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The works must be unpublished and refer to topics of surgery, physical exercise, physiotherapeutic treatment, thermotherapy, muscular physiology program, ultrasound, rehabilitation, augmented reality, articulated prosthesis and other topics related to Medicine and Health Sciences.

Presentation of Content

As first article we present, *Effect of L-carnitine supplementation on anthropometric measurements in overweight women who practice CrossFit*, by HERNÁNDEZ-CORONA, Diana M., GONZÁLEZ-HEREDIA, Tonatiuh, MÉNDEZ-DEL VILLAR, Miriam and MERAZ-MEDINA, Tzintli, with adscription in the Universidad de Guadalajara, as second article we present, *Physical training programs that affect muscle mass in adult women. Systematic review*, by VILLARREAL-SALAZAR, Angelly Del Carmen, ZAMBRANO-AYALA, Stephanie Denise, ESTRADA-SÁNCHEZ, Ivonne Azeret and ENRÍQUEZ-REYNA, María Cristina, with adscription in the Universidad Autónoma de Nuevo León, as third article we present, *The limbic system as a neuroanatomical link between obesity and depression. Neuroimaging findings*, by FLORES-OCAMPO, Paola M., TENORIO-BORROTO, Esvieta, MARTÍNEZ-ALVA, Germán and VIEYRA-REYES, Patricia, with secondment at the Universidad Autónoma del Estado de México, as last article we present, *Molar-incisive hypomineralization syndrome and associated factors in three siblings*, by MARTÍNEZ-ORTIZ, Rosa María & TAVIZÓN-GARCIA, Jesús Andrés.

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Effect of L-carnitine supplementation on anthropometric measurements in overweight women who practice CrossFit**Efecto de L-carnitina en las medidas antropométricas en mujeres con sobrepeso que practican CrossFit**

HERNÁNDEZ-CORONA, Diana M.†*, GONZÁLEZ-HEREDIA, Tonatiuh, MÉNDEZ-DEL VILLAR, Miriam and MERAZ-MEDINA, Tzintli

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Abstract

Objective: The aim of the study was to evaluate the effect of 1.5 grams of L-Carnitine on anthropometric measurements in overweight adult women who practice Cross-fit exercise routine, as an adjuvant non-pharmacotherapy for weight loss.

Methods: A randomized, double-blind, placebo-controlled clinical trial was carried out in women age 18 to 40 who practice Cross-fit. Anthropometric measurements, weight, percentage of fat mass and muscle mass were taken in all patients; brachial and waist circumference were measured. The body mass index was calculated according to the World Health Organization. All the measurements were taken at the beginning and end of the clinical trial. The study and evaluations were carried out in a private Cross-Fit gym, in El Salto, Jalisco, México.

Contribution: Hernández Corona, Diana Mercedes: design, implementation of the study, field work, statistical analysis and write of the paper. González Heredia, Tonatiuh: field work, statistical analysis, writing under discussion, conclusion, methodology. Méndez del Villar, Miriam: protocol drafting, field work, results, conclusions. Meraz Medina Tzintli: protocol drafting, field work, drafting methodology.

Carnitine, Overweight, CrossFit**Resumen**

Objetivo: El objetivo del estudio fue evaluar el efecto de 1,5 gramos de L-Carnitina en las mediciones antropométricas en mujeres con sobrepeso que practican Crossfit para ejercitarse de manera rutinaria, como adyuvante no farmacoterapéutico para la pérdida de peso.

Métodos: Se llevó a cabo un estudio clínico aleatorizado, doble ciego, controlado con placebo en mujeres de 18 a 40 años que practican Cross-fit. A todas las pacientes se les tomaron medidas antropométricas, peso, porcentaje de masa grasa y masa muscular; otras medidas fueron tomadas como la circunferencia braquial, la circunferencia del brazo contraído y la circunferencia de la cintura. El estudio y las evaluaciones se llevaron a cabo en Hard Crossfit, en El Salto, Jalisco, México.

Contribución: Hernández Corona, Diana Mercedes: diseño, implementación del estudio, trabajo de campo, análisis estadístico y redacción del artículo. González Heredia, Tonatiuh: trabajo de campo, análisis estadístico, redacción en discusión, conclusión, metodología. Méndez del Villar, Miriam: Redacción de protocolo, trabajo de campo, resultados, conclusiones. Meraz Medina Tzintli: Redacción de protocolo, trabajo de campo, redacción de metodología.

Carnitina; Sobrepeso; CrossFit

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Introduction

Being overweight is a major risk factor for the development of various chronic degenerative diseases. A balanced diet and exercise are the cornerstones in the treatment of overweight and obesity,² and within this category, CrossFit has proven to be effective in terms of weight control and weight reduction, given that it is a sport characterised by a physical conditioning system based on functional movements, creativity and a variety of high-intensity, short-duration exercises. However, there is evidence that the use of supplements could provide additional benefits in weight control and weight reduction. Among these supplements is Levocarnitine (L-Carnitine), which is an amino acid derivative and an essential cofactor for fatty acid metabolism, which facilitates the entry of long-chain fatty acids into the mitochondria, thereby releasing substrates for oxidation and subsequent energy production.

Oral L-Carnitine supplementation reduces body weight, waist circumference, hip circumference and insulin resistance in women with polycystic ovary syndrome (PCOS). L-Carnitine supplementation may improve aerobic capacity and exercise tolerance during high-intensity constant work rate exercise testing in patients with mitochondrial myopathy. There is evidence that L-carnitine leads to significant weight loss and a decrease in body mass index (BMI).

Due to the above, the present study proposes to evaluate the effect of L-carnitine as an adjuvant in weight loss in overweight women who practice CrossFit.

Aim of the study

The aim of the study was to evaluate the effect of L-Carnitine on anthropometric measurements in overweight women practising CrossFit as an adjuvant therapy for weight loss.

Materials and methods*Type of study*

A double-blind, randomised, placebo-controlled clinical trial was conducted.

Selection criteria

Women aged 18-40 years who met the following selection criteria were included: diagnosed as overweight according to the World Health Organization definition of BMI 25-29.9 kg/m², practiced CrossFit regularly, had a stable weight for at least 90 days prior to the start of the study and signed the informed consent form.

Patients were excluded if they had smoking, comorbidities such as diabetes mellitus, hypertension, metabolic syndrome, liver disease, kidney disease, human immunodeficiency virus, thyroid disease, known allergy to L-carnitine, pregnancy or were breastfeeding, had undergone any type of weight control treatment six months prior to study entry, and had used any medication and/or supplement known to have an effect on metabolism.

The following criteria were considered grounds for elimination: patients who had less than 80% adherence to the L-Carnitine intervention or CrossFit, who did not follow nutritional recommendations, and who had serious adverse events that resulted in withdrawal from the study. All selected volunteers attended CrossFit on a regular basis, where they were invited to participate in the study. All participants were evaluated by the researchers, a complete medical history and anthropometric measurements were taken.

Study site

The study was conducted in a private gym, Hard CrossFit, under the supervision of the researcher in terms of monitoring anthropometric measurements and patient well-being.

Sample size and randomisation

The sample size was calculated using a formula for clinical trials,⁸ with a confidence level of 95% and a power of 80%. The standard deviation for fat percentage was 2%,⁵ with an expected difference between groups of at least 2.3%, resulting in a total of 10 women per group. For the other components such as BMI and body weight, the sample size calculation was equal or smaller.

Randomisation of the patients was performed by a person outside the research team, so that neither the researcher nor the patient was aware of the assigned treatment to ensure blinding; randomisation was performed using a random number table to assign all patients into two groups in a 1:1 ratio.

Pharmacological intervention

After randomisation, two study groups were formed, each consisting of 10 participants. The first group received L-Carnitine 1.5 g (contained in 5 ml of oral suspension) and diluted in 250 ml of plain water, while the other (control) group took an approved placebo (5 ml of rehydration serum) diluted in 250 ml of plain water, before the start of each CrossFit session, for a period of 8 weeks.

The CrossFit session and intervention period took place Monday through Friday from 8:00 to 9:00 a.m. for all participants; Saturday and Sunday were set as rest days. All patients received nutritional recommendations not to make major dietary modifications and to assess the effect of L-carnitine on CrossFit practice; they were also instructed not to modify their exercise habits. CrossFit sessions were based on the CrossFit Training Level 1 training guide and WODZILLA: The Ultimate WOD compilation to be standardised routines.

Anthropometry, tolerance and adverse effects were assessed at baseline and at the end of the intervention.

Anthropometric assessments

Women were assessed at baseline and at the end of the study from 8:00 a.m. to 10:00 a.m. while fasting. Body weight, fat mass and muscle mass percentages were assessed using the HBR-514C OMRON HEALTHCARE, INC.® (Illinois, USA) tetra-polar scale. Arm circumference, contracted arm circumference and waist circumference were measured with a Lufkin® w606 metal tape measure, manufactured in the USA. Arm circumference was measured with the biceps contracted and flexed at right angles; the measurement was taken at the midpoint between the acromion and the olecranon.

For the circumference of the relaxed arm, the measurement was taken with the arm relaxed at the side of the body, with the palm of the hand facing medially towards the thigh, the tape measure was placed around the arm at the midpoint between the acromion and olecranon, and waist circumference was measured at the midpoint between the highest point of the iliac crest and the lowest rib at the mid-axillary line. BMI was calculated according to the World Health Organisation definition, with the following formula: weight (kg) / height (m²). Figure 1 shows the enrolment process.

Statistical analysis

The Statistical Package for the Social Sciences version 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Quantitative variables are presented as mean \pm standard deviation (SD) and while qualitative variables as frequencies and percentages. Values are presented according to the international system of units. Non-parametric statistical tests were used given the non-normal distribution of the data. The Wilcoxon rank test was applied for intra-group differences, while inter-group differences were assessed with the Mann-Whitney U-test. Fisher's exact X² test was used to assess differences in qualitative variables. Data were considered statistically significant with a P-value of ≤ 0.05 .

Ethical statements

The study was conducted in a private gym where crossfit classes are offered. Data collection and anthropometric measurements were performed under the supervision of the investigator, with the aim of guaranteeing the safety and well-being of the participants in accordance with the General Health Law Regulation on Health Research of the United Mexican States.

