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ORIGINAL ARTICLE

Obesity is associated with a higher prevalence of musculoskeletal pain in middle-aged women

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Abstract

Musculoskeletal pain (MSP) has been recently linked with high plasma leptin levels. Our objective was to study if obese women, who have higher leptin levels, could have a higher frequency of MSP. We studied 6079 Latin-American women, 40–59 years old. Their epidemiological data were recorded and the Menopause Rating Scale (MRS), Golberg Anxiety and Depression Scale and Insomnia Scale were applied. MSP was defined as a score $\geq$2 on MRS11. Women with MSP were slightly older, had fewer years of schooling and were more sedentary. They also complained of more severe menopausal symptoms (29.2% versus. 4.4%, $p<0.0001$). Furthermore, they had a higher abdominal perimeter (87.2 ± 12.0 cm versus 84.6 ± 11.6 cm, $p<0.0001$) and a higher prevalence of obesity (23.1% versus 15.2%, $p<0.0001$). Compared to normal weight women, those with low body weight (IMC <18.5) showed a lower risk of MSP (OR 0.71; 95%CI, 0.42–1.17), overweight women had a higher risk (OR 1.64; 95%CI, 1.44–1.87) and obese women the highest risk (OR 2.06; 95%CI, 1.76–2.40). Logistic regression analysis showed that obesity is independently associated to MSP (OR 1.34; 95%CI, 1.16–1.55). We conclude that obesity is one identifiable risk factor for MSP in middle-aged women.

Keywords

Leptin, middle-aged women, menopause, obesity, pain

History

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Introduction

Musculoskeletal pain (MSP) is an important epidemiological problem since it affects a significant percentage of the older population and its treatment is not always efficient. Based on these premises, the International Association for the Study of Pain, established the year 2010 as the Global Year against Musculoskeletal pain [1]. The epidemiological relevance of MSP was highlighted in a multinational study, which found that 63.0% of women aged 40–59 years suffered this condition and in 15.6% pain was severe [2].

It has been recently reported that serum leptin levels are associated with body pain. In a re-analysis of data from 5676 healthy postmenopausal women from the Women's Health Initiative Study, Jounger et al., found a direct relationship between plasma leptin levels and self-reported body pain. The mean serum plasma leptin level was 13.8 ng/mL in women without pain and 23.0 ng/mL in those with severe pain [3].

Considering that the principal source of leptin is the adipose tissue, it is expected that higher body weight would be associated with increased leptin levels [4]. On this regard, it is worth mentioning that the menopausal transition is a condition characterized by accumulation of fat mass, mainly in the abdominal area [5].

The present study hypothesizes that obese middle-aged women, who are expected to have higher leptin levels, could have more MSP in comparison to normal low weight women.

Methods

Study design and participants

This present study represents a new analysis of a previous cross sectional study performed by the *Red Latinoamericana de Investigación en Climaterio* (REDLINC V), originally designed to evaluate menopausal symptoms and associated risk factors in middle aged Latino-American women (40–59 years of age), selected among accompaniers of patients from 20 health centers in different cities with more than 500 000 inhabitants from 11 Latin-American countries. All the characteristics of this study were previously described [6]. Black and indigenous women were excluded as well as women with mental deficiencies or physical illnesses which could interfere with the understanding of the questionnaire. Those who qualified to enter the study were invited to sign an informed consent, according to the Helsinki declaration [7]. The research protocol was reviewed and approved by the

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Ethics Committee of the Foundation PROSAM, Santiago, Chile. The Statistical software EPI-INFO 6.04, Center for the Control and Prevention of Health, Atlanta, GA, was used to calculate the sample size, obtaining a figure of 194 women for each research center, considering that each covered a population of at least 50 000 women [8]. Finally, a minimum of 250 participants were requested in each center.

Instruments and variables

General data

A detailed questionnaire was previously constructed and validated in 50 women before deploying in this study.

