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RESEARCH REPORT

Use of hyperbaric oxygen therapy for tissue ischemia after breast reconstruction

Neha Rajpal, BA [1]; Elliot T. Walters, MD [2]; Tammer Elmarsafi, DPM [2];
Troy A. Pittman, MD [3]; Kelly K. Johnson-Arbor, MD [2]

[1] Georgetown University School of Medicine, Washington DC, U.S.

[2] Department of Plastic Surgery, MedStar Georgetown University Hospital, Washington DC, U.S.

[3] Private Practice, Washington DC, U.S.

CORRESPONDING AUTHOR: Kelly K. Johnson-Arbor – *kkja@me.com*

ABSTRACT

Introduction: Mastectomy skin flap necrosis represents a significant complication of breast reconstructive procedures and is reported to occur in 30%-52% of patients undergoing breast reconstruction. Early identification of ischemia and early initiation of hyperbaric oxygen (HBO_2) therapy can mitigate the effects of ischemia and rescue otherwise non-viable breast flap tissue.

Methods: We retrospectively examined the outcomes of HBO_2 therapy in eight breasts with compromised mastectomy skin flaps between September 2015 and January 2017. Indocyanine green angiography (ICGA) was used to assess perfusion intraoperatively and post-HBO_2 administration.

Results: Seven patients were referred for HBO_2 within 24 hours of mastectomy. One patient failed to improve despite starting hyperbaric treatment within 24 hours. All other patients manifested successful healing of their mastectomy skin flaps with acceptable cosmesis after 10 HBO_2 treatments. The mean relative perfusion of the at-risk area was 13.8% (±3.7%) pre-HBO_2 and 101.6% (±37.3%) post-HBO_2. The average area at-risk pre-HBO_2 was 17.1 cm^2 and reduced to zero post-HBO_2. Relative perfusion values after HBO_2 were found to be 6.8 (±3.4) times greater than those measured prior to HBO_2.

Conclusions: A short course of HBO_2 may be sufficient to successfully rescue at risk post-mastectomy breast flaps. ICGA is a useful adjunct for evaluating post-mastectomy breast flap perfusion before and after HBO_2 therapy. ∎

KEYWORDS: hyperbaric oxygen therapy; skin-sparing mastectomy; indocyanine green fluorescent angiography; breast reconstruction

INTRODUCTION

A significant complication of breast reconstructive procedures, mastectomy skin flap necrosis may occur in 30%-52% of patients undergoing breast reconstruction [1,2]. Early implementation of hyperbaric oxygen (HBO_2) therapy may be particularly valuable among patients at risk for mastectomy skin necrosis. HBO_2 can enhance neovascularization and flap perfusion through improved oxygen tension, collagen synthesis and fibroblast function [3].

Evidence suggests that clinical judgment alone is a poor predictor of post-surgical complications [4,5]. Recently surgeons have expanded the application of indocyanine green angiography (ICGA) to plastic reconstructive procedures to determine flap viability [6,7]. ICGA has accurately detected nipple hypoperfusion intra-operatively and proved more accurate in predicting ischemia when compared to clinical judgment alone [4,5,8-21]. Intraoperative use of ICGA may also result in decreased postoperative complications [12].

When ICGA suggests flap hypoperfusion, HBO_2 may be administered to prevent progression to flap necrosis. While the benefits of HBO_2 for the treatment of breast flap compromise and necrosis are well established, the number, duration, and frequency of treatments required have not been well described. The primary aim of this paper is to present a regimen for the use of HBO_2 in patients with breast skin flap compromise, and to discuss the utility of ICGA in evaluating the efficacy of HBO_2 in the treatment of compromised skin flaps.

