Global Academic Nursing Journal

REVIEW ARTICLE

# Effects of ozone therapy on the treatment of adiposity: an integrative review

*Efectos de la ozonoterapia en el tratamiento de la adiposidad: una revisión integradora*

*Efeitos da ozonioterapia no tratamento de adiposidades: uma revisão integrativa*

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**How to cite this article:**
Dias IF, Jurado SR. Effects of ozone therapy on the treatment of adiposity: an integrative review. Glob Acad Nurs. 2021;2(2):e144. https://dx.doi.org/10.5935/2675-5602.20200144

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**Submission:** 12-08-2021
**Approval:** 03-09-2021

**Abstract**

The aim was to evaluate the effects of ozone therapy in the treatment of adiposity. An integrative review was carried out during the month of October 2020, in the SciELO, LILACS, PubMed and Academic Google databases, with the descriptors: oxygen-ozone therapy, adiposity and the corresponding ones in Portuguese and Spanish. Inclusion criteria: articles available in full, in Portuguese, English and Spanish and containing at least two descriptors in the title or abstract, published between 2000 and 2020. Five scientific articles were selected, one on obesity, two on lipomas and another two on submental fat (double chin). Ozone proved to be an excellent lipolytic agent, reducing adiposity with few applications and without side effects. However, more studies on ozone therapy and adiposity treatment are needed to establish the ideal concentrations and frequency of ozone application to guarantee better results for the treatment of aesthetic dysfunctions, such as localized fat and pathologies, such as lipomas.

**Descriptors:** Ozone; Adipocytes; Lipomas.

**Resumén**

El objetivo fue evaluar los efectos de la ozonoterapia en el tratamiento de la adiposidad. Se realizó una revisión integradora durante el mes de octubre de 2020, en las bases de datos SciELO, LILACS, PubMed y Academic Google, con los descriptores: oxigenoterapia, adiposidad y los correspondientes en portugués y español. Criterios de inclusión: artículos disponibles en su totalidad, en portugués, inglés y español y que contengan al menos dos descriptores en el título o resumen, publicados entre 2000 y 2020. Se seleccionaron cinco artículos científicos, uno sobre obesidad, dos sobre lipomas y otros dos sobre submentonismo. grasa (papada). El ozono demostró ser un excelente agente lipolítico, reduciendo la adiposidad con pocas aplicaciones y sin efectos secundarios. Sin embargo, se necesitan más estudios sobre ozonoterapia y tratamiento de la adiposidad para establecer las concentraciones ideales y la frecuencia de aplicación del ozono con el fin de garantizar mejores resultados en el tratamiento de disfunciones estéticas, como la grasa localizada y patologías, como los lipomas.

**Descriptores:** Ozono; Asipocitos; Lipoma.

**Resumo**

Objetivou-se avaliar os efeitos da ozonioterapia no tratamento de adiposidades. Realizou-se uma revisão integrativa, durante o mês de outubro de 2020, nas bases de dados SciELO, LILACS, PubMed e Google Acadêmico, com os descritores: *oxygen-ozone therapy, adiposity* e os correspondentes em português e espanhol. Critérios de inclusão: artigos disponíveis na íntegra, nos idiomas português, inglês e espanhol e que continham pelo menos dois descritores no título ou resumo, publicados entre 2000 a 2020. Foram selecionados cinco artigos científicos, um sobre obesidade, dois que versavam sobre lipomas e outros dois sobre gordura submentoniana (papada). O ozônio mostrou-se um ótimo agente lipolítico, reduzindo as adiposidades com poucas aplicações e sem efeitos colaterais. No entanto, mais estudos sobre ozonioterapia e tratamento de adiposidades são necessários para o estabelecimento das concentrações ideias e frequência de aplicação do ozônio a fim de garantir melhores resultados para o tratamento de disfunções estéticas, como gordura localizada e patologias, como lipomas.