Study variables

The following variables were recorded: age (years), personal study level (total schooling years), smoking, alcohol consumption, physical activity, parity, having a stable partner, natural or surgical menopause, anxiety and depressive symptoms, use of hormonal or alternative therapies for menopausal symptoms, oral contraceptive use and past history of chronic diseases. The physical evaluation included body weight (kg), height (cm) abdominal perimeter (cm) and body mass index calculated with the formula Weight (kg)/square of the height (m)

Definitions and instruments

Normal health was defined according to the National Center for Health Statistics as that condition which permits to accomplish all the routine daily activities [9]. A person who did not practice sports or any physical activity apart from work, during at least 30 minutes three times a week was considered sedentary [10,11]. Menopausal stages were defined according to STRAW criteria [12]. Menopausal symptoms were evaluated by the use of the MRS scale (Menopause Rate Scale) [13]. A MRS score greater than 16 was considered severe [14]. Smoking was defined as the consumption of ≥ 5 cigarettes/day [15]. Troublesome drinker was defined as the attainment of 3 or more points in the Brief Scale of Abnormal Drinking (BSAD) [16]. More than 12 years of schooling was considered as an adequate educational level [17]. Other definitions were: low body weight (BMI < 18.5 Kg/m^2), normal weight (BMI 18.5 a 24.9 Kg/m^2), overweight (BMI 25.0 a 29.9 Kg/m^2), and obesity (BMI ≥ 30.0 Kg/m^2); Hypertension was defined as a blood pressure $\geq$140/90 or the use of antihypertensive drugs; diabetes mellitus as a fasting blood glucose >125 mg/dL or the use of antidiabetic drugs. Insomnia was defined as a score ≥ 6 in the Athens Insomnia Scale [18]. Anxiety and depression were evaluated with the Goldberg Anxiety and Depression Scales [19]. Depressive symptoms were considered when more than three positive answers were recorded in the depression sub-scale and anxiety symptoms when more than four positive answers were recorded in the anxiety sub-scale [20].

Statistical analysis

All data were analyzed using the statistical program EPI-INFO (Version 6.04 and version 3.5.1 2008, Center for Control and Prevention of Diseases, Atlanta, GA; OMS, Basel Switzerland). Results are expressed as mean $\pm$ standard deviation, percentages, (confidence intervals, 95%CI) and odds ratios (OR). The Kolmogorov–Smirnov test was used to evaluate normality of the data distribution and the Levene test to evaluate variance homogeneity. The between groups comparison was done with the Student ''*t*'' test (continuous parametric data) or the Mann–Whitney test (non-parametric data). Squared chi test was used to compare percentages between groups.

A logistic regression analysis was used to determine the factors related to MSP. In these analyses, pain was considered a dependent variable. The independent variables considered were: severe menopausal symptoms (MRS >16), presence of vasomotor symptoms (yes: item 1 of the MRS scale >0; no = 0), insomnia (yes/no), obesity (yes/no), depressive symptoms (yes/no), anxiety (yes/no), hypertension (yes/no), diabetes mellitus (yes/no), current smoking (yes/no), troublesome drinker (yes/no), age ($\geq$ 50 years, median; yes/no), postmenopausal status (yes/no), surgical menopause (yes/no), medication use (contraceptives or menopausal hormone therapy (yes/no), having a stable partner (yes/no) and adequate education (>12 years of schooling, yes/no). The inclusion of different variables in the model was done through a stepwise procedure, considering significantly a level of 5%. We also considered the different interactions between the variables found statistically significant in the univariate analysis. The Hosmer–Lemeshow test was used to determine the regression model adequacy. In all analysis, a p value <0.05 was considered statistically significant.