METHODS

This was a single center, retrospective, IRB-approved case series of eight female breast cancer patients who received nipple-sparing mastectomy (NSM) with recon-

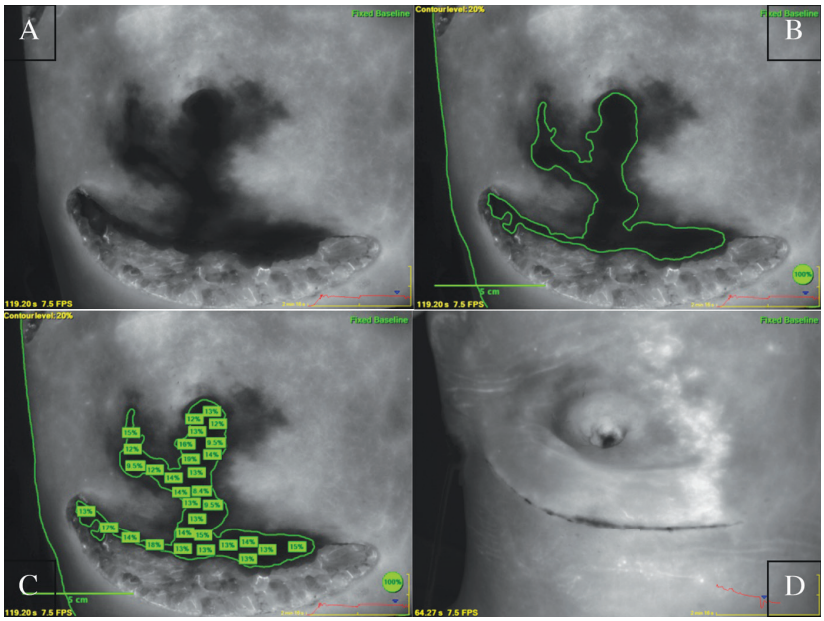

FIGURE 1
(Post-mastectomy ICGA images)

A) Dark regions represent areas of hypoperfusion.

B) Contour (green tracing) applied around region with <20% fluorescence.

C) Relative fluorescence values within the contour region.

D) Improved perfusion is noted after 10 HBO_2 treatments.

struction and HBO_2 between September 2015 – January 2017 at MedStar Georgetown University Hospital.

All eight patients underwent NSM. One patient was identified as having severely compromised flaps prior to reconstruction; consequently, immediate reconstruction was deferred in this patient. The remaining seven patients received immediate breast reconstruction using tissue expanders or implants. Tissue expanders were not inflated with saline until after the completion of HBO_2 therapy. Breast closure was performed without tension.

Intraoperative skin flap viability was evaluated by a single reconstructive surgeon using ICGA immediately following mastectomy and reconstruction. For the ICGA procedure, a 5cc bolus of indocyanine green dye was administered through a peripheral intravenous line followed by a 10cc saline flush. A SPY camera (Novadaq Technologies, Inc., Toronto, Canada) was positioned appropriately over the breast so as to include the xiphoid process, and a 120-second video of the infusion was obtained. Still images were captured at approximately 100 seconds. Perfusion was assessed by comparing the fluorescence of the darkest area of interest to the fluorescence at a control area located over the xiphoid process. The decision to treat the patient with HBO_2 was made at the end of each surgery based on the post-closure ICGA fluorescence. In line with the standard of care at our institution, ICGA fluorescence values of ≤20% of the control area indicates tissue at risk for postoperative ischemia (Figure 1a) and prompts a referral for HBO_2 treatment. ICGA images were assessed retrospectively using the SPY-Q Analysis Toolkit (Novadaq Technologies, Inc., Toronto) to determine relative perfusion (a percentage of fluorescence compared with the control area) of the at-risk region for pre- and post-HBO_2 images. ImageJ software (NIH, Bethesda, Maryland) was used to calculate the area (in cm^2) of the image with <20% relative fluorescence intensity for each breast, also known as the "contour" (Figure 1b) [22].

HBO_2 was performed using a monoplace hyperbaric chamber (Perry Baromedical Corp., Riviera Beach, Florida, U.S.) pressurized to a depth of either 2.0 or 2.5 atmospheres absolute (ATA). The treatment depth for each patient was determined by a hyperbaric medicine physician according to the patient's underlying medical comorbidities. Treatments were administered twice daily on weekdays, and once daily on weekends, for a minimum of 10 treatments per patient. Flap perfusion was assessed using ICGA immediately following the final hyperbaric treatment.

SAS 9.4 statistical software (SAS Institute, Cary, North Carolina, U.S.) was used for all statistical analysis.

