Original Article

Evaluation of efficacy of hyperbaric oxygen therapy as an adjunctive therapy in the management of thermal burns

ABSTRACT

Background: Hyperbaric oxygen therapy (HBOT) is an adjunctive therapy that has been proposed to improve outcome in thermal burns. It involves the therapeutic administration of 100% oxygen at environmental pressures >1 atmosphere absolute (ATA).

Methodology: An open, prospective, observational study was conducted for a period of 18 months which included fifty patients who were allocated to either adjunctive hyperbaric therapy in addition to the existing protocol of burn management (Group A) or only existing protocol of burn management (Group B) with daily dressing and debridement. All patients between the age of 18 and 60 years with 15%–60% of second and third degrees of thermal burns were included. HBOT was administered at 2.0 ATA in a "monoplace" chamber for 90 min, 6 days a week. A total of ten sessions were administered to each patient along with conventional treatment.

Results: The mean time of wound healing in Group A was 18.96 days, whereas in Group B, it was 43.64 days. The mean number of days of hospital stay in Group A was 32.04 days, whereas in Group B, those were 51.2 days. Similarly, the mean pain score and mean fluid requirement were less in Group A when compared to those of Group B.

Conclusion: With our study, we can conclude that HBOT is an effective adjunctive modality of treatment in the management of thermal burns.

Keywords: Burns, hyperbaric oxygen, therapy, thermal, wound healing

INTRODUCTION

Thermal burns remain an important source of morbidity and mortality. Every year, approximately two million people are burned, 80,000 are hospitalized, and 6500 die in the USA (Brigham 1996). Globally, there were 238,000 fire-related deaths in 2000, with low- and middle-income countries bearing 95% of the global burden. Mortality per 100,000 population is 1.3 in North America but 5.5 in Africa.[1] Increasing incidents of terrorism involving explosions in recent times have resulted in multiple system trauma along with burn injuries. The year 2008 claimed more than 210 lives and left more than 600 injured due to terrorist attacks in Jaipur, Ahmedabad, Delhi, and Guwahati. In India, during Diwali on October 28, 2008, more than 1000 fires were reported from all over country and firecrackers, most of them unsafe, worth rupees 600 crores were burst. There must be more than 5000 injuries and at least 100 of them very serious.

We do not have records of burn injuries in India; it is estimated by extrapolation of population figures that there are 700,000 major burn injuries every year and about 120,000 die of burns.

Burns are a difficult treatment challenge and ideally the province of specialized units with high-volume workloads. Such units do not exist in most parts of the world. Early treatment can positively influence mortality rate. It involves

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Submitted: 15-Sep-2019, **Revised:** 22-Dec-2019, **Accepted:** 22-May-2020, **Published:** 21-May-2021

Access this article online	
Website: www.ijburns.com	Quick Response Code
DOI: 10.4103/ijb.ijb_25_19	

How to cite this article: Kumar N, Tiwari VK. Evaluation of efficacy of hyperbaric oxygen therapy as an adjunctive therapy in the management of thermal burns. Indian J Burns 2020;28:44-50.

appropriate fluid resuscitation, usually involving attainment of resuscitation targets using consensus formulas for initial fluid administration,[2] together with topical agents to control pain, limit direct fluid losses, and slow bacterial growth.

Hyperbaric oxygen therapy (HBOT) is an adjunctive therapy that has been proposed to improve outcome in thermal burns. HBOT is the therapeutic administration of 100% oxygen at environmental pressures >1 atmosphere absolute (ATA).

Administration involves placing the patient in an airtight vessel, increasing the pressure within that vessel, and administering 100% oxygen for respiration. In this way, it is possible to deliver a greatly increased partial pressure of oxygen to the tissues.

