Effects of hyperbaric oxygen therapy on clinical and economic outcomes in patients with deep second-degree burns

Article *in* Undersea and Hyperbaric Medicine · January 2023

DOI: 10.22462/01.01.2023.18

CITATIONS
0

READS
167

6 authors, including:

Merve Akın
Dumlupinar University
55 PUBLICATIONS **398** CITATIONS
SEE PROFILE

Murathan Erkent
Baskent Üniversitesi Ankara Hastanesi
48 PUBLICATIONS **77** CITATIONS
SEE PROFILE

UNDERSEA & HYPERBARIC MEDICINE

Effects of hyperbaric oxygen therapy on clinical and economic outcomes in patients with deep second-degree burns

Ümit Özdemir, MD [1]; Merve Akin, MD [2]; İsa Sözen, MD [3]; Murathan Erkent, MD [4]; Selçuk Tatar, MD [5]; Ahmet Çinar Yasti, MD [6]

[1] Eskişehir Osmangazi University, Department of Gastroenterological Surgery, Eskişehir, Turkey
[2] Ankara City Hospital, Department of General Surgery, Ankara, Turkey
[3] Süleyman Demirel University, Department of General Surgery, Isparata, Turkey
[4] Baskent University, School Of Medicine, Department of General Surgery, Ankara, Turkey
[5] Ankara Gaziler Physical Therapy and Rehabilitation Education and Research Hospital, Underwater Medicine and Hyperbaric Medicine
[6] Health Sciences University, Department of General Surgery, Ankara City Hospital, Burn Treatment Center

CORRESPONDENCE: Merve Akin – *merveakin.2002@gmail.com*

ABSTRACT

Özdemir Ü, Akin M, Sözen İ, Erkent M, Tatar S, Yasti AC. Effects of hyperbaric oxygen therapy on clinical and economic outcomes in patients with deep second-degree burns. Undersea Hyperb Med. 2023 First Quarter; 50(1):29-37.

Introduction: Deep second-degree burn injuries are the most challenging situations for the burn surgeon in the treatment of adult cases. While waiting for spontaneous closure increases the risk of hypertrophic scar and keloid, early excision and grafting pose the risk of donor site wound and permanent color differences. Unlike many studies in the literature, the current study was planned in a way to minimize factors other than burn wounds to investigate the effect of adding hyperbaric oxygen (HBO_2) therapy to conventional treatment in deep second-degree burn wounds.

Material and Method: This prospective observational study included patients with burn injuries who underwent conventional treatment alone and those who underwent conventional plus HBO_2 treatment performed by a single experienced surgeon and who met the study criteria.

Results: Thirty-eight patients completed the study. Mean burned total body surface area (TBSA) was. 9.22 ±3 43% (range 5% to 20%). There was no difference between the two groups in terms of age, burned TBSA, and burn etiology. The need for surgery and grafting was lower in patients who received HBO_2 in addition to conventional treatment ($p=0.003$ and $p=0.03$, respectively). The patients in the HBO_2 group had a shorter hospital stay, and their wounds epithelialized in a shorter time ($p=0.169$ and $p<0.001$, respectively). They also had a higher satisfaction level and lower treatment cost ($p=0.03$ and $p=0.36$, respectively).

Discussion: The results of this prospective study, in which co-factors were eliminated, showed that adding HBO_2 to the conventional treatment of deep second-degree burns had a significant positive effect on patient outcomes, as well as reducing treatment costs.

KEYWORDS: burns; hyperbaric oxygen treatment cost; length of stay; wound healing

INTRODUCTION

Burns are injuries caused mostly by coagulative damage to the skin and adjacent organs. Burn injury is usually caused by thermal damage, but chemicals, radiation or electricity can also damage tissues directly [1]. Burns are the fourth most common type of trauma after traffic accidents, falls, and violence. According to the most recently updated (2018) data of the World Health Organization (WHO), there were 10.9 million burn cases across the world in 2004, and according to the annual data in 2008, 410,000 burn cases were seen in the United States and 1 million in India [2].

