

Recent Advances in Clinical Trials

Relevance of Ozonotherapy in Treatment of Patients Affected By Painful and Chronic Inflammatory Processes

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ABSTRACT

In order to draw a trajectory of use and utility of the conventional technique such as ozone therapy going through its historical trajectory and its effectiveness, mainly with regard to the treatment of painful and chronic inflammatory processes. The technique called "ozone therapy" is recommended for the use of ozone gas (5%) and oxygen (95%), being used to treat injuries, especially wounds and having been described in scientific articles as an alternative to suffering pain, inflammation, infection and wound healing. Scientific publications evidence or benefit ozone, it as an important option in the treatment or association of treatment of patients with chronic diseases. Such as example in the other techniques under supervision and validation, there are recommendations from new studies that establish the safety of the use of ozone in health and aesthetic procedures. Therefore, this study aims to present a literature review that includes relevant information on the ozone therapy technique, investing in information about the processes and methods used in various diseases, and especially in the treatment of chronic painful and inflammation. After applying the article selection, selecting 39 articles published in the years 2019 and 2020, describing the use of ozone therapy to treat pain and inflammation in various pathologies. The results that ozone therapy is presented as a therapeutic option, minimally invasive and inexpensive, can be used in conjunction with other therapeutic measures to enhance the beneficial results of resources and can be integrated into Alternative and Complementary Practices.

Keywords

Ozone, Chronic pain, chronic inflammation.

Introduction

Depression is defined as a mood disorder, which presents as main characteristics changes in sleep, appetite, loss of interest in pleasurable activities, depressed mood, among others. With regard to psychiatric disorders, depression is the one that is most associated with weight gain, which accumulated excessively is characterized as obesity [1,2].

Obesity is characterized as a chronic disease, of not yet fully understood etiology, characterized by the accumulation of fat in adipose tissue, being able to negatively affect the metabolic system as a whole, compromising the health of the individual, which may lead individuals to cardiovascular diseases and systemic arterial hypertension, dyslipidemias, obstructive sleep apnea and psychological disorders, among others of complex clinical management [3,4].

The most used method for classifying obesity is body mass index (BMI), which defines obesity as BMI greater than or equal to 30. This definition is subdivided into: Obesity class I - BMI 30 to 34.9; Obesity class II - BMI 35 to 39.9 and Obesity class III - BMI greater than or equal to 40 (also known as severe, extreme or massive obesity) [5].

As a treatment for extreme obesity, in addition to the change of lifestyle, bariatric surgery is indicated, conceptualized as the entire surgical procedure that causes weight reduction from gastric mechanical restriction, resulting in lower food intake and feeling of early satiety. In addition to weight loss, surgery brings many benefits to the individual, such as recovery from associated diseases, and finally, improvement in quality of life [6].

Linartevichi, [2] points out that surgical therapy has successful results, however, it should be carefully evaluated to reduce risks during and after the operation. The criteria include patients with $> \text{BMI}$ of 40 kg/m^2 or $\text{BMI} > 35 \text{ kg}/\text{m}^2$ associated with comorbidities, with at least 05 years of obesity evolution with failure of conventional treatment methods performed by qualified professionals. However, despite the benefits, bariatric surgery causes anatomical and physiological disorganization, evidencing the need for multidisciplinary follow-up throughout the treatment period. This role is mainly played by the nutritionist and psychologist, who together help in the prevention or treatment of mental disorders and change of eating habits, thus avoiding other complications [7]. However, some studies have shown that there is a lack of information from patients about future transformations, the effects of the procedure, the possibility of complications and weight gain, which negatively influences the mental health of the patient [8].

In a cross-sectional study conducted by Teles et al., [9], it was estimated that 9% of the individuals submitted to the procedure

did not have depression and developed after surgery. On the other hand, 5.9% lived with the disorder and remained with him even after surgery. In addition, White et al., [10], demonstrated that 45% of patients submitted to bariatric patients had significant depression. After 12 months postoperatively, 13.3% prevalence and after 24 months, 17.5%, suggesting that the time due after surgery is part of the process of development of depressive disorder [10].