Typically, treatments involve pressurization to between 1.5 and 3.0 ATA, for periods between 60 and 120 min once or more daily.[3] It has been suggested since 1965 that HBOT might improve the outcome following thermal burns.[4] HBOT has been shown to reduce edema and preserve microcirculation in a number of injury models, including burns, through vasoconstriction with enhanced oxygen delivery, a direct osmotic effect, and the inactivation of white cell adhesion.[5-7] HBOT also exerts beneficial effects on infections in hypoxic tissues through a variety of mechanisms.[8]

Burn wounds typically have a central zone of coagulation surrounded by a zone of stasis, in turn surrounded by a zone of hyperemia. HBOT was noted to reduce the capillary stasis in the zone of stasis and reduce the increase in the size of the zone of coagulation as occurs in burns. Thus, HBOT assists in tissue preservation. This mechanism might be of particular value in the case of burns in esthetically or functionally important zones (face, hands, and perineum) or with delicate vascularization (cartilaginous-ears, nose). Further, HBOT may exert beneficial effects by way of its anti-sludging effect in the microcirculation and prevention of injury by oxygen-free radicals.[9]

Despite nearly 40 years of interest in the delivery of HBOT in these patients, little

clinical evidence of effectiveness exists. By conducting this study, we were trying to evaluate the efficacy of HBOT as an adjunctive therapy in addition to the conventional therapy for the management of thermal burn patients.

METHODOLOGY

An open, prospective, observational study was conducted involving fifty patients who were divided equally into either adjunctive hyperbaric therapy in addition to the existing protocol of burn management (Group A) or only the existing protocol of burn management (Group B) with daily dressing and debridement for a study period of 18 months. Ethical clearance was obtained from the Institutional Ethics Committee with Ref. No. TP (DM/M. Ch)(5/2016)/IEC/PGIMER/RMLH-7953/16. Patients were informed about their allocation before surgery. All patients between the age of 18 and 60 years with 15%–60% of second and third degrees of thermal burns were included, whereas those with electrical or chemical burns or with a history of upper respiratory tract infection, active lung pathology, pregnancy, otitis media, claustrophobia, and on concurrent chemotherapy, i.e., bleomycin or cyclophosphamide, were excluded from the study.

Hyperbaric oxygen therapy

HBOT was provided as soon as patient was received within 24 h postburn injury. HBOT was administered at 2.0 ATA in a "monoplace" chamber for 90 min, 6 days a week. A total of ten sessions were administered to each patient along with conventional treatment. Patients' blood pressure, pulse rate, and respiratory rate were monitored during initial treatment and as necessary thereafter.

Existing protocol of burn management

It involved the resuscitation with Ringer's lactate solutions, regular daily burn dressing with 1% silver sulphadiazine cream, debridement, and infection control using appropriate intravenous antibiotics and intravenous analgesics.

RESULTS

Different variables were being analyzed between the two groups using appropriate statistical methods namely Chi-square test, Student's *t*–test, and Fisher's test. *P* value equal or less than 0.050 is considered significant for confidence interval of 95%.

In Group A, there were 11 males and 14 females out of the total of 25 study participants, whereas in Group B, there were 9 males and 16 females. However, the difference was not statistically significant ($P = 0.773$).

The mean age of the study participants in Group A was 44.64 years with range varying from 25 to 60 years, whereas in Group B, it was 45.30 years ranging from 20 to 60 years. There was no statistically significant difference in the distribution of the ages in the two groups ($P = 0.8031$).

In Group A, there were about 23 patients with mostly second degrees of burns and two were with mostly third degree of burns, whereas in Group B, there were about 24 patients

with mostly second degrees of burns and one was with mostly third degree of burns. By conventional criteria, the distribution of degrees of burns between the two groups was not statistically significant ($P = 1.000$).

The mean body surface area (BSA) burn was 31.76% in Group A, whereas in Group B, it was 32%. There was no statistically significant difference in the mean BSA burn in the two groups ($P = 0.7901$).

There was no death in either of the group. The mean time of wound healing as evident by the epithelization in Group A was 18.96 days [Figures 1 and 2], whereas in Group B, that was 43.64 days with $P = 0.0001$, with standard deviation (SD) as 1.40 and 3.28, respectively, and standard error of mean deviation (SE) as 0.2800 and 0.6560, respectively [Table 1].

By conventional criteria, this difference was considered to be statistically significant ($P = 0.0001$).

Wound infection was evident in 2 out of the 25 patients in Group A, whereas infection was observed in 9 out of 25 patients in Group B. By conventional criteria, this difference was considered to be statistically significant ($P = 0.0374$). Wound infection was confirmed by culture sensitivity of burn wound discharge. *Pseudomonas aeruginosa* was the most common organism isolated in cultures [Table 2].

It was found that in 10 out of the 25 patients, debridement and subsequent grafting was required in Group B, whereas grafting was needed in only 2 out of 25 patients in Group A [Table 3]. By conventional criteria, this difference was considered to be statistically significant ($P = 0.0181$).