First- and second-degree burns are defined as superficial dermal burns, and it is generally accepted that they will heal without surgery when using different wound dressings. Injuries involving the deeper layers of the dermis are defined as deep dermal burns. In third- and fourth-degree burns, since all layers of the dermis are damaged, dermal stem cells required for spontaneous healing are not present; therefore, these burns need to be closed using various surgical techniques.

Deep second-degree burns are the most discussed and challenging cases for the surgeon in terms of decision-making. While various schools recommend grafting, others suggest follow-up with dressings [3,4]. However, leaving deep second-degree burns to heal spontaneously after applying dressings delays wound healing, which increases hypertrophic scarring and future keloid formation. These complications cause loss of joint function and contractures, as well as cosmetic problems. In the case of grafting of these burns, creating a new wound in the donor site and graft take-rates remain major clinical concerns. The treatment of deep second-degree burns is still debated in the field of burn surgery, with no consensus having been achieved.

Burn depth assessment is important in burns management decision-making. Burn depth is a dynamic injury and if not managed adequately in the clinical course, the Jackson intermediate zone can progress to necrosis zone. There are several methods to assess the depth of the burn wound including biopsy, laser Doppler lmaging (LDI) analysis, indocyanine green, thermography, a number of dermoscopy techniques, hyperspectral imaging, and MR; all have limited accuracy. However, these methods, although reliable, are not always available from a cost, practitioner experience and/or practical perspective. In their article Monstrey et al. suggest LDI as almost the gold standard [5]. However, from the meta-analysis of Shin and Yi, it is clearly understood that in diagnosis of deep burns, LDI should be performed with careful clinical assessment by experienced surgeons [6].

Clinical evaluation is by far the most widely used method of burn depth assessment. This involves a subjective assessment of the characteristics of the burn to diagnose its depth [6,7]. On direct examination, there are four elements that should be assessed – bleeding, sensation, appearance, and blanching to pressure [7].

Hyperbaric oxygen (HBO_2) therapy involves breathing 100% oxygen under high pressure, which increases oxygen diffusion into the tissues. Hyperoxia in tissues and the resulting relative hypoxic environment contribute to wound healing in chronic wounds by increasing fibroblast proliferation and angiogenesis. It has been reported that HBO_2 is beneficial in the treatment of acute and chronic ischemia, crush injuries, risky grafts, flaps, and burn wounds, and it also has an antiedema effect in burn injuries [8-10].

In parallel with the developments in every field of medicine, progress has also been made in the treatment of burns. A better understanding of the pathophysiology of burn shock and appropriate treatment management have resulted in a significant reduction in mortality rates [11,12]. Despite the increasing survival rate, especially in non-life-threatening partial-thickness dermal burns, the length of hospital stay (LOHS), treatment cost, need for surgery, infections, inability to work for a long time, and patient satisfaction remain challenging issues, even in outpatients. Although there are studies on HBO_2 in burn wounds

in the literature, the above-mentioned parameters have not been discussed in partial-thickness burns. While some studies have shown the benefit of applying HBO_2 as supportive treatment in burns, others have reported no difference compared to conventional treatment alone. The Cochrane group has emphasized the need for additional studies in this area [13]. In the current study, the effect of HBO_2 on treatment and cost in partial thickness dermal burns was investigated by comparing it to conventional treatment alone.

METHODS

This prospective observational study was conducted in our burn treatment center, which is a reference center with an average of 2,500 patient presentations and 300 hospitalizations per year. The study included patients aged 18 to 65 years presenting to our center between February 1 and June 30, 2018, with deep second-degree dermal burns within the first 24 hours of injury. All lived in the province of Ankara and were eligible for outpatient follow-up. The exclusion criteria were requiring intensive care follow-up, having any comorbidity, using any regular medication, having a previous history of burn injury, smoking, any addiction, and having wound site infection or suspicion of sepsis. All patients had paracetamol as a pain-killer and antibiotics when required.

