Lack of Association between Serum Serotonin, Eating Patterns, and Depression in Obese Women

Falta de associação entre serotonina de soro, padrões de alimentação e depressão em mulheres obesas

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ABSTRACT

Objective: The objective of this study was to determine the association between circulating serotonin concentrations, depressive symptoms, and dietary patterns in obese women. **Methods:** We studied 47 patients using the Beck Depression Scale, the 24-hour food registry, biochemical tests, and serum serotonin levels by high-performance liquid chromatography (HPLC). **Results:** The mean age of patients was 41.0 ± 10.0 years and their body mass index (BMI) was 36.9 ± 6.2 kg/m^2. Depression was present in 34.0% of patients. There were no significant differences in serum serotonin concentrations between patients with or without depression (156.4 ± 63.5 vs. 147.7 ± 71.2 ng/mL; p = 0.357). The percentage of patients with abnormal serum serotonin concentrations and the presence of

depression according to the degree of obesity were as follows: Class I 56.5% and 30.4%, Class II 54.5% and 36.5%, Class III 38.5% and 38.5%; *p* = .5 and *p* = .9, respectively). There were no significant correlations between serum serotonin concentrations and eating patterns related to calorie intake (r = 0.09, *p* = 0.5), carbohydrate intake (r = 0.03, *p* = 0.8), fat intake (r = 0.1, *p* = 0.2), or protein intake (r = 0.24, *p* = 0.09). **Conclusion:** We found that in adult women with obesity, there were no relationships between serum serotonin and nutrient intake, the presence of depression, or obesity severity.

Keywords: circulating serotonin, obesity, food consumption, depression, endocrinology.

RESUMO

Objetivo: O objetivo deste estudo era determinar a associação entre as concentrações de serotonina circulante, sintomas depressivos e padrões alimentares em mulheres obesas. Métodos: Estudamos 47 pacientes utilizando a Escala de Depressão Beck, o registro alimentar de 24 horas, testes bioquímicos e níveis de serotonina sérica por cromatografia líquida de alto desempenho (HPLC). Resultados: A idade média dos pacientes foi de 41,0 ± 10,0 anos e seu índice de massa corporal (IMC) foi de 36,9 ± 6,2 kg/m2. A depressão estava presente em 34,0% dos pacientes. Não houve diferenças significativas nas concentrações de serotonina sérica entre pacientes com ou sem depressão (156,4 ± 63,5 vs. 147,7 ± 71,2 ng/mL; p = 0,357). A porcentagem de pacientes com concentrações anormais de serotonina sérica e a presença de depressão de acordo com o grau de obesidade foram as seguintes: Classe I 56,5% e 30,4%, Classe II 54,5% e 36,5%, Classe III 38,5% e 38,5%; p = .5 e p = .9, respectivamente). Não houve correlação significativa entre as concentrações de serotonina sérica e os padrões alimentares relacionados à ingestão de calorias (r = 0,09, p = 0,5), ingestão de carboidratos (r = 0,03, p = 0,8), ingestão de gordura (r = 0,1, p = 0,2), ou ingestão de proteínas (r = 0,24, p = 0,09). Conclusão: Constatamos que em mulheres adultas com obesidade, não havia relação entre serotonina e ingestão de nutrientes, a presença de depressão ou gravidade da obesidade.

Palavras-chave: serotonina circulante, obesidade, consumo de alimentos, depressão, endocrinologia.

1 INTRODUCTION

Serum serotonin is synthesized and secreted mainly (90% to 95%) by enteroendocrine or enterochromaffin cells, and through this neurotransmitter, the intestinal microbiota interacts with the human host. (1,2) This interaction has many effects on inflammation, glucose homeostasis, hepatic gluconeogenesis, mobilization of free liver fatty acids. In addition, it acts on energy conservation by decreasing the thermogenesis of brown adipose tissue and the darkening of white adipose tissue. These effects may contribute to metabolic disorders such as type 2 diabetes and obesity. (2) However, most regulatory mechanisms underlying the metabolism of serotonin remain unknown. (3)

The prevalence of obesity in the population aged 18 years or older is high as it occurs in 11% of men and 15% of women, representing more than half a billion adults, and has shown a sharp increase over the last four decades. (4)

Besides obesity itself, eating disorders and depression may also be associated with abnormal dietary patterns and behavior (5–7). Thus, it is believed that the size of a meal, the quality of the food, and its caloric content are what stimulate receptors on the number of nutrients stored in the gastrointestinal tract. This stimulation occurs through the secretion of intestinal peptides and neuronal signals that act directly on different areas of the brain (the gut-brain axis). (8)

The present study aimed to assess the pattern of food consumption and symptoms of depression and their relationship with circulating serotonin concentrations in an attempt to fill the current gap in the existing literature regarding the clinical use of serum serotonin.

