REVIEW ARTICLE
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Hyperbaric oxygen therapy for complications of breast cancer surgery

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ABSTRACT

In 2020, there were approximately 2.3 million new cases of breast cancer worldwide. Breast-conserving surgery followed by adjuvant radiotherapy has replaced radical and modified radical mastectomy as the standard treatment for patients with early-stage breast cancer, with equivalent overall survival and disease-free survival rates. Oncoplastic techniques consist in removing the tumor from the breast and applying plastic surgery techniques for breast reconstruction. The use of oncoplastic techniques may increase the number of women who experience postoperative complications or who are recalled for biopsy. Complication rates of around 16% can be considered acceptable, with the most common immediate complications being delayed wound healing, fat necrosis, and infection, while late complications being fibrosis and breast asymmetry. The use of hyperbaric oxygen therapy (HBOT) appears as an alternative for the treatment of these conditions. The Undersea and Hyperbaric Medical Society recognizes 14 valid medical indications for HBOT. Among these, those that stand out with interest in mastology are: chronic wounds; compromised flaps and grafts; radiotoxicity and soft tissue infections. Although most of the evidence is the result of observational studies or is extrapolated from the use of HBOT in other areas, its use may contribute to better outcomes in patients undergoing surgical treatment for breast cancer.

KEYWORDS: hyperbaric oxygenation; mastectomy; breast neoplasms; mammaplasty.

INTRODUCTION

In 2020, there were approximately 2.3 million new cases of breast cancer worldwide, equivalent to an estimated risk of 47.80 cases per 100,000 women. In the same period, in Brazil, there were 17,825 deaths from female breast cancer, corresponding to a risk of 16.47 deaths per 100,000 women[1]. Breast-conserving surgery techniques followed by adjuvant radiotherapy have replaced radical and modified radical mastectomy techniques as standard treatment in patients with early-stage breast cancer, with equivalent overall survival and disease-free survival rates[2]. Oncoplastic techniques consist of removing the tumor from the breast and applying plastic surgery techniques to reconstruct the breast. When comparing the use of oncoplasty with traditional breast-conserving surgery techniques, no significant differences were observed in overall and disease-free survival[3].

The use of oncoplastic techniques may contribute to reducing the number of surgical approaches required for oncologic resection and result in greater patient satisfaction and better assessment by the surgeon of the appearance of the breast after the procedure. However, it may increase the number of women who have complications in the postoperative period or who are recalled for biopsy[4]. Complication rates of approximately 16% can be considered acceptable, with the most common immediate complications being delayed wound healing, fat necrosis, and infection, while late complications being fibrosis and breast asymmetry[2]. Common strategies for managing complications in reconstructive surgeries include wound care, debridement, vacuum dressings, and new reconstruction procedures. The use of hyperbaric oxygen therapy (HBOT) appears as an alternative for the treatment of these conditions[5]. The use of HBOT in the

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treatment of chronic wounds is a well-established practice, and recent studies suggest benefit in acute or developing lesions[6].

The aim of this review is to discuss the applications of hyperbaric oxygen therapy in postoperative complications of patients treated for breast cancer.

METHODS

This work is a narrative review of the scientific literature based on several medical publications related to the application of HBOT in patients undergoing breast surgery. The initial search was performed in PubMed, using the MeSH descriptors: "breast neoplasms" and "hyperbaric oxygenation", with a filter for articles in English, Spanish and Portuguese published in the last 10 years. A total of 20 studies were found, most of them reports or case series related to flap ischemia and radiotoxicity. Articles listed in the bibliography of these studies were also consulted, as well as books and publications related to HBOT and the surgical treatment of breast cancer carried out by Cochrane, professional councils and specialist societies for contextualization purposes.

RESULTS AND DISCUSSION

Hyperbaric oxygen therapy

The first report of the use of HBOT dates back to 1662, when the British physicist Henshaw first used compressed air for hyperbaric therapy in a chamber called "Domicilium". Its use began to expand in the early 20th century, and in the 1960s it began to be used in the treatment of chronic wounds[7].

HBOT consists in subjecting the patient to an environment with high pressure and 100% oxygen concentration. The minimum value usually applied is 1.4 atmospheres absolute (ATA), which can be simplified as a 40% increase in atmospheric pressure at sea level. HBOT treatment is generally applied in hyperbaric chambers that can be individual (only 1 patient) or collective (multiple patients). The standard treatment consists in exposing the patient to 2 to 3 ATA for approximately 90 minutes[8].