**Descritores:** Ozônio; Célula Adiposa; Lipoma.

## Introduction

Fat accumulation (adiposity) is related to overweight and obesity. Obesity is a risk factor for several diseases, including diabetes, cancer and cardiovascular problems[1].

Adiposities are in different regions of the body, such as the submental region, pre-axillary region, abdomen, back, flanks, hips, arms, thighs and negatively alter the patient's self-esteem. Small esthetic changes, such as a reduction in localized fat, have the potential to establish a better relationship between the individual and self-image and thus also improve mental health[2].

The accumulation of adipose tissue cells (adipocytes) surrounded by a fibrous capsule and located in the subcutaneous tissue, muscles, nerves, bones, internal organs or in the abdominal cavity comprises a pathological condition called lipoma and is not associated with obesity[3]. The etiology of lipoma is still unknown and controversial[4].

Localized adiposities and possibly lipomas are associated with oxidative stress, inflammatory processes, and excessive release of reactive oxygen species (ROS)[5,6]. Therefore, the body needs a detoxifying and antioxidant system to combat oxidative stress. The transcription factor Nrf2, when properly activated, can restore redox homeostasis and improve human health[7,8].

Activation of Nrf2 by several different mechanisms (caloric restriction, ozone therapy, hyperbaric oxygen, physical exercise) can be ways to improve health[7]. Thus, the use of ozone therapy as an alternative and adjuvant therapy needs to be better studied in the case of pathologies and aesthetic dysfunctions involving adiposity.

Currently, ozone therapy (O2-O3) is considered a minimally invasive, safe, and effective treatment method, with applications in different concentrations and locations of the body, in the form of gas, water and/or oil[9] and very useful for reducing adiposity located.

Since the discovery of ozone by the German chemist Christian Friedrich Schönbein, in 1840, medical use has increased in different parts of the world and there has been greater interest by health professionals in knowing how it works and what its benefits are[10].

Reports of its use are already in the First World War, when medical resources were few and ozone was used as an alternative to treat post-traumatic wounds and gas gangrene, due to its antibacterial, anti-inflammatory, hemodynamic and analgesic functions[11].

In Brazil, ozone therapy is considered an integrative complementary treatment by Ordinance No. 702 of March 21, 2018[12] and is offered by the Unified Health System (SUS).

Despite the Ministry of Health's recognition of the efficacy and safety of ozone therapy in the treatment of various pathologies, this integrative practice has not received the approval of the Federal Council of Medicine (CFM) in the country. However, the Federal Council of Nursing (COFEN) regulated ozone therapy as a practice of nurses in Brazil through Normative Opinion No. 01, of February 20, 2020[13].

Among the therapeutic effects of ozone include antioxidant action against free radicals[14]; increased flexibility of erythrocytes, facilitating their passage through blood vessels and ensuring greater tissue oxygen supply due to the increase in 2,3-diphosphoglycerate (responsible for transferring hemoglobin O2 to tissues); reduced platelet aggregation; analgesic effect; anti-inflammatory; bactericide, fungicide and viricide[6, 15-17].

Medicinal ozone also has actions on metabolism, promoting lipolysis and breaking down unsaturated fatty acids into water-soluble compounds; participation in protein metabolism due to its affinity with sulfhydryl groups, thus reacting with essential amino acids, such as methionine and tryptophan or with cysteine, containing sulfur; increased glycolysis, which increases the availability of ATP in cells and therefore tissues, especially nerves[15,18].

Therefore, the aim of this study was to verify the existing scientific evidence of ozone therapy in the treatment of localized fat and lipomas and to answer the guiding question: What are the effects of ozone therapy in the treatment of adiposity?

## Metodologia

This is an integrative literature review, in which the scientific papers used in the research were collected, via online, in the electronic databases Latin American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library Online (SciELO), PubMed and Google Scholar. The survey of publications was carried out using the following descriptors, in English, oxygen-ozone therapy, adiposity, and the corresponding ones in Portuguese and Spanish.

