of dietary treatment.

Regarding sensitivity, insulin resistance, as well as fasting insulin and pancreatic B-cell responsiveness, 3 of the studies [6,20,24] reported that there were no additional advantages of performing ICR versus CCR. In addition, Pinto AM et al. [20] added that the reductions produced had no therapeutic relevance. On the other hand, 3 of the studies [11,21,23] did find improvements in fasting insulin, insulin resistance, insulin sensitivity and pancreatic B-cell responsiveness.

Regarding improvements in lipid profile, 2 of the studies [21,24] report improvements in HDL cholesterol when RCI protocols are carried out, in contrast to the results found by Sutton et al. [23] who found no changes in HDL cholesterol during the study. Moreover, there were also no changes in HDL in studies performed in people with MS [16,19,22]. LDL cholesterol was not affected either in the study by Sutton et al. [23]. The TG results were significantly increased in the RCI group in 2 of the studies [20,23], contrasting with the improvements found in the study by Sundfor et al. [21].

In a study by Trepanowski et al. [24] reported a high dropout rate in the ADA group. For this reason, they decided to conduct a secondary study [25] in order to clarify the reasons why they had dropped out of the study. The null hypothesis was that ADA regimens could lower leptin and other adipokines in such a way that adherence to the dietary regimen would be difficult for participants. This hypothesis was not confirmed; it was established that circulating leptin and other adipokine levels increased in both intervention arms during the study.

Table 3.

Articles addressing the effectiveness of intermittent fasting in people diagnosed with metabolic syndrome compared to continuous caloric restriction

Author, year, type of study, sample size and characteristics	Study groups and regimens applied	Body composition	Glucoregulatory markers	Lipids
Kunduraci YE et al. 2020 [22] Randomized Controlled Trial 70 participants with a diagnosis of MS 12 weeks of duration	GI: RCC time-restricted feeding ART (<25% kcal) GC: RCC <25% kcal	Both significantly decreased weight	Fasting glucose, HOMA-IR and HbA1c decreased significantly in both groups	Total cholesterol, triglycerides and LDL in both groups decreased significantly.
Parvaresh A et al. 2019 [19] Randomized clinical trial 69 participants with a diagnosis of MS 8 weeks duration	GI: AFD (alternate day fasting) GC: CCR 25% per day	The ADF protocol showed significant weight reductions compared to the ADF protocol with RCC	The ADF protocol significantly reduced fasting glucose compared to CCR. There were no significant differences in HOMA-IR or fasting insulin concentrations between the two groups.	No significant differences were observed in TG, total cholesterol and HDL between the groups.
Wang X et al. 2021[18] Systematic review and meta-analysis of 4 studies. Participants with SM 8-12 weeks	GI: Different RCI regimes GC: CCR 25% OF kcal/day	ICR was more successful for weight loss than CCR	No significant differences were found in HbA1c or fasting glucose between groups.	There was no statistical difference in total, HDL and LDL cholesterol levels.

Table 4.

Articles addressing the effectiveness of intermittent fasting in overweight and obese individuals compared to continuous caloric restriction

Author, year, type of study, sample size and characteristics	Study groups and applied regimens	Body composition	Glucoregulatory markers	Lipids
Rynders CA et al. [6] 2019 Literature review 11 clinical trials Overweight persons and obesity Duration >= 8 weeks	GC: RCC GI: Different RCI strategies	There are no significant differences in weight loss or in the loss of body fat	There are no advantages in the improvement of cardiometabolic health when comparing both groups.	It was not studied.
Welton S et al. [11] 2020 Systematic review of 41 items Overweight people and obesity Duration between 2 and 26 weeks	QA: following a diet with RCC GI: monitoring of different rCI protocols	Similar weight loss in both groups	Glucose levels in the blood fasting and fasting insulin decrease significantly with rCI protocols, however, may be at risk of hypoglycemia for diabetic people.	It is not rated at the study.

Pinto AM et al. [20] Randomized clinical trial 43 participants with central obesity 4 weeks duration	GI: diet 5:2 CC: RCC Protocol	Similar weight loss in both intervention groups	It increased insulin sensitivity, decreased insulin resistance, serum insulin and blood glucose in both intervention arms. The magnitude of the change was not relatively therapeutic.	Intervention group increased fasting TG concentrations.
Sundfor et al. [21] 2018 Randomized controlled trial 112 overweight and obese participants Duration 6 months and a further 6-month maintenance phase	GI: ADA fasting (400-600 kcal) every other day GC: RCC Protocol	Similar weight loss in both groups, and recovery at 6 months was also minimal and similar. Decrease in waist circumference with no significant differences among the different groups.	There were improvements in HbCA1 in the ADA group compared to RCC. Insulin sensitivity was also improved.	Improvements in TG and HDL cholesterol were observed in the intervention group.
Sutton E et al. 2018 [23] Randomized controlled trial 8 participants with overweight and obesity 5 weeks duration	GI: ART early feeding restricted in time CC: Normal power supply 12/12 Both performed the intakes under supervision throughout the study	Similar weight loss in both groups.	TRF improved insulin sensitivity, B-cell responsiveness and reduced insulin levels. It did not improve glucose levels.	TRF increased resting heart rate, TG and total cholesterol. HDL and LDL cholesterol were not modified.

Trepanowski J et al. [24] 2017 Randomized clinical trial 100 obese participants 1 year duration (6 months of intervention + 6 months of maintenance)	GI: fasting on alternate days ADA (25% caloric restriction on fasting days) GI: continuous caloric restriction (75% of TSG every day) GC: no intervention	Similar weight loss in the continuous caloric restriction and ADA groups.	There were no significant differences in fasting glucose concentrations, insulin resistance and fasting insulin between the intervention groups, but there were significant differences with respect to the control group.	It increased LDL cholesterol in the group performing ADA at month 6 significantly, but not at month 12 compared to CCR. HDL cholesterol was significantly elevated in the month 12 in the ADA participants compared to the ADA group RCC.

Discussion and conclusions

RCI protocols in people with MS appear to result in greater weight and fat mass loss in the short term than CRS. In the long term there is no evidence of an advantage of RCI over RCC for weight loss in the treatment of obese individuals. On the other hand, the results on the improvement of glucoregulatory parameters with ICR versus CCR are contradictory and inconclusive. As for changes in the lipid profile, there were equivalent reductions in LDL cholesterol and triglycerides without changes in HDL cholesterol.

Therefore, both interventions have similar effects on the control of cardiometabolic parameters; however, it remains to be resolved whether the cardiometabolic effects mediated by RCI are due solely to the caloric deficit generated. ICR is a safe protocol, however, caution should be exercised in those treated with antidiabetics due to the risk of hypoglycemia. It should be noted that all the studies analyzed were of short duration and with a small sample size, so more studies are needed, with a sufficiently large sample size to be extrapolated to all people with MS.

More clinical trials comparing the efficacy of ICR in people with MS vs. CCR are needed, as most studies include overweight and obese people.

The following recommendations are proposed for future studies:

- A consensus document should be drawn up to define the definition and characteristics of ICR regimens so that accurate comparisons can be made between the various studies.
- Studies should include the dietary recommendations and the menu prescribed for each diet, as well as the percentage of macronutrients in the diet, since most of them only mention the daily amount of restricted energy.
- Development of studies that include a large sample of people diagnosed with MS. In addition, it would be advisable for them to be of long duration in order to observe whether there are metabolic changes and good adherence that could be an advantage over CCR.
- Take into account confounding variables in future studies that may affect the results, such as physical activity or adherence to the prescribed diet by the participants.

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