The greatest weight loss in the post-surgery period, according to Ribeiro and collaborators [11], occurs until the first 23 months and then has a tendency to stabilize between 23 and 59 months, and may increase after 60 months. With this, weight stagnation can provoke feelings of dissatisfaction in the patient. In addition, increased skin sagging causes difficulties not expected by these individuals, such as walking problems and hygiene. Thus, a perception arises that the surgery does not provide the desired alterations, which corroborates the development of depressive disorder months after submission to the procedure.

According to Schuelter-Trevisol [12], the surgery promotes a major body change in a short time, but psychological changes do not follow symmetrically the same time, especially the brain that continues to receive information that was sustained by an obese body and that used to need great nutrition. Bariatric surgery, even presenting a relevance in the treatment of severe obesity, presents psychopathological characteristics such as binge eating, which interferes with weight loss and compromises postoperative results [13].

According to the Diagnostic and Statistical Manual of Mental Disorders 5 edition, [14] binge eating is a mental illness, which is characterized by the ingestion of an exaggerated amount of food without any form of control over the amount of what is ingesting. This disease is prevalent in obese candidates for bariatric surgery.

Given the above, it is essential that the patient is aware of the changes that will occur, for psychological preparation and the consequent success in treatment, because many patients are dissatisfied with their body image even after surgery. This fact occurs due to the idealized expectation of the perfect body, which leads to frustration, mainly due to excess skin and weight recovery that happens to approximately 20% of patients in the first two years post-bariatric, due to psychological problems, more commonly, mood changes and binge eating [15].

Finally, the present study aims to obtain data for a future creation of guidelines for obese patients who are subject to bariatric surgery, relating to possible pathologies that may be present in this process of rapid weight loss, especially in the postoperative period.

Research Methodology

This study consists of a systematic review, classified as exploratory and descriptive. The preparation of the research

was bibliographical research in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of smarter (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*). The work carried out is of a qualitative character. The qualitative analysis of the data was performed intuitively and inductively during the survey of the theoretical framework. It is also quantitative by the use of the multi-criteria method. In addition, there is also a numerical experimental study in order to simulate a selection situation of articles based on the observed criteria. From bibliographic research, located in the databases: *US National Library of Medicine* (Pub Med), *Scientific Electronic Library online* (SCIELO), Latin American System of Information in Health Sciences (LILACS), Science Direct (Elsevier) and Embase.

The search in the databases was performed using the terminologies registered in the Descriptors in Health Sciences created by the Virtual Health Library developed from *the Medical Subject Headings of the U.S. National Library of Medicine*, which allows the use of common terminology in Portuguese, English and Spanish. The keywords used in Portuguese for research in the databases were: Depressive disorder, postoperative, bariatric surgery. As a tool to support the decision in the selection and prioritization of articles, a set of criteria were considered as essential to represent the state of the art of the theme object of the research. This method has the following characteristics: (i) rigorous logic allows the acceptance of the method as a decision support tool; (ii) simple to be understood and applied with easy-to-interpret results. After all, the result obtained totaled 10 (ten) articles that contemplated the desired characteristics for the study.

Results

A comprehensive systematic search of the literature yielded a total of 630 articles. Of these studies, 46 articles were adequate for full-text screening and 20 articles were included for data extraction. Of these, 10 studies were excluded due to data overlap. Here, 10 articles were included for systematic review, in addition to a study identified through manual search.

The ten articles reported the prevalence of post-bariatric depression. Data grouping revealed a prevalence rate of 15.3% (95% CI: 15.0-15.5%, $p < 0.001$) [10,16-24].

The impact of depression after bariatric surgery on the mental component was evaluated in 4 studies. In the random effects model ($p < 0.001$, $I^2 = 98\%$), the grouping of effect sizes revealed a statistically significant association between post-bariatric depressive manifestations and mental component. The subgroup analysis among patients with depression revealed that the prevalence of severe depression was 1.9%, the prevalence of moderate depression was 5.1%, while the prevalence of mild and minimal depression was 12.7%. Three studies evaluated the correlation between post-bariatric depressive manifestations and eating disorders. There was a statistically significant positive association (correlation 0.164; 95% CI: 0.079-0.248; $p < 0.001$)

between postoperative depression and eating disorders in the random effects model.