The study was approved by the institutional research ethics committee (IRB / 448/2017 on 19 October 2017) and registered in the Clinical Trial (NCT03436277).

Results

A total of 19 overweight women were evaluated (L-Carnitine group n=9 and placebo group n=10), with a mean age of 27.5 ± 5.8 years in the placebo group and 32 ± 3.3 years in the L-Carnitine group ($P=0.073$).

No statistically significant differences in anthropometric measurements were observed between each group before the intervention (Table 1). One volunteer in the L-Carnitine group decided to drop out of the study and therefore withdrew her informed consent.

After the 8-week intervention, statistically significant differences were found in the placebo group in body weight (74.7 ± 11.6 versus 73.6 ± 11.7 kg, $P= 0.040$), BMI (27.8 ± 1.7 versus 27.4 ± 1.9 kg/m², $P= 0.041$), waist circumference (86 ± 6.4 versus 82.3 ± 7.4 cm, $P= 0.005$), body fat percentage (29.8 ± 3.5 versus 27.1 ± 2.4 , $P= 0.003$) and muscle mass (36.2 ± 3.4 versus 38.7 ± 2.3 , $P = 0.003$) (Table 2).

The L-Carnitine group demonstrated significant differences in waist circumference (89.4 ± 6.1 versus 87.1 ± 6.3 cm, $P = 0.018$), body fat percentage (31.5 ± 2.9 versus 29.1 ± 2.7 , $P = 0.008$) and muscle mass (34.7 ± 3.5 versus 37.1 ± 3.3 , $P = 0.008$) (Table 2).

Adherence to treatment was greater than 80% in all participants. Study flow diagram: Figure 1 shows the enrolment process.

Deviations: No deviations were found during the study, everything proceeded according to protocol.

Adverse events: One case of insomnia was reported in one of the patients in the placebo group, which was not considered statistically significant ($P= 1.000$)

Annexes

	Placebo n = 10	L- carnitine n = 10	P
Age	27.5±5.8	32±3.3	0.07
Weight (kg)	74.7±11.6	74±6.6	0.65
Height (m)	1.6±0.1	1.6±0	0.70
BMI (kg/m ²)	27.8±1.7	28.6±1.5	0.52
Arm relaxed (cm)	30.4±2.1	31.5±2.2	0.30
Arm contracted (cm)	31.2±2.1	31.7±2.3	0.70
Waist (cm)	86±6.4	89.9±6.1	0.17
Hip (cm)	107.3±8.8	107.1±4.2	0.94
Body fat (%)	29.8±3.5	31.5±2.9	0.27
Muscle mass (%)	36.2±3.4	34.7±3.5	0.34

BMI: Body Mass Index

Table 1 Baseline clinical characteristics of the study groups

Source: Own elaboration

	Placebo		L-carnitine	
	Basal (n = 10)	Final (n = 10)	Basal (n = 10)	Final (n = 9)
Weight (kg)	74.7±11.6	73.6±11.7*	74±6.6	74.1±7.3
BMI (kg/m ²)	27.8±1.7	27.4±1.9*	28.6±1.5	28.3±1.5
Arm relaxed (cm)	30.4±2.1	29±2**	31.5±2.2	30.5±2.5
Arm contracted (cm)	31.2±2.1	30.6±2.7	31.7±2.3	31.4±1.8
Waist (cm)	86±6.4	82.3±7.4*	89.4±6.1	87.1±6.3*
Hip (cm)	107.3±8.8	105.4±8.1	107.1±4.2	106±3.9
Body fat (%)	29.8±3.5	27.1±2.4**	31.5±2.9	29.1±2.7**
Muscle mass (%)	36.2±3.4	38.7±2.3**	34.7±3.5	37.1±3.3**

* $p < 0.05$, ** $p < 0.01$ between baseline-final measurement of both groups.

BMI: Body Mass Index

Table 2 Baseline-final measurement of both groups

Source: Own elaboration

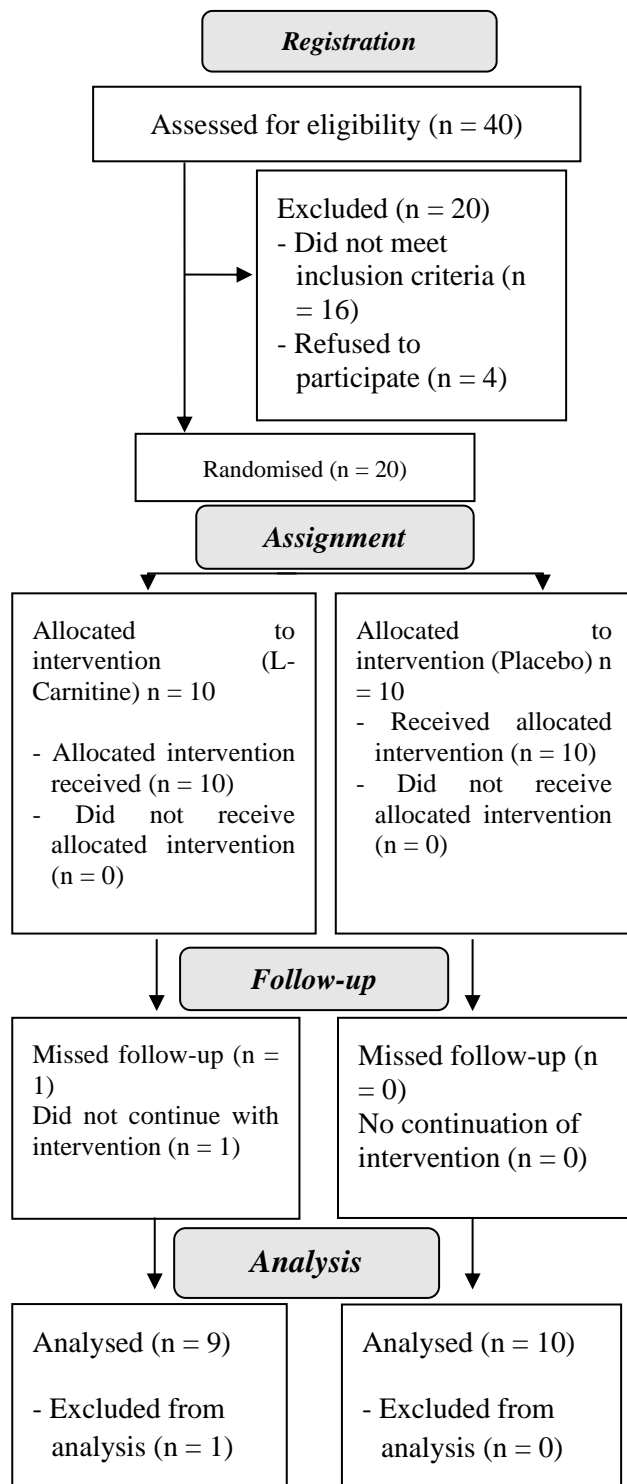


Figure 1 Patient selection flowchart

Source: Own elaboration

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Conclusions

We can conclude that the administration of 1.5 grams of L-Carnitine to overweight adult women practising Cross-fit as an exercise routine over a period of 8 weeks contributed to a decrease in waist circumference and body fat percentage.

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Physical training programs that affect muscle mass in adult women. Systematic review

Programas de entrenamiento físico que afectan la masa muscular en mujeres adultas. Revisión sistemática

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Abstract

Loss of muscle mass and strength is the main factor limiting functionality in activities of daily living. There are transition periods in which women reduce the practice of activities focused on maintaining muscle mass and strength, which affects their functionality. Interventions that promote the development or maintenance of adequate muscle mass and strength in adult women are effective strategies to prevent motor deficits that lead to physical disability. Objectives: to examine the characteristics of physical activity or exercise interventions that have evaluated changes in muscle mass in adult women under 60 years of age. Methodology: A literature search was carried out in the digital databases: PubMed, Cochrane and Redalyc. Experimental studies of physical training programs published between 2016 and 2021 were included, which included women under 60 years of age, who counted the impact on muscle mass among their results. Contribution: it is necessary to know the characteristics of training programs with influence on muscle mass in adult women, in order to support evidence-based practice for the promotion of physical-functional health.

Exercise, Training, Women

Resumen

La pérdida de masa muscular y fuerza es el principal factor que limita la funcionalidad en las actividades de la vida diaria. Existen períodos de transición en los cuáles las mujeres disminuyen la práctica de actividades enfocadas al mantenimiento de la masa muscular y la fuerza, lo cual repercute en su funcionalidad. Las intervenciones que favorecen el desarrollo o mantenimiento de una adecuada masa muscular y fuerza en mujeres adultas son estrategias eficaces para prevenir las deficiencias motrices que conducen a la discapacidad física. Objetivo: examinar las características de las intervenciones de actividad física o ejercicio que han evaluado los cambios en la masa muscular en mujeres adultas menores de 60 años. Métodos: Se realizó una búsqueda de literatura en las bases de datos digitales: PubMed, Cochrane y Redalyc. Se incluyeron estudios experimentales de programas de entrenamiento físico publicados entre 2016 y 2021, que incluyeron a mujeres menores de 60 años, que contaran dentro de sus resultados el impacto sobre la masa muscular. Contribución: es necesario conocer las características de los programas de entrenamiento con influencia sobre la masa muscular en las mujeres adultas, con la finalidad de apoyar la práctica basada en evidencias para la promoción de la salud físico-funcional.

Ejercicio, Entrenamiento, Mujeres

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Introduction

The optimal functioning of the musculoskeletal system is vital for the performance of the activities of daily life and an adequate metabolism. Loss of muscle mass and strength is the main factor that limits functionality in activities of daily living (Pano-Rodríguez et al., 2020; Skelton & Mavroedi, 2018). During the fourth decade of life, women experience various changes in metabolism, body composition, and the functioning of the musculoskeletal system. Abdulnour et al. (2016) point out that the loss of muscle mass and strength in this period is greater in women compared to men of similar ages. A consequence of the loss of muscle strength in the lower limbs is a decrease in balance, which increases the risk of falls in middle-aged women (Anek & Kanungsukasem, 2015).