The mean numbers of days of hospital stay in Group A was 32.04 days, whereas in Group B, those were 51.2 days, with SD as 1.54 and 1.94, respectively, and SE as 0.31 and 0.39, respectively. On applying Student's *t*-test, *P* value came out to be as 0.0001. By conventional criteria, this difference was considered to be extremely statistically significant [Table 4].

The mean pain score as per Visual Analog Scale (0–10) after day 1 was 7.0 in HBOT Group A and 6.84 in Group B ($P = 0.7214$). By conventional criteria, this difference was considered to be statistically nonsignificant.

The mean pain score as per Visual Analog Scale (0–10) after day 7 was 2.44 in HBOT Group A and was 5 in Group B ($P = 0.0001$). By conventional criteria, this difference was considered to be statistically significant [Table 5].

The total fluid required changes using Parkland formula measured in terms of ml/kg/%BSA from day 1 of treatment till day 7 were as follows:-

Figure 1: A 27-year-old male with 30% mostly second-degree thermal burns on admission. (a) Anterior view, (b) lateral view, (c) and (d) healed wounds after adjuvant hyperbaric oxygen therapy

Figure 2: (a) A 30-year-old female with 25% mostly third-degree thermal burns on admission, (b) healing of most of the wounds after adjuvant hyperbaric oxygen therapy

Table 1: Wound healing

Group	Number of patients	Mean time of wound healing (days)	SD	SE	*P*
Group A	25	18.96	1.40	0.2800	0.0001
Group B	25	43.64	3.28	0.6560	

SD: Standard deviation, SE: Standard error

After day 1 of treatment

The mean fluid requirement after day 1 of the treatments was 4.668 L in Group A and 4.640 L in Group B with SD as 0.621 and 0.580 groups, respectively. By conventional criteria, this difference was considered to be statistically nonsignificant ($P = 0.8698$).

After Day 7 of treatment

The mean fluid requirement after day 7 of the treatments [Table 6] was 2.136 L in Group A and 3.14 L in Group B with SD as 0.119 and 0.129 groups, respectively. By conventional criteria, this difference was considered to be extremely statistically significant ($P = 0.0001$).

The mean number of days in which wound became ready for grafting was 6 days and 9.6 days, in Group A and Group B, respectively [Table 7]. By conventional criteria, the difference between the two groups was statistically significant ($P = 0.0111$). None of the patients in the HBOT group reported any adverse effects from the administration of HBOT.

Table 2: Wound infection

Group	Wound infection		Total	*P*
	Yes	No		
Group A	2	23	25	0.0374
Group B	9	16	25	
Total	11	39	50	

Table 3: Requirement for further debridement/graft

Group	Debridement/grafting		Total	*P*
	Yes	No		
Group A	2	23	25	0.0181
Group B	10	15	25	
Total	12	38	50	

Follow-up was done at 2 weeks, 1 month, and 3 months after the treatments

The mean pain score as per Visual Analog Scale (0–10) also varied significantly in the two groups after 2 weeks. The mean pain score was 0.72 in HBOT Group A and 1.24 in Group B ($P = 0.0283$). By conventional criteria, this difference was considered to be statistically significant [Table 8].

It was found that in 4 out of the 25 patients, debridement and subsequent grafting was required in Group B, whereas no grafting was needed in Group A. By conventional criteria, the difference was considered not to be statistically significant ($P = 0.1099$).

The mean number of days required to return to activities of daily living measured after getting discharge from the hospital in Group A was 7.24 days, whereas in Group B, it was 14.24 days. *P* value came out to be 0.0001. By conventional criteria, this difference was considered to be very statistically significant [Table 9].

Further debridement or grafting was not required in either of the groups during 1-month and 3-month follow-up.

Postburn hypertrophic scarring was observed in one patient in Group B and none in Group A after 1 month of follow-up period ($P = 1.000$), whereas scarring was evident in one patient in Group A and in four patients in Group B after 3 months of follow-up period ($P = 0.3487$). In both the cases, the difference between the two groups was considered statistically nonsignificant.