Exposure to this environment leads to greater diffusion of oxygen gas into the blood, with an increase in the partial pressure of O_2 (pO_2) in arterial blood, and consequently, greater oxygen supply to the tissues. The increase in oxygen concentration in the tissues stimulates neovascularization and has an immunomodulatory effect, activating fibroblasts, reducing inflammation, increasing the synthesis of growth factors, potentiating antibiotics, improving antioxidant response and alleviating ischemia-reperfusion injury[7].

HBOT is a technique considered safe, with few reported contraindications. Its side effects are related to pressure variation and oxygen toxicity and include auditory barotrauma and transient visual changes. The most worrisome complications are pulmonary toxicity, practically nonexistent with current protocols, and neurotoxicity, which has a low incidence (1:10,000 treatments)[9]. Undrained pneumothorax is the main absolute contraindication due to the risk of transforming a simple pneumothorax into a tension pneumothorax[8].

Complications of post-treatment surgery

Oncoplastic surgeries are complex procedures that combine two different procedures at the same surgical site, accumulating the risk of complications from both procedures. In addition, the defect provides areas of fragility and thinner flaps compared to non-oncological surgeries, because of the resection of the tumor. The risk of postoperative complications is also related to the surgeon's experience and the patient's characteristics, such as body mass index (BMI), breast size, history of smoking and skin care[3].

Immediate complications include surgical wound dehiscence, ischemia and necrosis of the dermoglandular flap, necrosis of the nipple-areola complex, hematoma, seroma and surgical wound infection, while the most frequent late complications are fat necrosis and breast asymmetry[3].

In addition, patients with breast cancer are often subjected to radiotherapy, adding the sequelae of this treatment to the risks already described. Among the complications of radiotherapy is late radiotoxicity, which is characterized by pain, fibrosis, edema, reduced mobility of the arms and unsatisfactory aesthetic results[3,10].

When to indicate HBOT

The Undersea and Hyperbaric Medical Society recognizes 14 valid medical indications for HBOT (Table 1). Among these are indications of interest in mastology: chronic wounds, flap and graft involvement, radiotoxicity and soft tissue infections. The above-mentioned indications are also recognized by the Brazilian Society of Hyperbaric Medicine and the Federal Council of Medicine[11,12].

The application of HBOT in chronic wounds is well established in cases of diabetic foot and venous ulcers. A meta-analysis carried out by Cochrane in 2020 demonstrated that the use of HBOT in diabetic feet improves healing in the short term (relative risk [RR]=2.35; 95% confidence interval [95%CI] 1.19–4.62; p=0.01), but did not observe any difference in the long term. HBOT may also be beneficial in reducing wound size in patients with venous ulcers (mean difference [MD]=33.00%; 95%CI 18.97–47.03; p<0.00001) or with different types of ulcers (MD=61.88%; 95%CI 41.91–81.85; p<0.00001)[13]. Regardless of the etiology of chronic wounds, tissue hypoperfusion is a common mechanism in their pathophysiology, and HBOT corrects oxygen deficiency. HBOT improves oxygenation of the wound bed by providing adequate oxygen to the surrounding vascularized tissue, stimulating the local immune response, tissue repair and angiogenesis[11].

The pathophysiology of late radiotoxicity is a complex and only partially understood process. The mechanisms suggested in

Table 1. Indications for Hyperbaric Oxygen Therapy per Undersea and Hyperbaric Medical Society.

Air or Gas Embolism	Severe Anemia
Acute Thermal Burns	Compromised Grafts and Flaps
Refractory Osteomyelitis	Intracranial Abscess
Decompression Sickness	Acute Traumatic Ischemia
Arterial insufficiency: Central Retinal Artery Occlusion and Selected Problem Wounds	
Delayed Radiation Injuries: Soft Tissue and Bony Necrosis	
Carbon Monoxide and Cyanide Poisoning	
Idiopathic Sudden Sensorial Hearing Loss	
Necrotizing Soft Tissue Infections	
Clostridial Myositis and Myonecrosis (Gas Gangrene)	

Adapted from: Indications for Hyperbaric Oxygen Therapy[11].

its pathophysiology include obliterative endoarteritis and fibrosis associated with tissue atrophy. Thus, the benefit of HBOT would be the result of stimulating neoangiogenesis and consequently tissue oxygenation. Basic research studies have shown that the prophylactic use of HBOT can reduce tissue fibrosis and stimulate the mobilization of stem cells to irradiated tissues[11].