Reduced functional capacity is known to be one of the main causes of disability, mortality, and other negative health outcomes (Pano-Rodríguez et al., 2020). Lifestyle-related factors such as a protein-deficient diet and physical inactivity affect the quantity and quality of muscle mass (Aretson-Lanz et al., 2019).

Regarding physical inactivity, Barranco-Ruiz et al. (2019) point out that its prevalence is higher in the female population, both in developed and developing countries. In Mexico, according to the National Health and Nutrition Survey (ENSANUT) 2018-2019 (Shamah-Levy et al., 2020) and the Women and Men Survey 2020 of the National Institute of Statistics and Geography [INEGI] (2020), the constant of physical inactivity is observed throughout all the stages of development of this population group, especially from adolescence. Thus, 53.5% of adolescents between 15 and 19 years old are physically inactive, while 65.6% of women older than 18 years do not exercise or practice sports (INEGI, 2019; Shamah-Levy et al., 2020).

Skelton and Mavroedi (2018) report that there are transition periods, such as the beginning of university life, marriage, pregnancy and menopause in which women reduce the practice of activities focused on maintaining muscle mass and strength, which affects its functionality.

Interventions that favor the development or maintenance of adequate muscle mass and strength in adult women are effective strategies to prevent motor deficiencies that lead to physical disability; in sum, women who maintain an adequate level of muscular strength in the lower limbs from early adulthood experience a lesser decline in said conditional ability and have fewer disturbances in balance during middle adulthood (Wu et al., 2017). The quantity of the muscular mass and the quality of this evaluated with respect to the resulting physical condition, are indicators associated with the physical functionality and quality of life.

It is necessary to know the characteristics of training programs with influence on muscle mass in adult women, in order to implement them appropriately in the professional practice of the multidisciplinary health team. The objective of the present systematic review is to examine the characteristics of physical activity or exercise interventions that have evaluated changes in muscle mass in adult women under 60 years of age.

This study presents the sections of methods, results, discussion and conclusions. The methods section describes the literature search process, the inclusion and exclusion criteria of articles, as well as the evaluation of the quality of the literature found. The results section describes the characteristics of the studies included in the systematic review in consideration of the research objectives. In the discussion section, the contrast between the methodologies of the training programs is exposed. In the conclusions, the limitations found in the analyzed studies are identified and areas of opportunity for research are identified.

Methods

A literature search was carried out in the digital databases: PubMed, Cochrane and Redalyc. The keywords used in English were exercise AND muscle mass AND women NOT elderly or older and exercise AND muscle mass AND adult women NOT elderly or older.

The search was carried out from September to December 2021.

Experimental studies of physical training programs were included, which were evaluated as high-quality evidence, published in the period from 2016 to 2021, which included women under 60 years of age, who counted the impact on muscle mass among their results. Articles that could not be found in extensive, exercise programs with a duration of less than six weeks, that did not have the description of the training, in participants with an average age of over 60 years, studies that included physically active men or women were excluded. Fourteen documents were removed, and it was not possible to find the full text.

The quality level evaluation was obtained according to the criteria of the Grading of Recommendation Assessment, Development and Evaluation -GRADE- (Manterola, Asenjo-Lobos & Otzen, T., 2014). Three investigators conducted the electronic database search, title and abstract analysis, and cross-checked the report. The data analysis was carried out in descriptive tables of the training programs considering the indicators of the impact on women.

Results

The systematic literature search yielded a total of 328 articles in the three databases considered: PubMed, Cochrane and Redalyc. Once the selection criteria were reviewed, 14 articles were analyzed in this literature review (Figure 1).

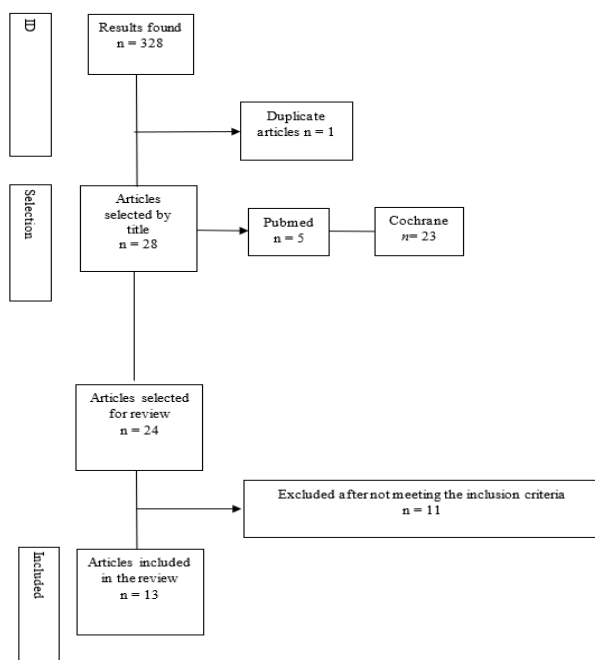


Figure 1 Flowchart for selecting articles for review

Table 1 shows the descriptive characteristics of the articles considered in the review. The characteristics of the experimental groups are distinguished, the design and classification according to the type of program evaluated.

Reference	GE(n)	GC(n)	GE Age (years ± SD)	GC Age (years ± SD)	Design	Type
Barranco-Ruiz et al., 2019	31/GE2: 23	22	38 ± 6.4*	NE	Randomized clinical trial	RA
Cholewa et al., 2018	11	12	20.7 ± 1.4	21.2 ± 1.3	Randomized clinical trial	BC
Daly et al., 2020	122	121	45-65	45-65	Randomized, double-blind, placebo-controlled trial	BC
de Oliveira Júnior et al., 2020	13/GE2: 13	14	58.53 ± 8.03 GE 2= 59.31 ± 8.37	59.80 ± 9.43	Randomized clinical trial by control group	RM
Dutra et al., 2018	15 /GP: 12	15	23.7 ± 1.6	23.6 ± 3.6	Randomized, double-blind, placebo-controlled trial	BC
Franco et al., 2019	14	18	24.3 ± 6.4.8	24.3 ± 6.4.8	Randomized controlled trial	RM
Hernández-Reyes et al., 2019	24/ GE2: 27	29	42.97 ± 10.84	46.10 ± 10.57	Randomized trial	RA
Hettchen et al., 2021	27	27	53.6 ± 2.0	54.5 ± 1.6	Randomized trial	BC
Jendricke et al., 2019	45	45	38.3 ± 8.7	41.6 ± 6.9	Randomized, double-blind, placebo-controlled trial	BC
Miller et al., 2020	30	30	37.9 ± 7.69	35.9 ± 10.3	Randomized clinical trial	BC
Orsatti et al., 2017	16	16	58.8 (8.9)	56.8 (6.6)	Randomized placebo-controlled trial	BC
Said et al., 2017	16	16	30.58 ± 3.8	29.66 ± 4.2	Randomized controlled intervention trial	RA
Zeng et al., 2021	18/ GE3: 18	18	21.13 ± 1.64	22.13 ± 1.96	Randomized clinical trial	RA

Note: GE = experimental group; GC = Control group; GP = placebo group; RA = Aerobic endurance; BC = Multicomponent; RM = Muscle endurance. * NE: They do not specify by group

Table 1 Characteristics of high-quality experimental studies evaluating muscle mass in adult women
Source: check full data in references

Table 2 describes the characteristics of the evaluated programs, the indicators to evaluate muscle mass and the results related to this indicator. For the description of the programs, the explanation of frequency, intensity, time, type, volume and progression was considered in accordance with the recommendations for physical training programs. Table 2 presents the aerobic resistance training programs; the muscular resistance training programs are presented in Table 3 and finally, the bicomponent programs are described in Table 4.

Reference	Experimental group 1 program	Description	Control or experimental group program 2	Description	Muscle mass	Results
Barranco-Ruiz et al., 2019	Zumba classes	F: 3 s / s I: EB (0-10) T: 60 min	Zumba Fitness classes + GE2 muscle resistance exercise: 10,000 steps daily walk + Bodybump muscle resistance training	F: 3 s / s I: EB (0-10) T: 80 min (60 min of Zumba and 20 min of strength exercises)	Anthropometry ISAK = ec. de Lee (Lee et al., 2000)	In both groups, MG decreased (p < .01) and MM increased (G1 p = .05 and G2 p < .01)
Hernández-Reyes et al., 2019	10,000 steps daily walking program (GE1)	F: daily I: 60% T: 60 min V: 10,000 steps METS: 5-8	CG: 5000 steps daily walk + hypocaloric diet Low impact aerobic exercise program + muscular resistance exercises (LIAS)	GE2 F: 4 s / s I: 70% VO2max T: 60 min V: 10,000 steps F: Bodybump: 3 s / s METS: > 8	Electrical bioimpedance (Tanita BWB 300-A)	There was a greater increase in MM in GE2 compared to GE1 (β ₁ = 0.182 vs. β ₂ = 0.008)
Said et al., 2017	High Impact Aerobic Exercise Program (HIA)	F: 4 s / s I: 60% of HR max (week 1-4); 75% of HR max (week 5-14); 86% of HR max (week 15-24) T: 30-60 min	GE2: high intensity interval aerobic exercise (HIIT) program	GC F: daily T: 30 min V: 5000 steps METS: 1-4	Anthropometry + ec. Womersley & Durmin (Womersley & Durmin, 1977)	Significant increase in fat-free mass in the HIA group compared to the HIA group (p < .05)
Zeng et al., 2021	Continuous aerobic exercise program for maximum fat oxidation (FAT max)	F: 3 s / s T: 45 min V: 5 min warming + 40 min exercise	GE3: muscular endurance training program	LIAS F: 4 s / s I: EA: 50-55% of HR max (week 4-14); 60-65% of HR max (week 15-24) I ER: 80-80% of 1 RM T: 50 min EA of exercise and 20 min of ER V ER: 2 sets with 15 s rest between exercises. 3 min rest between sets.	Electrical bioimpedance (INBODY 7.0, model ec-265B, South Korea).	Muscle mass increased in the 3 groups, being higher in the GE3 group (p < .05).