DISCUSSION

Adjunctive HBOT has been shown in previous studies to reduce the length of stay and cost of care in conjunction with

Table 4: Total duration of hospital stay in number of days

Group	Number of patients	Mean number of days in Hospitals	SD	SE	*P*
Group A	5	32.04	1.54	0.31	0.0001
Group B	5	51.2	1.94	0.39	

SD: Standard deviation, SE: Standard error

Table 5: Pain scores (Visual Analog Scale) on posttreatment day 7

Group	Number of cases	Mean pain score (0-10)	SD	SE of mean deviation	*P*
Group A	25	2.44	1.26	0.25	0.0001
Group B	25	5.0	1.47	0.29	

SD: Standard deviation, SE: Standard error

Table 6: After day 7 of treatment

Group	Number of cases	Mean fluid requirement day 7 (l)	SD	SE of mean deviation	*P*
Group A	25	2.136	0.119	0.0240	0.0001
Group B	25	3.14	0.129	0.0260	

SD: Standard deviation, SE: Standard error

Table 7: Number of days in which wound became ready for graft

Group	Number of cases	Mean number of days requirement for grafting	SD	SE of mean deviation	*P*
Group A	2	6	1.41	1.00	0.0111
Group B	10	9.6	1.51	0.48	

SD: Standard deviation, SE: Standard error

Table 8: Pain score after 2-week follow-up in either groups

Group	Number of cases	Mean pain score (0-10)	SD	SE of mean deviation	*P*
Group A	25	0.72	0.74	0.15	0.0283
Group B	25	1.24	0.88	0.18	

SD: Standard deviation, SE: Standard error

Table 9: Return to activities of daily living

Group	Number of patients	Return to activities of daily living (days)	SD	SE	*P*
Group A	25	7.24	1.01	0.20	0.0001
Group B	25	14.24	1.20	0.24	

SD: Standard deviation, SE: Standard error

early excision and comprehensive burn management. While HBOT is advocated as an adjunctive treatment for thermal burns in some centers, there are surprisingly few comparative reports that support its use.

It was previously suggested that hyperbaric oxygen (HBO) supports tissue viability by preventing microvascular damage, minimizing edema, and providing the necessary oxygen for normal cellular metabolism mainly to the dermis beneath thermally damaged skin.[10]

After the acute damage has been stabilized and wound healing processes have taken place, HBO has been shown to promote fibroplasia, angiogenesis, and re-epithelialization.[11]

The success of therapeutic measures taken during the first 24 h following the burn, aimed at halting the progression of tissue injury, may be critical to the final outcome.

Previous studies regarding the role of HBO in burn management failed to include both the control groups required. Ketchum *et al*.,[12] Korn *et al*.,[13] and Nylander *et al*.[14] reported reduced infection, less systemic edema, greater capillary proliferation and epithelial regeneration, and shorter healing time in HBO-treated animals.

In our study, there were no significant difference in age, gender, degree of burn, and the mean surface area burn.

In 1987, Niu *et al*.[15] in a large clinical series compared 266 HBO-treated thermal burn patients with a mean age of 27 years ranging from 2 to 82 years with 609 non-HBO-treated burn patents with a mean age of 26 years ranging from 7 to 82 years. Similarly, the mean total burn surface area was 34% (7%–90%) in the HBO group and 36% (5%–85%) in the non-HBO group.

Cianci *et al*. stated that adjunctive HBOT has drastically reduced the healing time in major burn injury, especially if the wounds are of deep second degree.[15-18] There is theoretical benefit of HBO therapy for obviously less well-defined third-degree burns.[19]

Again, the distribution of mean body surface of area of burn was also not significant statistically with mean BSA of 31.76% in Group A, whereas in Group B, it was 32%.

Cianci *et al*. in 2013 had proposed that the HBOT was recommended to treat >20% total BSA (TBSA) and/or with involvement of the hands, face, feet, or perineum that are deep partial- or full-thickness injury.[20]

In our study, the mean time of wound healing as evident by epithelization in Group A was 18.96 days, whereas in Group B, these was 43.64 days. The difference was found to be extremely statistically significant.