Another meta-analysis conducted by Cochrane in 2023 evaluated the use of HBOT in the prevention and treatment of late complications of radiotherapy, observing complete resolution or significant improvement in cases associated with necrosis or tissue damage (RR=1.39; 95%CI 1.02–1.89; I2=64%; number needed to treat=8). However, only 2 studies included patients with breast cancer, and no benefit of HBOT was found in the primary outcomes evaluated: improvement in lymphedema and brachial plexopathy[14]. In contrast, two more recent observational studies observed an improvement in quality of life, even without objective improvement in lymphedema[15,16]. Although HBOT is the recommended treatment for late radiotoxicity, it still lacks high-level evidence. The Honey Trial is an ongoing randomized study to evaluate the efficacy of HBOT in patients with late radiotoxicity treated for breast cancer and should provide new information to this field[10].

HBOT is not indicated in cases of viable grafts and flaps; however, it can be applied in the recovery of patients who have graft or flap compromise[11]. A case series of women undergoing NSM included 17 patients and 25 breasts that presented with early signs of ischemia and venous congestion or partial tissue necrosis postoperatively. Flap recovery was observed in 22 breasts, and only 3 breasts required a new surgical approach[17]. Another case series included 44 patients and 50 breasts with mastectomy flap necrosis referred to an HBOT referral center in the Netherlands. The outcomes evaluated included the need for surgical reapproach and reduction of tissue necrosis using the SKIN score. Despite the worsening of necrosis depth observed during the study, the affected area was significantly reduced with HBOT. Twenty-one breasts (42%) required a new surgical approach, a rate that is within the range found in the literature for patients who received other treatments for ischemia (5%-67%)[18].

In addition to therapeutic use, HBOT can be used in the perioperative period in cases of flap or graft compromise to reduce the risk of progression to necrosis and the need for new surgical approaches[5]. A retrospective case series of 8 women who underwent nipple-areola complex-sparing mastectomy and immediate reconstruction followed by HBOT showed a >6-fold increase in pre- and post-HBOT perfusion. Tissue viability was assessed intraoperatively with indocyanine green angiography (ICGA). Intraoperative fluorescence values in IVGA <20%, relative to the control area, indicated a risk of postoperative tissue ischemia and immediate referral for HBOT[6].

Although breast surgery is considered a clean procedure, rates of surgical site infections range from 1% to 20% after mastectomy and from 1% to 35% after breast augmentation with implants. Standard treatment consists in antibiotic therapy and debridement of devitalized tissue in selected patients[19,20]. However, necrotizing soft tissue infections are rare, with only 20 cases described in the literature, including cases without prior breast surgery and unrelated to cancer[21-23]. The use of HBOT in the treatment of these infections contributes to reducing mortality, the need for amputation and other complications[11,24].

CONCLUSION

The development of oncoplastic techniques, allowing for better aesthetic results and ensuring oncological safety, has led to an increase in the number of procedures performed. Consequently, complications related to this procedure have occurred more frequently, which requires that mastologists have knowledge of the methods available to manage them, providing better outcomes for patients. HBOT appears to be a possible intervention in cases of complications associated with oncoplasty and other surgical treatments for breast cancer. Although most of the evidence is

the result of observational studies or extrapolated from the use of HBOT in other areas, its use can contribute to better outcomes in patients undergoing surgical treatments for breast cancer. Cases associated with late radiotoxicity and compromise of grafts and flaps stand out because they present more solid evidence compared to other applications of HBOT in mastology. Difficulties regarding cost and availability should also be considered. Knowledge about HBOT by specialists and the public in general is another limiting factor for expanding the use of the method. However, offering HBOT in the management of these conditions expands the therapeutic arsenal available to patients who present with complications at this fragile time in their life.

AUTHORS' CONTRIBUTIONS

CBF: Data curation, Methodology, Writing – original draft. RJSV: Conceptualization, supervision, writing – Review & editing. MB: Writing – review & editing. EN: Writing – Review & editing. MAB: Writing – review & editing. CRC: Conceptualization. MHRRK: Conceptualization. MAP Conceptualization.

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