Note: F = frequency; s / s = weekly sessions; I = intensity; EB = Borg scale; T = time; min = minutes; V = volume; P = progression; ISAK = International Society for the Advancement of Kineanthropometry; VO2 max = maximum oxygen consumption; GE2 = experimental group 2; CG = control group; HR max = maximum heart rate; EA = aerobic exercise; ER = resistance exercise; RM = maximum resistance; GE3 = experimental group 3.

Table 2 Description of changes in muscle mass evaluated in aerobic resistance training programs for adult women
Source: check full data in references

Reference	Experimental group 1 program	Description	Control or experimental group program 2	Description	Instrument to evaluate muscle mass	Results
De Oliveira et al., 2020	High Volume Muscle Endurance Training (HRVT) Program	F: 3 s / s I: 30-90% of 1 RM per exercise series V: 6 s from 8-12 r	Low Volume Resistance Program (LRVT)	F: 3 s / s I: 30-90% of 1 RM per exercise series V: 3 s of 8-12 r	DEXA (Lunar iDXA GE, Madison, WI, USA).	Increased FFM in the thigh in the HRVT group (p < .01) compared to the LRVT group
Franco et al., 2019	Low Load Muscle Endurance Training Program (LL)	F: 2 s / s I: 20-90% RM V: 3 s from 30-35 r	High Load Muscle Endurance Training Program (HL)	F: 2 s / s I: 20-90% RM V: 3 s of 8-10 r	DEXA (GE / Lunar iDXA Corp, Madison, WI, USA)	In both groups there was a gain in MM in the legs (p < .05), being greater in the LL group [95% CI: 0.4 kg; 0.2 kg]. HL group [95% CI: 0.2 kg; 0.0 kg]. The GF was similar, no differences were observed between groups

Note: F = Frequency; s / s = weekly sessions; I = intensity; RM = repetition maximum; V = volume; s = series; r = repetitions; MLG = fat free mass; MM = muscle mass; GF = strength gain

Table 3 Description of changes in muscle mass evaluated in muscular resistance training programs for adult women.
Source: check full data in references

Reference	Experimental group 1 program	Description	Control or experimental group program 2	Description	Muscle mass	Results
De Oliveira et al., 2020	High Volume Muscle Endurance Training (HRVT) Program	F: 3 s / s I: 30-90% of 1 RM per exercise series V: 6 s from 8-12 r	Low Volume Resistance Program (LRVT)	F: 3 s / s I: 30-90% of 1 RM per exercise series V: 3 s of 8-12 r	DEXA (Lunar iDXA GE, Madison, WI, USA).	Increased FFM in the thigh in the HRVT group (p < .01) compared to the LRVT group
Franco et al., 2019	Low Load Muscle Endurance Training Program (LL)	F: 2 s / s I: 20-90% RM V: 3 s from 30-35 r	High Load Muscle Endurance Training Program (HL)	F: 2 s / s I: 20-90% RM V: 3 s of 8-10 r	DEXA (GE / Lunar iDXA Corp, Madison, WI, USA)	In both groups there was a gain in MM in the legs (p < .05), being greater in the LL group [95% CI: 0.4 kg; 0.2 kg]. HL group [95% CI: 0.2 kg; 0.0 kg]. The GF was similar, no differences were observed between groups

Note: ERM = muscular endurance training; F = frequency; s / s = weekly sessions; Intensity = intensity; RM = repetition maximum; HR max = maximum heart rate; T = time; min = minutes; V = volume; P = progression; s = series; r = repetitions; Sup = supplementation; MsSs = upper limbs; MsIs = lower limbs; MM = lean mass; EA = aerobic exercise; EB = Borg scale; gr = grams; ml = milliliters; MLG = fat free mass; EG = experimental group; CG = control group

Table 4 Description of bicomponent programs - supplement / diet and muscular resistance training- for adult women included in the review
Source: check full data in references

Discussion

Research on the characteristics of training programs that include the evaluation of changes in muscle mass in adult women is relevant, given the high levels of physical inactivity reported in this population group. Physical inactivity is known to be one of the main contributing factors to muscle wasting.

The studies analyzed suggest that programs focused on muscle resistance training can generate benefits on the amount of muscle mass. Barranco-Ruiz et al., 2019 and Hernández-Reyes et al., 2019 compared the effects of aerobic exercise programs against muscular resistance programs, obtaining a greater increase in muscle mass in the latter. Other authors (Hettchen et al., 2021; Jendricke et al., 2019; Orsatti et al., 2017) evaluated muscular resistance training programs with the addition of nutritional supplements without achieving significant changes in the indicators considered to measure muscle mass. In addition, Miller et al., 2020 report that the combination of an energy-restricted diet and exercise does not produce changes in muscle mass.

Regarding the characteristics of the training programs, it was found that the methodology used to estimate exercise intensity was based on MRI (Cholewa et al., 2018, De Oliveira et al., 2020, Dutra et al., 2018, Franco et al., 2019, Orsatti et al., 2020 and Zeng et al., 2021), the Borg Scale (Daly et al., 2020), maximum HR and MR (Said et al., 2017). In contrast, Hernández-Reyes et al. (2019) estimated energy expenditure based on the METS unit of measurement. Despite the diversity in the methods used, positive changes in muscle mass were observed in all studies.

Different research indicators are considered for the evaluation of muscle mass. Electrical bioimpedance was the most used method (Dutra et al., 2018, Hernández Reyes et al., 2019, Hettchen et al., 2021, Jendricke et al., 2019, Orsatti et al., 2017 and Zeng et al., 2021); Dual energy X-ray absorptiometry (DEXA) considered the gold standard was the second most frequent method used (Daly et al., 2020, De Oliveira et al., 2020, Franco et al., 2019, Martins et al., 2018 and Miller et al., 2020). Two projects used formulas based on anthropometric measurements to estimate body composition (Barranco-Ruiz et al., 2019; Said et al., 2017) and only one report used air displacement plethymography (Cholewa et al., 2018). Verifying the validity and reliability of the indicators according to the study population is important for the comparative analysis of findings. The heterogeneity of indicators responds to the possibilities of each investigation. The evaluation of the quality of the muscle mass in addition to the quantity persists as an area of opportunity in this type of project.

Conclusions

The objective was to examine the characteristics of physical activity or exercise interventions that have evaluated changes in muscle mass in adult women under 60 years of age. Muscle resistance training programs appear to be effective in improving muscle mass in untrained adult women. This highlights the importance of resistance training for maintaining adequate levels of muscle mass during adulthood. Although the quality of the design of this type of project has many strengths, it is still necessary to promote the unification of the indicators used to evaluate muscle mass, consider the quality of muscle mass and the description of training programs.

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The limbic system as a neuroanatomical link between obesity and depression. Neuroimaging findings

El sistema límbico como vínculo neuroanatómico entre obesidad y depresión. Hallazgos en neuroimagen

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Abstract

It has been described high comorbidity between depression, therefore, it becomes interesting to explore the activity of brain structures common to both conditions through neuroimaging studies. Objectives. First - to identify neuroimaging structures concerning to morbid obesity and mayor depression disorder. Second - to analyze the common structures to both conditions. Methodology. Articles were searched in Pubmed and Science databases with the following keywords: MRI (magnetic resonance imaging) obesity, mayor depression disorder, depression and brain activity; with publication dates from 2007 to 2021, no review articles were considered. Contribution. Obesity has a very high comorbidity with depression. In both pathologies the activation of prefrontal cortex, putamen and insula is altered. These neuroanatomical structures are part of the reward system, so the response to hedonic stimuli is mediated by them and altered in obesity and depression.

Obesity, Depression, Neuroimaging

Resumen

Se ha descrito una alta comorbilidad entre obesidad y depresión, por lo que resulta interesante explorar la actividad de las estructuras cerebrales comunes a ambas afecciones a través de estudios de neuroimagen. Objetivos. Primero – Identificar las estructuras de neuroimagen relacionadas con obesidad mórbida y trastorno depresivo mayor. Segundo - Analizar estructuras comunes en ambas condiciones. Metodología. Se buscaron artículos en bases de datos Pubmed y Science con las siguientes palabras clave: MRI (resonancia magnética) obesidad, trastorno depresivo mayor, depresión y actividad cerebral, con fechas de publicación de 2007 a 2021; no se consideraron artículos de revisión. Contribución. La obesidad tiene alta comorbilidad con depresión. En ambas patologías se altera la activación de la corteza prefrontal, el putamen y la ínsula. Estas estructuras neuroanatómicas forman parte del sistema de recompensa, por lo que la respuesta a los estímulos hedónicos está mediada por ellos y alterada en la obesidad y la depresión.

Obesidad, Depresión, Neuroimagen

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Introduction

Obesity has been called the epidemic of the 21st century (Barrera-Cruz, Rodríguez-González, & Molina-Ayala, 2013; Hernández Arteaga, Rosero Galindo, Coral, & Andrés, 2015). It has become one of the most challenging important aspects of public health (Contreras Landgrave et al., 2014) since it affects all dimensions of quality of life of those who suffer from it (Pimenta, Saruwatari, Corrêa, Genaro, & Aguilar-Nascimento, 2010). According to ENSANUT, 2018 in Mexico, 36.1% of the population suffered from obesity; 26.6% of men and 40.1% of women (ENSANUT, 2018). Unfortunately, from 2012 to 2018 the prevalence in Mexican women has increased by 13.5% (Shamah-Levy, 2019).

Obese patients are known to have a high prevalence of depression (Castellini et al., 2008; Scott et al., 2008); in addition to a strong relationship between somatic symptoms, waist circumference and body mass index (BMI) in girls (Aparicio, Canals, Voltas, Hernandez-Martinez, & Arija, 2013) and paranoia in women (Desai, Manley, Desai, & Potenza, 2009).

Obesity is coupled to structural and functional changes in the brain that are remarkably like those observed in depressive disorders, such as region-specific increases in cell density and compromised neural connectivity and excitability (Opel et al., 2021; Rapuano et al., 2020). The main common neurobiological substrate between obesity and depression is the limbic system and its connection with insular cortex. Neuroimaging studies demonstrate structural alterations in obesity, most consistently decreases in cortical grey matter that are strikingly comparable with those observed in individuals with mood disorders (Opel et al., 2021). Obese adults exhibit increased cellularity in the hippocampus and amygdala (Samara et al., 2019), whereas greater cell density in the nucleus accumbens, dorsal striatum, pallidum, hypothalamus, amygdala, and hippocampus correlates positively with waist circumference in adolescents (Rapuano et al., 2020).