2 STUDY POPULATION AND METHODS

The study was approved by the Ethics in Research Committee of the University of Pernambuco (CAAE: 94304418.6.0000.5207), with all participants signing the informed consent.

We included 47 female patients with obesity aged 19-58 years. The exclusion criteria were as follows: antidepressant and/or anxiolytic use, patients who underwent bariatric surgery, stage 4 chronic renal failure, cancer (except basal cell carcinoma), uncontrolled hypo- or hyperthyroidism, and pregnant and lactating women.

After answering a clinical questionnaire and the Beck Depression Scale or the Beck Depression Inventory (BDI) (9), patients underwent a complete physical examination, including anthropometric measurements.

A twenty-four dietary recall was also performed. The calculation of food consumption through nutritional composition tables of the DietBox® program was used for tabulation, in which the macronutrients carbohydrates (CH), proteins (PTN), and lipids (LIP) were evaluated in grams (g) and percentages (%), and the micronutrients fiber (g) and sodium in milligrams (mg).

After overnight fasting, blood samples were collected for biochemical and serotonin measurements. Fasting plasma glucose, serum creatinine (CR), total cholesterol, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG), very-low-density lipoprotein cholesterol

(VLDL-c), and glycated hemoglobin (HbA1C) were measured using an autoanalyzer (Cobas c311- F.Hoffmann-La Roche, Basel, Switzerland). Serum serotonin was measured by high-performance liquid chromatography (HPLC) (Chromosystems Chemicals, Grafelfing, Germany). The assay sensitivity was 1 ng/mL, reference range 20-150 ng/mL, with the intraaasay and interassay coefficient of variation of <2% and <1.5%, respectively.

3 STATISTICS

All information on the variables collected was entered into an Excel® spreadsheet version 2016, and the program used to perform statistical calculations was IMB SPSS® version 23. The margin of error used in the decision of the statistical tests was 5%.

Data was expressed through absolute and percentage frequencies for categorical variables and measures: means, standard deviations (mean ± SD), and coefficients of variation, medians, and 25th and 75th percentiles for numerical variables.

When comparing categories concerning numerical variables, a Student's t-test with equal variances was used, a Student's t-test with unequal variances or a Mann-Whitney test in the case of two categories. The F test (ANOVA) or Kruskal-Wallis test was used when comparing three or more categories. For variables with significant differences by the F test (ANOVA), Tukey's multiple comparison test was performed.

In the study of the association between two categorical variables, Pearson's Chi-square test or Fisher's exact test was used in cases where the condition for using the Chi-square test was not verified. The association between two numerical variables was assessed by obtaining Spearman's correlation coefficient, and the specific Student's t-test was used for the null correlation test.

Student's t-test and F tests (ANOVA) were used in situations where the normality of the data was verified, whereas the Mann-Whitney, Kruskal-Wallis, and Spearman's correlation tests were used in situations where there was a rejection of normality in at least one category or variable. The verification of normality was performed by the Shapiro-Wilke test, and the equality of variances was through Levene's F test.

4 RESULTS

The patients' mean age was 41.0 ± 10.0 years, and their body mass index (BMI) of 36.9 ± 6.2 kg/m^2 (Table 1). Depression was present in 34.0% of patients, 46.8% had hypertension, 19.1% diabetes, 48.9% dyslipidemia, 48% grade I obesity, 27.7% grade III

obesity, and 23.4% grade II obesity. Fifty-one percent had serum serotonin levels equal to or greater than 150 ng/mL; the majority (51.1%) had PTN intake greater than 90 g, followed by 29.8% less than 70 g, and the remaining 19.1% had 70 to 90 g; 63.8% had CH intake greater than 200 g. The highest percentage (44.7%) corresponded to those who had fiber intake from 10 to 20 g, 38.3% had fiber intake greater than 20 g, and the remaining 17.0% had less than 10 g a day. The presence of depression by BDI was found in 34.0% of patients; BDI scores below 10, 10 to 20, and >20 were 34.0%, 31.9%, and 34.0%, respectively.