The research followed the inclusion criteria a) scientific articles; b) be available in full text (original type, review, experience report, case study, observational descriptive study) free of charge; c) that contained at least two descriptors in the title or abstract; d) studies that addressed the specific theme; e) studies available in English, Spanish and Portuguese; f) time frame from 2010 to 2020.

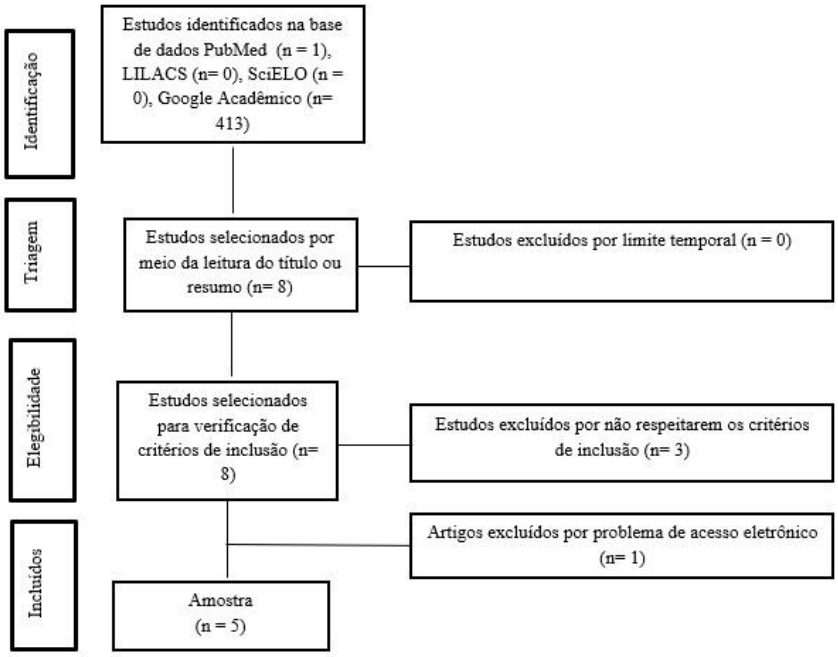
The choice of the initial year of the time frame is due to the increase in publications on the clinical applications of ozone therapy.

Works that did not meet the central theme were excluded; dissertations, theses, and studies in duplicates in more than one database.

For data collection and systematic analysis of publications, an instrument was used, which consisted of publication identification data (year, article title, authors), type of study and main results.

Data collection took place in October 2020, in an independent double-blind fashion.

**Figure 1.** Flowchart of this integrative review. Três Lagoas, MS, Brazil, 2020




## Results and Discussion

In the ten-year period (2010 to 2020), 414 articles were identified in the studied databases, however, after analysis and inclusion criteria, 5 works were selected in the study (Figure 1), which are listed in Chart 1.

**Chart 1.** Selected works from PubMed and Academic Google databases on ozone therapy in the treatment of adiposity. Três Lagoas, MS, Brazil, 2010-2020

| Year | Authors | Type of study | Type of pathology | Sample | Treatment | Results |
|---|---|---|---|---|---|---|
| 2011 | Ashem and Nagib[19] | Randomized | Grade II obesity | 30 patients aged 25 to 45 years, with grade II obesity of both sexes and with a Body Mass Index (BMI) of 30-40. They were randomly divided into two groups: Group 1: fifteen patients received ozone therapy with a low-calorie diet. Group 2: fifteen patients received only low-calorie diet | Each patient in group 1 received ozone therapy in the form of rectal insufflations with ozone concentration of 20 µg/mL, increased gradually up to 40 µg/ml. The volume ranged from 150-300 ml. The procedure was performed twice a week for 6 months | In both groups there was a significant decrease in BMI and waist circumference. However, the greatest reductions were denoted in the ozone group with a low-calorie diet, with a BMI of 39.53 to 30.67 kg/m2 and waist circumference of 119.47 to 100.20 cm |
| 2018 | Cardoso *et al.*[18] | Clinical | Painful lipoma | 20 patients, 16 women and 4 men, aged 30 to 80 years | 10 mL were applied per point (concentration of 4 µg/mL). 10 applications were performed per patient, twice a week | Reduction of approximately 4 cm of lipoma in each patient. All had a reduction in the score on the visual analogue pain scale (from 7 to 1 point), in addition, there was an improvement in motor skill in all patients |
| 2019 | Kara and Kara[25] | Clinical | Painful lipoma on the right forearm and non-painful lipomas on the left forearm and abdominal region | 31-year-old female with a family history of multiple lipomas | Local application of 10g (10 mL) of ozone in the lipoma of the right forearm. After a week, another application of 5g (5 mL) of O3 | Right forearm lipoma reduced from 3.05 x 0.72 cm (cross-sectional area: 1.63 cm2) to 1.09 by 0.63 cm (cross-sectional area: 0.61 cm2) in the first application. Furthermore, the pain decreases immediately after ozone therapy |