Due to the importance and neuroanatomical link of these two public health problems, obesity and depression, it will be analyzed reports of neuroimaging findings. We will begin by describing the limbic system neuroanatomy, later the magnetic resonance imaging as a tool for studying neuroanatomy; obesity; psychopathological comorbidity; functional neuroanatomy of obesity; depression; functional neuroanatomy of depression; and we will finish explaining the neuroanatomical link between obesity and depression.

Limbic system neuroanatomy

The term limbic comes from the Latin *limbo*, meaning edge or border (White et al., 2008). The neuroanatomical structures that conform it, are basically divided into two regions: the cortical region that includes the cingulate gyrus and parahippocampal gyrus, prefrontal and orbitofrontal cortex; and the subcortical regions that comprise the hippocampus, amygdala, septal nucleus, nucleus accumbens, striatum, mammillary bodies, hypothalamus, thalamus, ventral tegmental area, raphe nuclei and locus coeruleus (Laviolette, 2007; Maclean, Flanigan, Flynn, Kim, & Stevens, 1955).

There have been identified four tracts according to their projections and combined effects that imply different areas of the limbic system:

- a) Nigrostriatal pathway: projections from the substantia nigra pars compacta (SNc) to striatum (Taylor, 2001). It has been related to the motor control (Alcaro, Huber, & Panksepp, 2007; Marsden, 2006). In general, the dorsolateral striatum regions (caudate and putamen) are innervated by ventrolateral regions of the substantia nigra; while the ventrolateral regions of the striatum (nucleus accumbens), the globus pallidus and the cerebral cortex are innervated by the dorsal ventral tegmental area (Taylor, 2001). The basal ganglia are composed by: globus pallidus (inner and outer), putamen, caudate nucleus, nucleus accumbens (core and shell), olfactory tubercle and innominate substance. These nuclei and structures adopt different names depending on how they are grouped.

- b) Mesolimbic pathway: includes projections from ventral tegmental area to the nucleus accumbens, striatum and amygdala. This tract is associated with emotions and reward processes (Alcaro et al., 2007; Marsden, 2006).
- c) Mesocortical pathway: projections from the ventral tegmental area to prefrontal cortex and cingulate gyrus. This pathway is associated with reward processes (Afifi, 2005; Alcaro et al., 2007; Marsden, 2006).
- d) Tubero - infundibular pathway: projections that originate in the arcuate nucleus and paraventricular nucleus of the hypothalamus, to the median eminence (Lechan, 1980) and pituitary gland; it is associated with neuroendocrine regulatory functions (Alcaro et al., 2007; Marsden, 2006).

Magnetic Resonance Imaging (MRI) as a tool for neuroanatomy studies

The MRI images are based on the premise that when a mental process occurs, neurons involved require a greater amount of energy obtained from circulating oxygen from the blood of the nearby capillaries (Pauling & Coryell, 1936). The change in the blood-oxygen-level dependent (BOLD) resulting from a change in hemodynamic response, occurs due to cerebral process carried out at the time (Ogawa, Lee, Kay, & Tank, 1990). According to these authors, the generation of images from these processes involves: a) the increased flow of oxygenated blood to the neurons mostly involved in the process, b) the magnetic properties of the molecule that carries oxygen (oxyhemoglobin oxygen and deoxyhemoglobin without oxygen) c) changes in the brain in the above conditions after exposure to an external magnetic field (Armony, 2012; Ogawa et al., 1990; Pauling & Coryell, 1936).

One of the tasks used to study brain activity with this technique involves viewing images. For example, to study obesity, images of food with different calorie content are used, on the understanding that this task will facilitate the activation of brain areas associated with motivation for food (Rothmund et al., 2007).

On the other hand, to determine changes in brain activity in subjects suffering from depression, is quite common use the test "Pictures of Facial Affect" (POFA), test that makes use of facial expressions representing the six basic emotions: joy, anger, fear, sadness, surprise and disgust (Ekman, 1993).

Obesity

Obesity is a condition characterized by alterations in energy balance resulting in excessive body fat accumulation (Mataix Verdú, 2009).

According to the World Health Organization, WHO, 2021, the worldwide obesity has nearly tripled since 1975; in 2016, more than 1.9 billion adults, 18 years and older, were overweight; of these over 650 million were obese; 39% of adults aged 18 years and over were overweight in 2016, and 13% were obese; most of the world's population live in countries where overweight and obesity kills more people than underweight; 39 million children under the age of 5 were overweight or obese in 2020; over 340 million children and adolescents aged 5-19 were overweight or obese in 2016 (WHO, 2021a). Mexico ranks first worldwide overweight women and fourth in women with obesity (OMS, 2015).

Obesity is a condition characterized by alterations in energy balance. The obesity causes have been grouped on environmental and physiological. Within the first kind of causes are implied the type of diet mainly consumed, family eating behavior and physical inactivity; among the latter causes are involved changes in the factors that regulate body energy balance, intake and energy expenditure and excessive body fat accumulation (Baqai, 2015; Skelton, Irby, Grzywacz, & Miller, 2011).

Psychopathological comorbidity

Relationship between obesity and depression in different age groups, has been widely reported (Aparicio et al., 2013; Calderón, 2010; Castellini et al., 2008; Cebolla & Torró, 2011; Desai et al., 2009; Pompa Guajardo, 2011; Rosen, 2010; Scott et al., 2008).

However, regarding results about relationship between body mass index (BMI) and severity of depression are discrepant. While some authors report a positive relationship between BMI and severity of depression (Calderón, 2010; Scott et al., 2008) or BMI and the tendency to personality disorders (Desai et al., 2009); others reports not show such association (Castellini et al., 2008; Isnard, 2010). Another constant in the reviewed studies is the higher prevalence of obesity and depression in females (Desai et al., 2009; Scott et al., 2008), although it should be noted that in some studies more than 50% of the sample were women (Aparicio et al., 2013; Calderón, 2010; Castellini et al., 2008; Isnard, 2010). Among other psychopathological findings in people with obesity it has also being described the presence of low self-esteem (Brauhardt, Rudolph, & Hilbert, 2014; Cebolla & Torró, 2011), eating disorders (Calderón, 2010; Castellini et al., 2008; Isnard, 2010) and somatic symptoms (Aparicio et al., 2013).

It has even been reported relationship between race, obesity and depression (Rosen, 2010). In addition to social phobia, panic disorder and dysthymia in childhood and adolescence; all of them predictors of BMI increased in adulthood (Aparicio et al., 2013).

Functional neuroanatomy of obesity

Ahead are described, neuroimaging findings in obese subjects.

It has been reported, that when visualizing pictures of food with high calorie, obese women aged 21 to 40 years old, showed activation of areas associated with reward processes such as dorsal striatum (set of areas associated with reward anticipation and learning habits), anterior insula, and orbitofrontal cortex (areas involved in processing gustatory information), claustrum and anterior cingulate (emotionally relevant stimuli processing and memory) (Rothmund et al., 2007). These findings have supported the following hypothesis "hyperphagia compensates hypo-dopaminergic state of obesity" (Blum, Thanos, & Gold, 2014). It has been shown that obese subjects have fewer dopamine receptor 2 (D2) and less striatal response to food intake (Stice, Yokum, Burger, Epstein, & Small, 2011).

Other neuroimaging findings that support this hypo-dopaminergic hypothesis of obesity are:

- a) When to performing a test to measure impulsive choice for high calorie food, obese women showed less activation of areas associated with inhibitory control (lower superior frontal gyrus, frontal gyrus, medial frontal gyrus and inferior parietal lobe); which also was proved to be a predictor factor of greater weight gain in 1.3-2.9 years (Kishinevsky et al., 2012). Consistent with the above, it has also been informed that impulsive choices are associated with lower activity superior frontal gyrus, medial frontal gyrus and inferior parietal lobe in obese women (Stoeckel, Murdaugh, Cox, Cook, & Weller, 2013).
- b) Patients between 25 and 40 years of age prone to obesity, presented reduction in activity of insula and inferior prefrontal cortex; coupled with increased activity in medial prefrontal cortex when visualizing images of food after food consumption (Cornier et al., 2013).
- c) Obese children between 10 and 17 years of age, demonstrated increased activity of prefrontal cortex (superior frontal gyrus, medial frontal gyrus, inferior frontal gyrus) and insula during fasting while viewing pictures of food, in addition to increased activity of orbitofrontal cortex after food intake (Bruce et al., 2010).
- d) Investigating the brain activity of adolescents (age 15 + 2.9 years) with high risk of obesity when being rewarded with palatable food in fasting conditions, it has been showed increased activity of caudate, parietal operculum and frontal operculum in response to food (Stice et al., 2011).

- e) When visualizing images of high-calorie food, obese subjects had pre-prandially increased activation of anterior prefrontal cortex; and post-prandially increase in activity insula, dorsolateral prefrontal cortex, lateral orbitofrontal cortex, superior and medial frontal gyrus, anterior and posterior cingulate, entorhinal cortex, caudate, superior frontal gyrus, temporal lobe, temporal supramarginal gyrus, medial temporal gyrus; areas associated with high gustatory cortex, motivation and reward (Dimitropoulos, Tkach, Ho, & Kennedy, 2012).

Depression

Depression is a disorder of mood characterized by the presence of anhedonia (loss of interest and ability to experience pleasure) and feelings of sadness, hopelessness or irritability; it could be accompanied by somatic symptoms (physical aches and pains) functionally preventing the person (APA, 2000).

According to WHO, 2021, depression affects 264 million people worldwide. Each year more than 800,000 people commit suicide, and suicide is the second leading cause of death in the age group 15 to 29 years affecting mainly females. An estimated 76–85% of people suffering from mental disorders in these countries lack access to the treatment they need (WHO, 2021b).