Results

A total of 6598 women were invited to participate and 6079 (92.1%) of them were incorporated in the study. The remainder refused to participate. They were 40–59 years old with a mean of 49.8 years; their educational level was low (10.8 ± 4.9 years). Regarding their life style, 11.3% were smokers, 0.1% were troublesome drinkers and 63.9% were sedentary. Their obgyn history revealed a mean parity of 2.5, 57.6% were postmenopausal, 15.8% had a surgical menopause and 68.9% had a stable partner. Regarding the climacteric symptoms, the mean score in the MRS scale was 8.54, 12.2% had severe symptoms, 55% had vasomotor symptoms, 43.6% had insomnia, 46.5% had depressive symptoms and 59.7% had anxiety. Menopausal hormonal therapy (MHT) or oral contraceptives were used by 13.2 and 11.5%, respectively. Regarding the mean anthropometric characteristics their weight was 66.7 kg (18.5% were obese), height was 159.1 cm, BMI was 24.4 Kg/m^2, abdominal perimeter was 85.5 cm. Furthermore, 22.9% had hypertension and 8.5% had diabetes mellitus.

Comparing the characteristics of women without MSP with those who presented this symptom (Table 1) it is observed that there is no difference in smoking, excessive alcohol consumption or the use of MHT. Women suffering of MSP were slightly older, had less schooling years and were more sedentary. Regarding climacteric symptoms, women with pain were more prone to be postmenopausal (64.5 versus 54.4%, $p < 0.0001$), had higher frequency of severe symptoms (29.2 versus 4.4%, $p < 0.0001$), more insomnia (64.7 versus 34.0%, $p < 0.0001$), higher depressive symptoms (64.1 versus 38.5%, $p < 0.0001$) and more anxiety (78.8 versus 51.0%, $p < 0.0001$). Considering the anthropometric indices, women suffering of pain had greater abdominal perimeter (87.2 ± 12.0 cm versus 84.6 ± 11.6 cm, $p < 0.0001$) and were more obese (23.1 versus 15.2%, $p < 0.0001$). Hypertension was also more frequent in women with pain (28.7 versus 20.2%, $p < 0.0001$).

Table 2 shows that BMI is directly associated with the risk of presenting MSP. Compared with normal weight women, those with low body weight have a non-significant lower risk of MSP (OR 0.71, 95%CI 0.42–1.17); on the contrary, those who are overweight have an OR 1.64 (95%CI 1.44–1.87), which increases in obese women to an OR 2.06 (95%CI, 1.76–2.40)

On Table 3, it is shown the risk factors associated to MSP. We observe that musculoskeletal pain is independently and significantly associated with climacteric symptoms (insomnia, anxiety, vasomotor symptoms and depression), age and obesity.

Table 1. General characteristics of women according to the presence or absence of musculoskeletal pain.

Characteristics	Musculoskeletal pain		
	Absent	Present	$p<$
N° cases (%)	4184 (68.8)	1895 (31.2)	
Age (years)	49.4 ± 5.4	50.7 ± 5.3	0.0001*
Educational level (schooling years)	10.9 ± 4.9	10.5 ± 4.7	0.009†
Smokers (%, 95%CI)	11.7 (10.8–12.8)	10.3 (9.0–11.8)	ns‡
Troublesome drinker (%, 95%CI)	0.2 (0.1–0.4)	0.1 (0.0–0.4)	ns‡
Sedentarism (%, 95%CI)	62.8 (61.3–64.3)	66.3 (64.1–68.5)	0.008‡
Parity (number of children)	2.5 ± 1.5	2.6 ± 1.6	0.0004*
With a stable partner (%, 95%CI)	68.5 (67.0–69.9)	69.7 (67.6–71.8)	ns‡
Postmenopausal (%, 95%CI)	54.5 (53.0–56.0)	64.5 (62.3–66.7)	0.0001‡
Surgical menopause (%, 95%CI)	14.2 (13.2–15.3)	19.2 (17.5–21.1)	0.0001‡
Total MRS score¶	5.7 ± 4.9	11.1 ± 6.0	0.0001†
Severe menopausal symptoms§ (%, 95%CI)	4.4 (3.8–5.1)	29.2 (27.2–31.3)	0.0001‡
Vasomotor symptoms	49.9 (48.4–51.4)	67.7 (65.5–69.8)	0.0001‡
Insomnia (Athens)	34.0 (32.6–35.5)	64.7 (62.5–66.8)	0.0001‡
Depressive symptoms (Goldberg)	38.5 (37.1–40.0)	64.1 (61.8–66.2)	0.0001‡
Anxiety (Goldberg)	51.0 (49.5–52.5)	78.8 (76.9–80.6)	0.0001‡
MHT users (%, 95%CI)	12.8 (11.8–13.8)	14.2 (12.7–15.9)	ns‡
Hormonal contraceptive users (%, 95%CI)	13.4 (12.4–14.5)	7.4 (6.3–8.7)	0.0001‡
Body weight (Kg)	65.9 ± 11.4	68.2 ± 11.8	0.0001†
Stature (cm)	159.4 ± 6.5	158.3 ± 6.9	0.0001†
BMI (Kg/m^2)	26.0 ± 4.4	27.2 ± 4.5	0.0001*
Obesity (% IMC $\geq$ 30 Kg/m^2)	15.9 (14.8–17.0)	23.1 (21.2–25.1)	0.0001‡
Abdominal perimeter (cm)	84.6 ± 11.6	87.2 ± 12.0	0.0001*
Abdominal obesity (%, abdominal perimeter $\geq$88cm)	39.4 (37.9–40.9)	48.3 (46.0–50.6)	0.0001‡
Hypertension (%, 95%CI)	20.2 (19.0–21.5)	28.7(26.7–30.8)	0.0001‡
Diabetes mellitus (%, 95%CI)	7.6 (6.9–8.5)	10.8 (9.4–12.3)	0.0001‡