There were no significant differences in serum serotonin concentrations between patients with or without depression (156.4 ± 63.5 vs. 147.7 ± 71.2 ng/mL; $p = 0.357$). Likewise, there were no significant differences in eating patterns between those patients with normal or elevated serum serotonin concentrations: calorie intake (2092.70 ± 1036.92 vs. 2214.30 ± 816.39 Kcal; $p = 0.349$), protein intake (106.23 ± 55.40 vs. 92.85 ± 31.52 g; $p = 0.702$), carbohydrate intake (263.20 ± 139.42 vs. 269.61 ± 102.93 g; $p = 0.469$), fat intake (72.87 ± 43.04 vs. 86.83 ± 40.1 g; $p = 0.160$), fiber intake (18.71 ± 8.69 vs. 19.93 ± 11.15 g; $p = 0.958$), sodium intake (2178.16 ± 1026.50 vs. 2547.34 ± 3007.06 mg; $p = 0.61$) [Table 2]. The percentage of patients with abnormal serum serotonin concentrations and the presence of depression according to the degree of obesity were as follows: Class I 56.5% and 30.4%, Class II 54.5% and 36.5%, Class III 38.5% and 38.5%, $p = .5$ and $p = 0.9$, respectively) [Figure 1].

There were no significant correlations between serum serotonin concentrations and eating patterns related to calorie intake ($r = 0.09$, $p = 0.5$), carbohydrate intake ($r = 0.03$, $p = 0.8$), fat intake ($r = 0.1$, $p = 0.2$), or protein intake ($r = 0.24$, $p = 0.09$).

5 DISCUSSION

In the present study, we found no significant differences between the dietary pattern with depression, and depression and the degrees of obesity. Likewise, there was no relationship between depression, food patterns, or the degree of obesity with serum serotonin concentrations.

Predisposing factors to depression involve different genes and serotonin pathways (10), but antidepressant actions on serotonin occur through multiple receptors (11), which suggests that the peripheral amount of serotonin present in individuals is not the primary factor. This suggestion may explain the 34% prevalence of depression in our patients, with most of these individuals presenting elevated serum serotonin levels.

Several factors are related to the difficulties encountered when interpreting serum serotonin levels as outcome predictors. One of these factors may be linked to the serotonin transporter (SERT), which regulates the extracellular availability of serotonin in the intestine and brain. A study conducted in rats showed that, as they age, those with SERT deletion developed metabolic syndrome and had altered structure of the gut microbiome, suggesting a role of the serotonin pathway in maintaining homeostasis of intestinal microbiota. (12) A study demonstrated that germ-free mice had lower levels of plasma serotonin compared with controls, due to a decrease in the enzyme that synthesizes serotonin (tryptophan hydroxylase). (3)

In the present study, there were no differences in the number of calories or nutrient intake according to serum serotonin concentrations. In this regard, one study in mice showed that plasma concentrations of serotonin were significantly lower after a period ingesting a high-fat diet supplemented with whole rye bread when compared with the period after white bread ingestion, suggesting a potential role of the serotonin pathway on whole-grain intake and postprandial insulin responses. (13)

Another factor is related to the amount and availability of tissue serotonin. One study in which brain serotonin metabolism was evaluated showed that the consumption of a high-fat diet decreased anxiety and the expression of 5-hydroxytryptamine (5-HT) in the hypothalamus (14) and enhanced 5-HT in the hippocampus.

Decreases in the expression of adiponectin in adipose tissue are associated with the positive regulation of serotonin receptors in hypertrophic 3T3-L1 adipocytes. (15) In addition, platelet serotonin may be positively associated with plasma soluble leptin receptor concentrations. (16) Likewise, pre-adipocytes, when incubated with serotonin, may not differentiate into brown adipocytes because of reduced catabolism and mitochondrial activity, changing their metabolism to fat accumulation instead of oxidation. (17)

In contrast, one study showed a positive correlation between urinary serotonin and serum adiponectin in individuals with metabolic syndrome. (18) This finding makes the issue of serotonin measurement even more controversial.

In our study, there were no significant differences between the dietary patterns with the presence of depression. However, there was a high intake of processed foods, rich in refined sugars, fried foods, pasta, and sweets, whereas fruits, vegetables, and whole grains were consumed in small amounts, which can contribute to the worsening of depressive symptoms and weight gain. (19–25).

Our study has some limitations, including the cross-sectional design and the population studied (only females from a reference center). On the other hand, the scarcity of human studies addressing serum serotonin concentrations and dietary patterns in patients with both obesity and depression makes our study a valuable contribution at present. Further studies with a larger sample size would be welcomed.

In conclusion, we found that in adult women with obesity, there were no relationships between serum serotonin and nutrient intake, the presence of depression, or obesity severity.

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Authors Contribuitions

Estephanie Cavalcante de Lima: wrote the Project, submitted it to the ethics committee, collected data, wrote the article, submitted the article.

Talitha Mey César Kuroki: collected data, reviewed article, submitted article.

Alice Rego Barros Mendonça: collected data, researched content.

Francisco Alfredo Bandeira e Farias: advisor, reviewed article.

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