Among the causes of depression it has proposed several hypotheses involving the role of: monoamines (Krishnan & Nestler, 2008), neurotrophins, cytokines (Haase & Brown, 2015) and stress (Brouwer et al., 2005).

Functional neuroanatomy of depression

It will be described here the neuroimaging findings of depression.

Recently it was shown that challenged with a task of facial emotional identification, subjects with major depressive disorder (MDD) between 33 and 56 years had less activity in several regions of the right hemisphere, including: insula, temporal gyrus (medial and inferior) hippocampal gyrus, putamen, occipital gyrus (Brodmann area 18), fusiform gyrus and cerebellum. In addition, subjects with MDD and anxiety, had decreased activity in orbitofrontal cortex (Townsend et al., 2010).

This may imply that the mentioned areas have an important role in the visual processing of negative emotions (Townsend et al., 2010).

However, it has also been reported that when using a test of dysfunctional relationships (Operationalized Psychodynamic Diagnosis OPD) in MDD women and men between 20 and 64 years old, increased activity of the medial frontal gyrus and inferior, pre and post-central rotation, amygdala and basal ganglia was showed; this areas are associated with emotional processing. This shows that the type of task used may lead to a greater or lesser response, in this case, by using individualized statements associated with a particular situation, greater emotional involvement is generated (Kessler et al., 2011).

In women and men between 14 and 17 years old and MDD, it has being shown less cerebral blood flow (hypoperfusion) in frontal gyrus and dorsolateral prefrontal cortex; areas related to psychomotor and executive functions deficit present in patients with depression, they also showed hypoperfusion in the anterior cingulate cortex, amygdala and insula, which is explained as a reflection of reduced motivation or anhedonia. On the other side, cingulate subcallosum, right and upper right insula showed hyperperfusion; the former structure is considered as an interface between cognitive and emotional processing given its connections with frontal, limbic and paralimbic structures. Increased activity of insula was described as a reflection of experiencing negative emotions. Hyperactivity of the mentioned areas in subjects with depression may be associated with hyper-reactivity or inadequate regulation to negative stimuli. This is one of the few studies that reported hyper-perfusion putamen and explain its association with negative emotional stimuli assessment (Ho et al., 2013).

Other studies reflected that functional connectivity between amygdala and prefrontal cortex of men and women with MDD between 19 and 46 years old, during recognition of facial emotional expressions, decreased during fear emotion processing. It is proposed a minor inhibitory control from prefrontal cortex to amygdala, resulting in the delay of the extinction of the negative emotion (Kong et al., 2013).

In addition, it has been reported that women and men between 29.5 and 54.9 years old with MMD, which do not respond to transcranial magnetic stimulation in dorsomedial prefrontal cortex have: a higher level of anhedonia; less functional connectivity between ventral tegmental area and caudate nucleus with left ventromedial prefrontal cortex; and less functional connectivity between left prefrontal cortex (ventromedial prefrontal cortex, cortex, dorsomedial, dorsolateral cortex) and inferior parietal lobe and anterior insula. Therefore, two subtypes of depression were considered: one characterized by hypo-activity of the dorsomedial prefrontal cortex and intact hedonic response; and other characterized by hyper-activity and altered hedonic response (Downar et al., 2014).

Neuroanatomical link between obesity and depression

The main common neurobiological substrate between obesity and depression is the limbic system and its connection with insular cortex. The limbic system is miscellaneous in functions and diverse in areas, however, due to functional magnetic resonance imaging, a technique that allows us to study real-time changes in brain activity based on the need of blood supply, there have identified common active areas committed to both, obesity and depression. Such areas are integrated into basically three circuits: frontal area, basal ganglia and insula; the higher activity has been identified in frontal gyrus, putamen and insula; while the lower activity has being associated to prefrontal cortex, the activity of the specific areas implied in both conditions, regardless the type of study used are shown in Table 1.

Basal Ganglia	Putamen (Stice et al., 2011) Caudate (Dimitropoulos et al., 2012; Kishinevsky et al., 2012; Stice et al., 2011) Ventral striatum (Bruce et al., 2010)	---	Putamen, higher blood flow (Ho et al., 2013)	Putamen, lower blood flow (Townsend et al., 2010)
Insula	Insula (Bruce et al., 2010; Cornier et al., 2013; Rothmund et al., 2007; Stice et al., 2011)	---	Right superior insula (Ho et al., 2013)	Insula (Townsend et al., 2010) Inferior bilateral insula (Ho et al., 2013)

Table 1 Neuroanatomical link between obesity and depression

In this regard, a problem that was found when analyzing the published reports, is that depending on the type of technique used is higher or lower activity of the studied area, hence reports with conflicting results were found. For example, some authors reported decreased blood flow in amygdala and others report increased activity based on the level of oxygenation of the blood (Table 1).

Besides this, the task used in each study and gender to which reference is made, may also influence the results.

Therefore, the specific results that converge both pathologies will be discussed.

Discussion

Neuroimaging studies allow us to know and correlate brain activity in different pathologies to identify symptomatology similarities and make it possible found a common origin; in this review this was attended to obesity and depression.

It has been documented that in obesity exists a hypersensitivity to reward while the opposite has been described for depression, anhedonia. However, in both pathologies it has been found less activity in frontal area, which may result in less inhibitory control of some limbic areas. In obesity, loss of inhibitory control has been associated with low frontal gyrus activation, resulting in impulsive consumption choice of high-calorie food for the immediate reward it represents (Stice et al., 2011).

Structure	Obesity		Depression	
	High	Low	High	Low
Frontal area	Prefrontal cortex (Bruce et al., 2010; Cornier et al., 2013; Dimitropoulos et al., 2012) Superior frontal gyrus (Dimitropoulos et al., 2012) Frontal Operculum (Stice et al., 2011)	Frontal gyrus (Stoeckel et al., 2013) Prefrontal cortex (Kishinevsky et al., 2012)	Frontal gyrus (Kessler et al., 2011)	Poorer connectivity between prefrontal cortex and insula, (Downar et al., 2014) And between Prefrontal cortex – Ventral Tegmental Area/Caudate (Downar et al., 2014)

In depression, lack of inhibitory control of prefrontal cortex to amygdala, favors delaying the extinction of negative emotions (Kong et al., 2013); in addition, the lower activity of frontal area may be related to lower connectivity between prefrontal cortex and ventral tegmental area/caudate and insula (Downar et al., 2014).

However, it has also been reported increased activity in certain regions of the frontal area in obesity and depression; all this in relation to hyper-reactivity of the mesolimbic circuit in obesity (Bruce et al., 2010; Dimitropoulos et al., 2012; Kishinevsky et al., 2012; Stice et al., 2011); and increased of hemodynamic activity in limbic regions and subcortical structures including amygdala in depression (Dougherty & Rauch, 1997; Kessler et al., 2011). In obesity, the orbitofrontal cortex is actively involved in processing reward signals through the association of primary reinforcers (gustatory stimuli, olfactory, somatosensory) by afferents of taste and olfactory areas, amygdala, striatum, hypothalamus and insula (Rolls, 2004). However, in depression it has been reported increase metabolism in orbitofrontal area (Dougherty & Rauch, 1997) and the presence of greater frontal gyrus activity coupled with increased activity in putamen and amygdala; which is related to verbal emotional sensitivity caused by the evocation of personal experiences (Kessler et al., 2011).

As mentioned above, in subjects suffering from depression it has being showed increased putamen activity, a situation that has also being described in obese subjects. In obesity, the increase in activity of this areas is associated with hyper-reactivity of the mesolimbic dopaminergic system (Bruce et al., 2010; Cornier et al., 2013; Dimitropoulos et al., 2012; Rothmund et al., 2007; Stice et al., 2011); however in depression, the study of this area should be studied further because it is mentioned that the increased activity of putamen is linked with the patient's sensitivity to negative emotional situations (Fitzgerald, Laird, Maller, & Daskalakis, 2008), which is important but little investigated.

Regarding to insula, the third area where correlation of activity was found in the studied pathologies, is known to be involved in the integration of autonomic functions: viscerosensory, visceromotor and limbic ones (Gu, Hof, Friston, & Fan, 2013), because in this structure various sensory routes converge (taste, smell, touch) and interaction with other neural networks is present in order to attend or remember (salience network) (Menon & Uddin, 2010; Rolls, 2015). In obesity, it has being reported increased general activity of the insular area, which has also been attributed to hyper-reactivity of the mesolimbic system. In depression, detailed studies based on the insula cytoarchitecture, reported greater blood supply to upper right insula (Ho et al., 2013), an area that has been linked to processing somatosensory information, cognitive control and decision making (Klein, Ullsperger, & Danielmeier, 2013); while reduced blood supply to lower bilateral insula was observed, an area that is related to emotional processing, autonomic interoception and as part of the network of salience (brain network involving anterior insula, anterior cingulate cortex and subcortical structures whose function is to identify internal and external relevant stimuli for driving behavior) (Seeley et al., 2007); which has resulted in recognition deficit of experienced emotions in depressed subjects.

However, more studies are needed to enable the identification of the common causes of greater or lesser activity of these or other shared areas in the studied conditions, either from hemodynamics or neurochemical approaches, and furthermore to determine the cytoarchitecture of the precise area active in each condition, for example to identify the specific active areas of the frontal area. All this in order to prevent development of the disease and identify targets for specific treatment.

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Conclusions

- Obesity has a very high comorbidity with depression.

- In obesity and depression, the activation of prefrontal cortex, putamen and insula is altered.
- The former structures are part of the reward system, so the response to hedonic stimuli is mediated by them and altered in obesity and depression.