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|---|---|---|---|---|---|---|
| 2019 | Lopes, Matrone, Lopes[24] | Clinical | Submental fat (jowl) | 17 women, age group 20 to 55 years old | 3 mL of gas were applied (concentration of 5 µg/mL) at each point, once a week, totaling three applications, in three different points following a triangular shape of the double chin anatomy | Significant reduction in adipometry (from 38.77 to 21.53 mm) and pachymetry (from 97.41 to 71.93 mm) in the third week when compared to the beginning of treatment |
| 2020 | Varão[5] | Literature review | Submental fat (jowl) | Did not mention the number of articles found in the bibliographic review | 1 to 8 µg /mL of O3 in 12 local applications, twice a week and 250 mL of 0.9% saline solution with 3 to 5 µg /mL of O3 twice a week, totaling 6 systemic applications | The literature review work demonstrated that ozone therapy is better than liposuction or other aesthetic procedures in reducing double chin adiposity, with fewer side effects and combating the oxidative and inflammatory stress of adiposity |

A good weight loss program with a reduction in body weight, body mass index (BMI) and waist circumference should combine a low-calorie diet, physical exercise, and aesthetic treatments. In general, a caloric deficit of about 7,700 kcal leads to the loss of about one kilogram of fat[19].

It is known that a low-calorie diet provides a loss of 1.5 kg in one week, with a significant reduction in blood pressure levels, a 20 to 25% decrease in serum cholesterol and a considerable reduction in glucose levels in diabetics[20].

In the study of Ashem and Nagib[19], fifteen patients undergoing a low-calorie diet and ozone therapy in the form of rectal insufflation had a significant reduction in BMI (from 39.53 to 30.67 kg/m2) and waist circumference (from 119.47 to 100.20 cm). The authors justified that ozone promoted lipolysis, decreased insulin resistance, accelerated glycolysis, and increased metabolic activation parameters.

In relation to weight loss and reduction of localized fat, other factors should also be considered, such as regular physical activity and the maintenance of a balanced and healthy diet[21].

It is important to emphasize that one of the causes of excessive food consumption is the widespread use of oral antibiotics. Antibiotics destroy target bacteria, but they also kill those in the intestinal flora, which are necessary for healthy digestion. As a result, the feeling of hunger comes more often and lasts longer. Thus, the body tries to compensate for ineffective digestion, increasing the amount of food eaten and therefore leading to overweight and obesity[15].

When the physiological flora is balanced and in symbiosis with the body, it is beneficial for both, and is referred to as eubiosis. When, for various reasons, there is a functional change in the colonic mucosa and modification of the bacterial flora that resides in the intestine, we have dysbiosis[22].

The main symptoms of dysbiosis are poor digestion, bloating, constipation alternating with fecal dysentery, mood swings, sleep disturbances, vaginal thrush, dysmenorrhea, asthenia, halitosis, headaches and allergies[23].

A survey of 34 patients with intestinal dysbiosis who received three 125 ml glasses of ozonized water and three rectal ozone insufflations (40µg/mL concentration), totaling 250 ml per session, three times a week, for 45 days, showed a decrease of halitosis, gastralgia, asthenia, bloating and diarrhea episodes[15].