Data are presented as mean ± standard deviation or as % prevalence (95% confidence interval).
*Student's ''*t*'' test
†Mann–Whitney
‡Chi-square test
¶MRS score, excluding musculoskeletal pain
§MRS score >16 points.

Table 2. Association between musculoskeletal pain with different body weight categories.

BMI (kg/m^2)	No. of women	Women with pain (N, %)*	OR (95%CI)†
<18.5	113	21 (18.6)	0.71 (0.42–1.17)
18.5–24.9	2348	569 (24.2)	1.00
25.0–29.9	2491	858 (34.4)	1.64 (1.44–1.87)
≥30.0	1127	447 (39.7)	2.06 (1.76–2.40)

*Chi-squared for the tendency $p > 0.0001$
†OR in comparison to BMI 18.5–24.9

Table 3. Risk factors associated to musculoskeletal pain. Logistic regression.

Risk factor	OR	95%CI
Insomnia (Athens)	2.22	1.96–2.52
Anxiety symptoms (Goldberg)	2.05	1.77–2.38
Vasomotor symptoms	1.59	1.41–1.79
Depressive symptoms (Goldberg)	1.55	1.36–1.77
Age ≥50 years	1.48	1.32–1.67
Obesity (≥30 kg/m^2)	1.34	1.16–1.55

Among the symptoms, insomnia is remarkable, implying a higher risk of MSP (OR 2.22; 95%CI, 1.96–2.52). In a similar way, older age (OR 1.48; 95%CI 1.96–2.52) and obesity (OR 1.34; 95%CI, 1.16–1.55) were also associated with a higher risk of MSP.

Discussion

In the present study, we have found several factors independently associated to MSP in middle-age women. Among them, obesity, is one of the most important. From our data, we cannot conclude causality since our study had a transversal design. However, if we analyze the Bradford Hill Criteria for causality we can suggest that our results, complemented with other observations, satisfy several causality criteria, making it possible to postulate a potential causal relationship between obesity and the presence of body pain [21].

Statistical association is the main principle of the Bradford Hill criteria without which it is impossible to establish causality; it must exist a relation between the possible causal factor and the effect studied. We found a significant association in our logistic regression models between obesity and MSP.

The dose-response relationship is another important criterion. We must evaluate if the increase of a given variable, called *cause*, also induces an incremental effect in the variable called *effect*. On Table 2, it is shown how as BMI increases we observe a higher prevalence of MSP and that weight increment is associated with a higher and progressive risk of presenting pain. In summary, the relationship between obesity and pain meets this criterion.