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Molar-incisive hypomineralization syndrome and associated factors in three siblings**Síndrome hipomineralización molar-incisivo y factores asociados en tres hermanos**

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Abstract

Introduction: The Incisor-Molar Hypomineralization Syndrome is an enamel dysplasia due to a disorder that affects the maturation of ameloblasts during the secretion, mineralization, maturation, and amelogenic phases, according to the European Academy of Pediatric Dentistry (EAPD). Enamel affected by MIH is characterized by a reduction in the quantity and quality of minerals (reduced Ca and P content) and a reduced hardness and modulus of elasticity (including the transition zone). Furthermore, MIH affected enamel shows increased porosity, increased carbon and carbonate concentrations, and higher protein content than healthy enamel. Enamel crystals affected by MIH are less dense than healthy enamel crystals, with thicker prismatic sheaths and higher inter- and intraprismatic concentrations of organic particles. Bekes K. (2020). **Case presentation:** A 5-year-old female patient came to the clinic due to a contusion on the upper lip with rupture of the maxillary frenulum, when practicing swimming, the periapical X-ray did not find no significant findings, resin was performed compound, in tooth No. 36, two years later the mother reported an opalescence in tooth No. 32, when it erupted, it manifested pain due to changes in temperature (cold), Duraphat was indicated every 3 days, a year after a grade fracture 2 (Andreasen) in the upper right incisor, it was restored with glass ionomer and a liner (Dycal), the following year the lingual face of the lower left first molar was fractured, it was restored with glass ionomer and a bioactive material (vitrebond), instructing on hygienic measures, at 6 months he was seen for an atypical fracture in the distal face of No. 36. **Conclusion:** Carrying out a timely diagnosis of MIH will avoid pulp damage or tooth loss.

Resumen

Introducción: El Síndrome de Hipomineralización Incisivo-Molar es una displasia del esmalte debido a un desorden que afecta a la maduración de ameloblastos durante las fases de secreción, mineralización, maduración, amelogénica, según la Academia Europea de Odontología pediátrica (EAPD). El esmalte afectado por MIH se caracteriza por una reducción en la cantidad y calidad de minerales (contenido reducido de Ca y P) y una dureza y módulo de elasticidad reducidos (incluida la zona de transición). Además, el esmalte afectado por MIH muestra un aumento de la porosidad, un aumento de las concentraciones de carbono y carbonato y un mayor contenido de proteínas que el esmalte sano. Los cristales de esmalte afectados por MIH son menos densos que los de esmalte sano, con vainas prismáticas más gruesas y concentraciones inter e intraprismáticas más elevadas de partículas orgánicas. Bekes K. (2020). **Presentación del caso:** Paciente de sexo femenino de 5 años de edad, acudió a consulta debido a una contusión en el labio superior con ruptura del frenillo maxilar, al practicar natación, en la radiografía periapical no se encontraron sin hallazgos significativos, se le realizó resina compuesta, en el diente No. 36, dos años después la madre refiere una opalescencia en el diente No. 32, al erupcionar manifestó dolor a cambios de temperatura (frio), se indicó el Duraphat cada 3 días, al año acudió por fractura grado 2 (Andreasen) en el incisivo superior derecho, se restauró con ionómero de vidrio y un liner (Dycal), al siguiente año se fracturó la cara lingual del primer molar inferior izquierdo, se restauró con ionómero de vidrio y un material bioactivo (vitrebond), instruyendo sobre medidas higiénicas, a los 6 meses se acudió por una fractura atípica en cara distal del No 36. **Conclusión:** Realizar un diagnóstico oportuno de MIH, evitará un daño pulpar o pérdida del diente.

Hypomineralization, associated factors 3 siblings**Hipomineralización, factores asociados 3 hermanos.**

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Introduction

Incisor-Molar Hypomineralization Syndrome is an enamel dysplasia caused by a disorder that affects the maturation of ameloblasts during the early phase of amelogenic maturation, causing a qualitative enamel defect according to the European Academy of Pediatric Dentistry. (EAPD).

It affects the first permanent molars (one, two, three or four) with demineralization defects of the enamel and opacities in the incisors to different degrees. It is characterized by the alteration of the circumscribed, qualitative and quantitative calcification that is not necessarily symmetric. Without altering the primary dentition, the mineral concentration of the enamel of the affected teeth decreases from the amelodontal limit towards the subsurface zone of the enamel, the opposite situation to that found in normal enamel.

In 2000, Weerheij et al, proposed the name "Incisor-Molar Hypomineralization" to characterize the clinical pictures in which the mineralization of the first permanent and / or incisor molars is affected, with the appearance of white-opaque-yellow-brown spots. that sometimes leads to the progressive disintegration of enamel, differentiating them from other types of calcification disorders, such as hypoplasia and fluorosis and in an attempt to unify a varied terminology "Idiopathic Enamel Hypomineralization", "Hypomineralization of the first permanent molars", Cheese "Idiopathic opacities" Non-Fluorositic Hypomineralization ", appeared in the literature accompanying the same picture. Boxwood, (2011).

Medical and / or economic importance

It is an entity of unknown origin and in families their work and leisure schedules are disrupted due to pain, destruction, impairment of function and aesthetics (quality of life, psychosocial, emotional, aesthetic). They are anxious patients with fear of dental treatment for permanent and temporary teeth. It is important to differentiate types of treatments and which are the best preventive and treatment strategies for each type of tooth with hypomineralization. Children are puzzled because they adequately perform their oral hygiene and do not consume sweets, they do not understand the reason for this pathological entity that occurs in their mouth.

They refuse to chew and brush their teeth due to the great sensitivity that occurs and therefore increases the presence of dental caries in these teeth affected by MIH.

Background

The first documented case of hypomineralization dates from the year 1970, it was not until 2003 that it was accepted as a pathological entity at the Meeting of the European Academy of Pediatric Dentistry in Athens. Also in 1987, the origins of this syndrome as configured at this time, when Koch et al, published the results of a study on the prevalence of hypomineralization defects in permanent teeth, the first allusion to a specific alteration of mineralization in an acute and idiopathic form that affected the quality of the calcification of the first permanent and incisor molars. They did not use the index of developmental defects of the enamel (DDE) previously usual in this type of study and described the defects in terms of color and surface alterations. Cameron, (2018).

This index was established in 1982, to unify the collection of data in epidemiological studies, however it soon became difficult to complete it and successive modifications were presented in 1989 and 1992 to improve its application (MDDE). Alalusua et al, (1996). published a study with data on the prevalence of mineralization defects in permanent first molars, in which they exclude hypoplasia and fluorosis and also present degrees of severity. MIH prevalence is higher in medically compromised children, genetic predisposition is likely.

Etiology and Pathogenesis

The etiology of hypomineralization is multifactorial and involves genetic and environmental factors. Dental development follows a genetic code, but this can be affected by environmental factors, enamel defects are excellent indicators of episodes of stress, adaptation, subsistence and health in childhood. (archaeological studies). Mature enamel is the most mineralized tissue in the body with 95% organic content. Genetic or hereditary factors and also environmental factors. Coelho L. S, (2010).

Prenatal Factors

Episodes of maternal fever, asthma, viral infections in the last month of pregnancy, Prematurity, low birth weight, prolonged labor.

Postnatal Factors

(During the first year of life) high fevers and respiratory problems, otitis, alterations in Calcium-Phosphate metabolism. Exposure to Diagnostics, due to prolonged breastfeeding, environmental pollutants in breast milk, gastrointestinal disturbances, prolonged use of medication, mainly amoxicillin, chickenpox, vitamin D deficiency. Heart problems. Urinary infections. More recently the influence of environmental pollutants or certain antibiotics has been suggested. Srivastava V.K. (2011).

Suggested Treatments

It involves specific clinical problems such as: Sensitivity, from slight to very intense to thermal and mechanical stimuli, even when there is no loss of enamel. Even brushing causes intense pain, and avoiding it leads to an accumulation of bacterial plaque, especially when there is post-eruptive enamel rupture, it favors the appearance of cavities, whose progression is rapid and sometimes masks the defect.

Difficult analgesia occurs due to the presence of pulp inflammation and accumulation of immune cells even in the absence of caries in hypomineralized molars. (Behavioral problems due to not achieving adequate anesthesia, with a simple exploration, when introducing air, water or percussion with the explorer, it is not possible to seal the damaged piece). The rapid progression of caries, local risk factors due to sensitivity, caries occurs, the alteration in mineralization favors its very rapid progression. Srivastava V.K. (2011).

Determining how much tissue to remove is not always easy since the color of the opacity does not reliably indicate the intensity of the damage and often if all the visibly discolored enamel is removed the viability of the restoration is compromised and if required to limit the extension to Sometimes margin placement has to be intuitive. Choose the right material, adhesive materials are preferred because of the atypicality of the resulting cavities.

The working conditions limit the possibility of using adhesive techniques, since they are molars that have not completed their eruption, difficult to access and isolate, even with transiently subgingival margins.

The use of desensitizers, papain gel, is recommended, in case of hypersensitivity, the remineralization of the enamel is indicated through fluorotherapy and the use of toothpastes with CPP-ACP (casein phosphopeptide-amorphous calcium phosphate). In specific cases, rinses with 0.12% chlorhexidine digluconate aqueous solution are indicated for one week. Ionomeric sealants are indicated, which should be replaced by resinous sealants at the end of the eruption. Infiltrating resins (Icon-DMG, Germany) are used in the affected enamel, to improve adhesion and eliminate organic tissue, the use of sodium hypochlorite for 60 seconds at 5.25% is recommended. Use papain gel and follow normal adhesion protocols Srivastava VK (2011).

Presentation of the Case (identity card)

A 4-year-old female patient attends a private office, apparently generally healthy, with a ceo index of 1, oral hygiene index of 1, Class I Anterior Occlusion, Class I Molar, with a history of dental trauma (contusion in upper lip, frenulum rupture), at age 4, when swimming, at oral inspection: anterior diastema low insertion. canine class I right and left. anterior diastema and labial frenulum of low insertion, thick, interferes with aesthetics, causing an upper and lower diastema. When the tooth erupts, no. 41 there was a slight opalescence, with cold pain and chewing with hard food.



Figure 1 - 2 Girl 4 years. Maxillary frenulum frontal view. Upper and lower diasthema



Figure 3-4 Interim restoration with glass ionomer tooth No. 22. Marked mancha: 22, 42 and 43.



Figure 5 Demarcated cervical stain on the buccal side of tooth No. 36



Figure 6 Atypical caries tooth No. 36.