RESULTS

Demographics and comorbidities of the eight patients included in this study are listed in Table 1. Seven patients received immediate breast reconstruction with tissue expanders or implants prior to referral for HBO_2. Breast reconstruction was delayed in one patient due to extensive intraoperative ischemia with resultant necrosis and infection. Seven patients were referred for HBO_2 and began treatment within 24 hours of mastectomy. HBO_2 was administered at a depth of 2.5 ATA in seven patients, and at 2.0 ATA in one patient due to a history of seizures. There were no adverse events related to HBO_2 reported in this patient population.

One patient failed to improve despite starting hyperbaric treatment within 24 hours. Her pre-HBO_2 perfusion percentage was 11.7% and increased to 17.1% after completing 17 HBO_2 treatments. This patient failed to improve adequately and was returned to the operating room for debridement of the nipple-areola complex. All other patients manifested successful healing of their mastectomy skin flaps with acceptable cosmesis after 10 HBO_2 treatments.

Two patients did not complete the post-treatment ICGA and were excluded from the ICGA analysis. However, after completing HBO_2 treatment these patients' breast flaps recovered without requiring additional intervention. The remaining patients mean relative values of perfusion pre- and post-HBO_2 are illustrated in Table 2.

TABLE 1. Patient demographics

patient demographics	n=8	range
age	49.6 (±9.3)	40-65
race		
White	4 (50%)	
African American	3 (37.5%)	
other	1 (12.5%)	
BMI	25.6 (±9.7)	
comorbidities		
hypertension	2 (25%)	
hyperlipidemia	3 (38%)	
smoking	1 (12%)	

Table 2. Relative perfusion percentages pre- and post-HBO_2 within the at-risk region for patients with successful HBO_2 treatment

patient	pre-HBO_2	post-HBO_2	p-value
1	16.3±3.7	138.7±36.1	<.0001
2	13.3±2.3	117.8±35.0	<.0001
3	15.1±4.2	76.9±28.7	<.0001
4, right	12.0±3.5	114.3±30.5	<.0001
4, left	13.7±4.1	94.0±32.7	<.0001
5	13.8±2.9	65.3±27.6	0.0006
6	14.8±1.7	78.2±22.1	<.0001
mean	13.8±3.7	101.6±37.3	<.0001

DISCUSSION

Early initiation of HBO_2 following mastectomy has been shown to improve breast flap survival, thereby reducing the risk of infection, esthetic deformity, and implant extrusion [23-25]. The results of this case series demonstrated a greater than sixfold increase in relative perfusion values between pre- and post-HBO_2, indicating the potential of HBO_2 to improve flap viability and avoid skin necrosis.

Although HBO_2 is a recognized treatment for compromised skin grafts and flaps, the available evidence for HBO_2 therapy to treat mastectomy flap hypoperfusion is limited. Our results suggest that flap salvage can be accomplished with a limited number of HBO_2 treatments, especially when patients are referred for HBO_2 within 24 hours of mastectomy and reconstruction.

This case series demonstrates that ICGA represents a valuable adjunct for monitoring response in patients receiving HBO_2 therapy. Limitations of this case series include a small sample size and retrospective nature of the study. In this study, patients were referred for HBO_2 within 24 hours of mastectomy; as the referral patterns for HBO_2 are variable, the results of this study may not be generalizable to all institutions. In addition, ICGA poses additional limitations, as the timing of injection and image capture are operator-dependent. Future studies should explore the utility of ICGA for monitoring response of HBO_2 therapy over the course of the treatment, as this may help identify the point of maximal effect during the HBO_2 treatment course.

CONCLUSIONS

In this series of patients with intraoperative identification of mastectomy flap compromise, tissue expander and implant reconstructions were successfully salvaged with a short course of HBO_2. ICGA obtained in six

patients demonstrated a greater than sixfold increase in relative perfusion values between pre- and post-HBO_2, indicating the remarkable capacity of HBO_2 therapy to improve flap survival and prevent progression to necrosis. In patients with compromised skin flaps after mastectomy, ICGA can be used to guide and monitor a patient's response to HBO_2 therapy.

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