Ketchum *et al*. in 1967 observed a reduction in the healing time of burn wounds and number of infections,[12] which was also confirmed by Härtwig and Kirste in 1974.[21]

Similarly, the data presented by Merola and Piscitelli in a study done in 1978 showed faster wound healing of burn wounds in 37 patients when compared to nontreated wounds.[22]

In a 2005 randomized controlled study, Bilic evaluated the effects of HBO on burn wound healing. He showed that HBOT had a beneficial effect on time to epithelial regeneration and healing of burn wounds.[23]

Hart *et al*. reported a sham-controlled randomized series showing mean healing time ($P < 0.005$) in 10%–50% of TBSA burn patients treated with HBO when compared to controls and to United States National Burn Information Exchange Standards.[24] Hart reported mean healing time significantly shorter – 19.7 versus 43.8 days ($P < 0.001$).

In 1965, Wada observed improved healing of burns in coal miners being treated for carbon monoxide poisoning with HBO. Later, a clinical series by Ikeda *et al*., Wada *et al*., Lamy and Hanquet, Tabor and Grossman and Grossman[25-30] showed improved healing.

Cianci *et al*. had demonstrated in previous studies that Adjunctive HBOT has drastically reduced the healing time in the major burn injury, especially if the wounds are deep second-degree.[15-18]

The evidence of wound infection was found in 2 out of 25 patients in group A in comparison to 9 patients in group B. The difference was found out to be statistically significant. These findings have been supported by the Ketchum *et al*. in 1967,[12] Härtwig and Kirste in 1974[21] as and Niu in 1987.[15]

Debridement and subsequent grafting was required in 10 out of 25 patients in non HBOT Group whereas grafting was needed in only 2 out of 25 patients in HBOT Group. In a retrospective paired controlled series of burn patients treated with HBO2, Waisbren reported a 75% reduction in the need for grafting ($P < 0.001$) in the hyperbaric group.[31]

Our study had shown that the mean duration of hospital stay was 32.04 days in HBOT group whereas it was 51.2 days in non-HBOT group. Cianci had also shown a significant reduction in length of hospital stay in burns up to 39% TBSA.[16] Ikeda *et al*., Wada *et al*., Lamy and Hanquet, Tabor, and Grossman and Grossman[25-30] also demonstrated decreased length of hospital stay in their clinical series.

Cianci had also reported reduced surgeries ($P < 0.03$) and reduced length of hospital stay (53%) in 40%–80% TBSA burns.[32] Similarly, Maxwell *et al*. also reported reduced total hospitalization time.[33]

Our study has shown that HBOT is effective in reducing the pain in thermal burn patients by causing faster wound healing and epidermization of the burn wounds.

From the review of the studies done in the past, it was found that there was not much details provided in regard of any change in the pain experienced by thermal burn patients. In this context, a change in the pain score in our study in HBOT-treated patients is an important observation.

A statistically significant difference was seen with change in mean fluid requirements in two groups from day 1 to day 7. In the first trial, Hart *et al*. in 1974,[24] as previously discussed, reported reduced fluid requirements when compared to controls (mean: 2.2 ml/kg vs. 3.4 ml/kg, no statistical analysis reported).

Ikeda *et al*., Wada *et al*., Lamy and Hanquet, Tabor, and Grossman and Grossman[25-30] showed decreased fluid requirements (30%–35%). Cianci *et al*. observed similar results in a series of patients averaging 28% TBSA burns.[17] In a small blinded review, Cianci's group reported a 25% reduction in resuscitative fluid requirements ($P < 0.07$). Niu *et al*. in 1987 in a clinical series also reported reduction in fluid requirement by 30%–35% in the HBO-treated group.[15]

Our study had shown a statistically significant difference in the number of days required for a wound to get prepared for grafting. It was again an important observation made in our study. Although the debridement and subsequent grafting was required in less number of HBOT-treated patients, HBOT which helped in controlling in the wound infection faster, was found to be beneficial in preparing the wound bed for grafting in less number of days when compared to the non-HBOT group.

CONCLUSION

With our study, we can conclude that the HBOT is an effective adjunctive modality of treatment in the management of thermal burns that has shown reduced length of hospital stay, early wound healing, and improved morbidity in conjunction with comprehensive burn management.

Limitation of study

1. Short period of follow-up. Three-month of follow-up was not enough to comment upon the occurrence of hypertrophic scar/keloid and requirement of further debridement and grafting
2. Parameters studied such as pain scores by Visual Analog Scale are more of a subjective assessment, which may vary from patients to patient and not objective.

Informed consent

Duly informed written consent was obtained from all patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given

their consent for their images and other clinical information to be reported in the journal. The patients understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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