Localized adiposity can be avoided in most cases with an adequate diet and healthy lifestyle, but the study by Ashem and Nagib[19] pointed out ozone therapy as an adjuvant treatment for weight loss and localized fat reduction.

Two studies demonstrated the effects of ozone therapy in the treatment of submental adiposity[5,24]. The accumulation of fat in the submental region represents a significant aesthetic disadvantage, causing a double chin and implies a serious health problem, as it is associated with sleep apnea, oxidative stress and even death from cerebral hypoxia and respiratory failure[5,24].

Many clinical studies are needed to establish a treatment protocol that is effective for the volumetric reduction of adipose tissue with ozone therapy in the submental region, as the ozone concentration, route of administration and frequency of application differ in the literature studied. Varão described local and systemic applications of ozone, the first at a concentration of 1 to 8 µg/mL twice a week, totaling 12 applications, and systemic, with 250 mL of 0.9% saline solution with 3 to 5 µg/ mL of O3 twice a week, totaling 6 applications[24].

Although randomized studies of ozone therapy in the treatment of lipomas are lacking, a survey of 20 patients who had painful lipomas showed that oxygen-ozone injections reduced lipoma size and pain intensity by an average of 4 centimeters (mean visual analogue scale score decreased from 7 to 1) in 10 sessions[18].

Another study showed a reduction of one third in the size of the painful lipoma on the right forearm in a 31-year-old patient, who had other lipomas on the left forearm and abdominal region. The cross-sectional area of the lipoma was reduced from 1.63 cm2 to 0.61 cm2 with just one application of 10 g (10mL) of ozone[25].

Therefore, there is no doubt that ozone acts efficiently as a lipolytic agent because this gas dissolves in interstitial water and lipids are its preferred substrates,

being broken down into lipoperoxides, hydroperoxides and low molecular weight lipid oxidation products[26].

Ozone therapy is scientifically approved and is a highly effective treatment for lipodystrophy[6]. This effectiveness is achieved because oxygen-ozone exerts its action through three main mechanisms: i) breaking down long fatty acids into short chains and, therefore, hydrophilic; facilitating the transport of these by bodily fluids and allowing their elimination by the body; (ii) facilitates the removal of stagnant interstitial fluids (edema); (iii) oxygen-ozone binds to the membrane of red blood cells, delivering more oxygen to tissues and, therefore, activating local metabolism and improving venous and lymphatic circulation[18].

Paradoxically, ozone at low concentrations (5 to 10 µg O3/mL) in adipose tissue stroma-derived adult stem cells (hADAS) in vitro induced adipogenesis, even in the absence of adipocyte factors[27].

hADAS cells can differentiate in vitro into meso, ecto, and endodermal cell lines and can be reprogrammed into pluripotent stem cells more efficiently than other cell types. These cells are therefore considered a powerful tool in regenerative medicine and tissue engineering[28]. However, higher ozone concentrations (20 µg/mL) has been shown to cause destruction of stem cells by increased oxidative stress[27].

Therefore, there is significant evidence of the use of ozone therapy as an adjuvant therapy in the treatment of lipomas and localized adiposities. For the nurse, it is necessary to have technical competence in the administration of this gas and as this is a new growing field as a therapeutic technique, nursing professionals will be confronted daily with scientific advances in ozone therapy, with the same in-depth studies and constant improvements being required.

## Conclusion

Adequate nutrition and regular physical exercise increase the chance of positive results in relation to ozone therapy for the treatment of localized adiposity. In the case of lipomas, ozone therapy reduced pain and reduced size with few applications.

In this sense, ozone therapy proved to be effective in the treatment of localized fat and lipomas. However, more clinical studies with large samples are needed to establish protocols, especially with concentrations and frequency of ozone application, as well as longer-term follow-up of patients to verify the effectiveness of the treatment in the long term.

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