The temporal sequence implies that it is necessary to show that the risk factor, obesity in this case, was present before the suspected effect, in our case the pain. A representative sample of the whole Chilean population shows that the mean BMI of increases in women from 24.5 kg/m^2 between 15 and 24 years old to 28.1 in those between 25 and 44 years old and then remains in the same range in older women [22]. On the contrary, non-traumatic MSP prevalence continues to climb progressively with

age until 65 years and beyond, making it possible to suggest that body weight increment starts slightly before or simultaneously with pain. In the same direction, a 20 years' longitudinal study showed that obesity increases the risk of having MSP during the follow-up (OR, 1.54, 95%CI, 1.04–2.28) [23].

To speak of a causal relationship, it is necessary the existence of a biological plausibility which may logically explain how a particular factor may cause a health problem. Although we did not measure leptin levels, it is well known that this hormone is elevated in obese subjects [4,24] and in a recent re-analysis from the Women's Health Initiative Study, Jounger found a direct relationship between plasma leptin levels and self-reported body pain, a result that gives plausibility to our findings [3].

The constancy and consistency criteria refers to the fact that results from a study must remain constant and reproducible for any investigator in any circumstance. A Brazilian study showed that obesity in women is a factor, among several others, associated to a higher risk of presenting MSP (OR, 2.25, 95%CI, 1.27–3.98) [25]. Another study also showed that body weight increment is associated to a higher prevalence of MSP [26]. The same relationship between obesity and musculoskeletal pain has been demonstrated in adolescents; one study which evaluated quality of life in this age group showed that obese people have more body pain and that this condition deteriorates their quality of life [27]. Several other studies have shown the association between obesity and body pain, although they do not suggest a causality relation as we do [28–30].

Another Bradford Hill criterion is the reasoning by analogy. If one risk factor produces a health effect, another factor with similar characteristics should produce the same result, or at least not contradict the concept studied. Our study shows that depression as well as obesity, are associated to a greater risk of MSP and the mechanism involved, according to a previous study [3], would be the increased leptin levels. It has been postulated that this peptide is involved in the genesis of both, depression and obesity [31]. Hence it would not be surprising that leptin was one of the pathogenic factors which may explain the MSP observed in the depressive women in our study.

According to Bradford Hill criterion a causal relationship should be coherent, i.e. starting with a theory, in our case the role of leptin in the genesis of MSP, we can deduce other relationships. As we mentioned before, we have suggested the association between obesity and depression with pain. In both conditions, it seems that leptin is involved showing the coherence between our results and the theoretical postulates [32].

In our study, we do not need to meet the specificity criterion, since in the logistic regression model we used there were several and various risk factors associated with MSP. This condition is a general rule for different diseases since, as it is known that pathogenic factors are frequently multiple and that specific associations do not practically exist. In the same way, our study does not fulfill the criterion that one must have an experimental probe. From an ethical point of view, we cannot induce a group of women to increase their body weight in order to observe if MSP appears.

Among the weaknesses of our study is the fact that it is a transversal type of study, which implies that we can only describe associations but not causal relationships, even though the theoretical postulates analyzed support these relationships. In addition, we focus our analysis on the relationship of pain to obesity, but we must also consider that pain is an equivalent of depression and anxiety (somatization) [33], two psychological symptoms that we find in our study with a higher prevalence than obesity. Logistic regression analysis shows that both anxiety and depression are associated with a greater risk of pain than obesity; however, that statistical analysis indicates that obesity is a factor independent of higher risk of MSP. Finally, our population has a low level of education, a situation that could also influence our results, since it is associated with a higher prevalence of pain [34]. Among our strengths, it is worth highlighting the fact that we included a large number of women and applied validated instruments for the evaluation of symptoms.

In conclusion, our study shows that obesity is a risk factor for musculoskeletal pain in middle-aged women. As a pathogenic factor, the high levels of leptin, characteristic of this condition, could be considered.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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