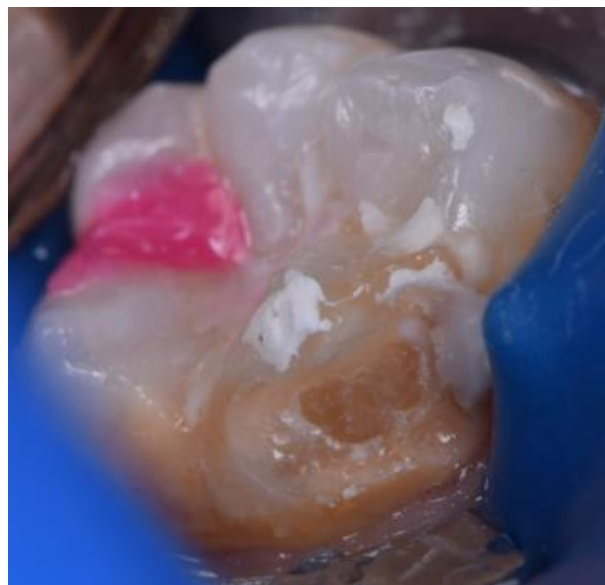


Figure 7 Cavity Preparation

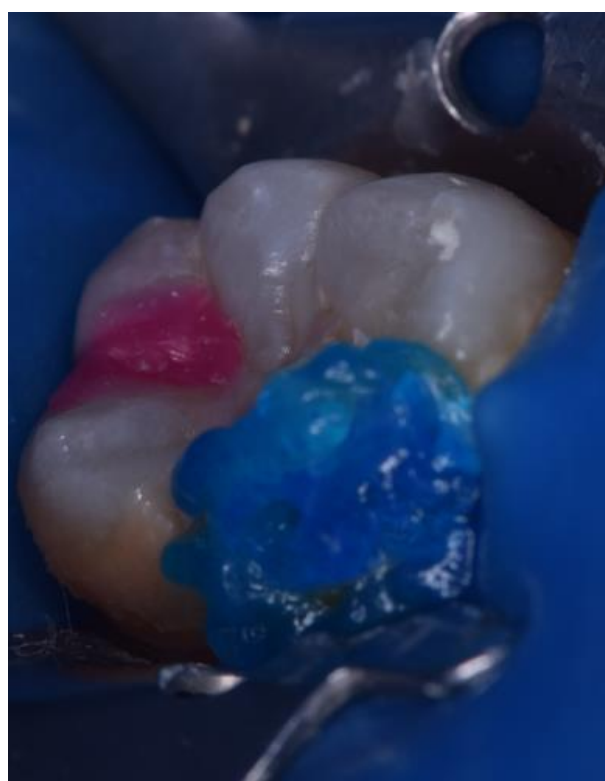


Figure 8 Total acid etching of tooth No. 36 with hypomineralization



Figure 9 Appearance of the cavity after full etching. (White chalk cavity regular edges)



Figure 10 Final Restoration with Molar Composite Resin with Hypomineralization



Figure 11 Panoramic X-ray of the Patient.

Diagnosis

Incisor-Molar hypomineralization following dental organs: upper right lateral incisor, lower right molar No. 36 radiographic diagnosis (orthopantomography). It was classified based on the criteria of Mathu-Muju, year 2006, * A differential diagnosis was made with dental fluorosis, hypoplasia, imperfect amelogenesis, dental caries, nature, color, brightness, shape, limits, structural integrity, location, distribution, family history, amelogenesis phase.

Treatment

The child's cooperation was achieved through effective pain control inferior regional anesthesia, to determine how feasible it would be to place a provisional or permanent restoration to remineralize the enamel, and preserve vitality, taking into account dental age through radiography (proximity of the mineralization fracture), the immaturity of the affected tooth, the occlusal relationships and the collaboration of the parents in the future, among others, were also taken into account. Extraction was ruled out and it was decided to preserve the tooth, it was determined how much tissue should be removed, if the TRAC (Atraumatic Restoration) technique is used before restoring, an ionoseal liner was chosen, and vitrebond, this material is more compatible with the resulting preparation and verified that the necessary working conditions can be achieved (absolute isolation), and a good result was achieved. The sensitivity was previously treated with Durephat. For 4 weeks every 3rd day. From tooth No. 41.

Preventive treatment

Remineralized and desensitized with professional application of fluoride monthly or quarterly depending on the risk and daily use of mouthwashes and products with casein phosphopeptide and amorphous calcium phosphate (Recaldent), which provide calcium and phosphate ions to promote remineralization. However, the usefulness of these procedures in hypomineralized molars must be observed with caution, since it is not a question of replacing a lost mineral but rather a mineral that the molar has never had. Prevention of caries and postuptive ruptures, establishing good daily hygiene as soon as possible, reducing the cariogenic and acidogenic potential of the diet and sealing fissures and retentive areas as soon as possible as long as it can be done effectively.

In order to reduce sensitivity, a soft brush and desensitizing toothpastes were recommended, while a remineralization program was established to achieve correct plaque removal on a daily basis as soon as possible. Occasionally, retentive areas, grooves and some small enamel breaks were covered with a glass ionomer until the molar can be isolated and another protection or restoration procedure can be undertaken with better moisture control conditions.

Discussion

The number of studies on the prevalence of MIH and associated factors has increased in the last ten years. Not all studies use the same criteria or interpret the criteria in the same way. In this case, the age at which this syndrome was detected was 8 years old according to the EAPD, the most conducive age to diagnose this syndrome is between 8 to 10 years, when the first molars and incisors were already erupted and possibly not are still severely affected by caries, previously it was believed that it was only a dysplasia in permanent dentition, but recent studies show that there is a positive correlation of hypomineralization in the second primary molar it is very likely that in permanent dentition it is present, allowing a correct diagnosis of the condition. McDonald and A. (2018).

In this case, the literature consulted is consistent with the association of MIH with the need for treatment and the average number of teeth with experience of caries, decayed teeth, and missing teeth ($P < 0.05$), individuals with MIH have 2.1 to 4.6 more experience caries in permanent dentition than these without MIH. In this case it was compared with the caries experience of his two brothers with 0-1 DMFT.

According to studies, although the majority of affected teeth present a medium degree of MIH, these with moderate and severe degrees have a more complex treatment due to the development of the pulp. Because the enamel exposure is porous with a large interprismatic space which allows the penetration of bacteria into dentin, resulting in chronic inflammation of the pulp and difficulty in obtaining adequate local anesthesia. Thus children may be more anxious about treatment, which will require better behavioral management techniques. The treatment modality available for MIH is broad, including prevention for MIH, restoration and extraction. The decision of which treatment to use is complex and depends above all on the severe factors and severity of the condition, the age of the patient and the social expectations of the family. Bezerra da Silva. (2018).

MIH teeth cause pain to the patient and affect individual life on a daily basis. Which coincides with this reported case.

According to the etiological factors explored in this study, the number of variables analyzed in the prenatal period, fever during pregnancy had a significant association with MIH. These data coincide with the literature. This study shows that fever has a negative effect on amelogenesis.

In this case, other possible factors were presented, such as the period when the birth occurs (According to, before or after the probable date of delivery), cesarean delivery, prolonged labor.

None of these variables was however associated with MIH. The variables analyzed during the postnatal years of life were diarrhea / dehydration, chickenpox, bronchitis, sinusitis, rhinitis, high fever, malnutrition, and use of antibiotics. They were not associated with MIH. Which agrees with the reported studies. Vinay Kumar Srivastava (2011).

Prematurity is also reported as a predisposing factor because children are more susceptible to some alteration during amelogenesis. Nutritional conditions, such as low vitamin D levels, are reported as another factor, as this participates in the amelogenesis process. In this case, it is believed that it is related to these nutritional conditions.

The clinical history was investigated for environmental factors that the mother recalled perinatal factors such as birth, delivery route, gestational age, early detection of the disease at the time of tooth organ No. 32 eruption, contributed to avoiding its progression, decreasing tooth sensitivity and the risk of cavities. The two siblings of the patient presented mild to moderate incisor-molar hypomineralization.

Conclusions

- Take a comprehensive medical history about prenatal history, such as nutrition, anemia, medications, stress, smoking, alcohol, and perinatals such as preterm birth, low birth weight, complications at birth (hypoxia, cesarean), and postnatal: nutrition, breastfeeding prolonged asthma, respiratory infections, childhood illnesses, otitis media, hyperpyrexia, antibiotics, environmental pollutants. In order to relate some risk factor for inciso-molar hypomineralization.

- Rule out if there are any other relatives (siblings-parents) with the presence of HMI. In this case, if two brothers had mild to moderate hypomineralization, the sister only in one tooth No. 26 and the brother demarcated areas No. 13 and 14 in cusps.
- Use bioactive materials to mineralize affected dental tissues such as enamel and dentin. In order to avoid the loss of the dental organ with all the future implications that the loss of a permanent molar may entail.

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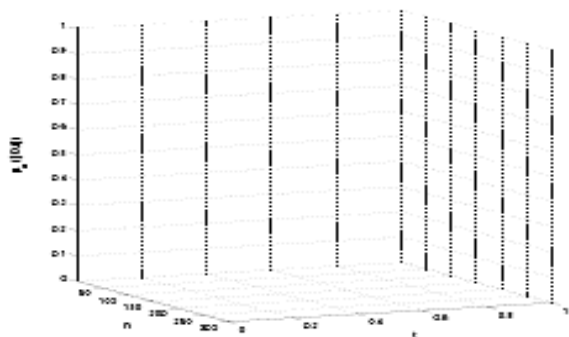
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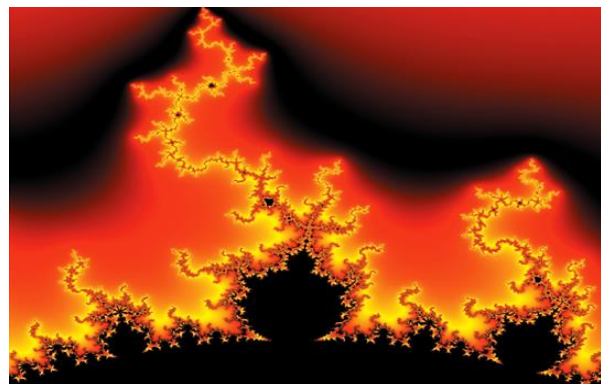


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