The association between post-bariatric depression and weight loss has been reported in three articles. In the random effects model ($p = 0.048$, $I^2 = 67\%$), there was a statistically significant negative association between postoperative depression and weight loss (correlation -0.135; 95% CI: -0.176 to -0.093; $p < 0.001$). On the other hand, there was no statistically significant association between depression after bariatric surgery and BMI.

Discussion

Bariatric surgery is associated with weight reduction with improved associated comorbidities and increased life expectancy. The physical and mental aspects of patients are improved positively, which means an increase in quality of life, including the return to daily activities, improvement of social relationships, sexual life, self-esteem and body image, reflecting on eating behavior, which is now more appropriate to healthy conditions [25].

However, although in most cases there is a general improvement in mental disorders, there is an individual variation of patients who may present a worsening of their psychological health status [26,27]. Of these reports, there are not many consistent literatures on the impact of surgery on psychological outcomes, and this review is performed for the survey of depressive manifestations after bariatric surgery [28,29].

This systematic review reveals that one in five patients undergoing this surgical procedure has depression within three years after surgery. According to research, the proportion of patients is high, as about 50% of candidates may develop minimal depression. In the short term, follow-up of bariatric surgery may not have a significant impact on weight gain. Instead, initial weight reduction is mainly related to metabolic alterations induced by bariatric surgery, and not to behavioral or psychological factors [30-32].

In most cases, weight reduction occurs during the first year after surgery, where this rapid weight loss is gratifying for patients. However, weight loss tends to stabilize after this period, requiring patients to take more restrictive nutritional and behavioral behaviors in the long term, avoiding additional weight gain [33]. Furthermore, after rapid loss of body weight, the skin tends to become flaccid and aesthetically compromised, which results in disorders due to body image dissatisfaction, which are associated with unrealistic expectations of the image itself, resulting in more depressive disorders, anxiety and stress [34,35].

For this reason, patients at higher risk of developing depression after bariatric surgery should undergo more careful monitoring, including careful and exhaustive investigation of depression and other psychological disorders associated with drug intervention and psychological follow-up [36,37].

In the long run, these measures increase weight reduction by increasing the effectiveness of surgery and improve quality of

life. However, in order to understand these long-term effects, more studies are needed that can cover the trajectory of all depressive manifestations involved in weight regain, under conditions that one is dependent on the other [38,39].

Psychiatric disorders and anxiety exist when obesity contributes to the increased incidence of obesity problems. In genetically predisposed individuals, the consumption of foods rich in fat and sugar, as well as sedentary lifestyle, seems to explain the incidence of metabolic diseases and obesity. However, to understand the risk factors for psychological disorders in these patients, treatment approaches should be changed in favor of integrated and multidisciplinary care [40,41].

In some cases, suboptimal weight loss after bariatric surgery is associated with binge eating, eating disorders, anxiety, and depression. There is a strong association between rebound weight gain and depressive manifestations, also associated with food adaptation, which is considered an important factor in long-term weight gain. However, according to the studies, there are not enough data for a definitive conclusion [17,42,43].

The role of psychiatry professionals is to identify additional problems that may be associated with severe comorbidities in the treatment of patients undergoing bariatric surgery, which will exacerbate neuropsychological changes, and may result in the development of metabolic syndromes and systemic arterial hypertension [44].

There should be the presence of a multidisciplinary team in the care of these patients, with postoperative care involving activities that include counseling, awareness and change of mental, body and eating practices, where the set of therapies that can contribute to significantly improve the results [45,46].

In general, most of the articles available are from research with an observational design, where selection errors may occur, and overly heterogeneous groups, with various population characteristics, unscientific evaluation methods, and differentiated surgical techniques. Therefore, the prevalence of depression in patients after bariatric surgery and underestimated in the long term, where the impact on bariatric surgery on mental health cannot be evaluated in a short follow-up.

Final Considerations

It is concluded that there is a high demand of patients who underwent bariatric surgery with depression in the post-surgery period. These conditions come from emotional unpreparedness for body changes, effects of the procedure, the possibility of complications, weight gain and binge eating, fundamental factors that, if not properly worked, will end up affecting the patient's mental health.

The analysis of the studies shows that there is a concern to seek better results in the treatment of obesity and motivate the

development of more conclusive studies, and it is of paramount importance to carry out educational actions to avoid depression, discussing the most appropriate approach to be adopted to improve the mental health of the target audience.

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