Within the scope of the study, age, gender, burn etiology, burn area, epithelialization time, number of HBO_2 sessions, surgery requirement, operations performed, infection development, patient satisfaction, length of hospitalization, and treatment cost were compared between two groups: an HBO_2 treatment group and a control group. In all the patients, the evaluation of burn depth was performed by the same surgeon, who had been tending to burn injuries since 1998 and had been responsible for the burn treatment center since 2001.

Patients eligible for the study were asked to have HBO_2 treatment and were included to the study group – except the last six patients; as the study group had reached a sufficient number, the last six patients were included in the control group. Thirty patients were included in the study group that received HBO_2 + conventional treatment, and 30 patients were included in the control group, which received conventional treatment alone. In all patients, conventional treatment was started by applying daily silver sulfadiazine dressing and washing when necessary. Following the appearance of epithelialization and/or epithelial bulging in the burn site and clinical confirmation of the absence of any infection, daily dressing was continued using paraffin gauze closures.

In addition to conventional dressing, the HBO_2 study group received HBO_2 five days per week (excluding Saturdays and Sundays). HBO_2 was planned as a maximum of 21 sessions, one (3 x 30 minutes of O_2 at 2.4 ATA with five-minute air breaks) session per day, and performed in multiperson hyperbaric chambers with the supervision of a nurse, a specialist doctor, and an operator. Patients hospitalized on Friday, Saturday or Sunday were given HBO_2 on Monday, and these additional hospitalized days were added to the total LOHS. As the full epithelialization was achieved, the HBO_2 therapy was discontinued, and the number of sessions recorded.

In debrided patients, eschar tissue was removed from the wounds. During this procedure, sharp debridement was avoided, and hydrosurgery (Versajet®, Smith & Nephew, UK) was used when necessary. In patients with grafts, the donor sites were dressed with paraffin gauze. On the first postoperative day, the dressings on the donor site were opened, and the paraffin gauze that was adhered was left in place. The grafts were opened on the fourth day and covered with daily antibiotic cream, and then the patients were followed up. The patients were discharged from the hospital on the day their wounds were considered suitable for outpatient follow-up. At this time, hospital stay was terminated, and outpatient follow-up was started. On the day of the discharge decision, patient satisfaction was also evaluated by asking the patients to rate their satisfaction with the treatment they received using a rating from 1 to 4: unsatisfied (1), partly satisfied (2), somewhat satisfied (3), and satisfied (4).

Descriptive statistics were used in the statistical analyses of data. In the comparison of the treatment and control groups, the normality of distribution of quantitative data was checked using the Kolmogorov-Smirnov test, and normally distributed data were compared using the independent-samples t-test (Student's test). For qualitative data, the chi-square and Fisher's exact tests were applied; $p < 0.05$ was considered statistically significant.

Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Health Sciences University Ankara Numune Healthcare and Research Center with the decision number 1704/2017 dated 03.01.2018, and necessary permission was taken from the Turkish Medicines and Medical Devices Agency with the letter numbered 93189304-514.05.01-E.34718, 2018.

RESULTS

Two of the patients initially included in the study were excluded because they were lost to follow-up. The study was completed with 58 patients, of whom 29 were in the HBO_2 group and 29 in the control group. Power analysis was performed with the number of patients participating in the study; Type I error was taken as 5% , and the power of the study was found to be more than 80% at the 95% confidence level.

The overall sample consisted of 29 women and 29 men with a mean age of 41.26 ± 14.74, (range 18 to 65) years, and the mean burned total body surface area was 9.22 ± 3.43% (range 5% to 20%). The most common cause of burn injuries was scalding (38 patients, 65.5%), while flame burns were observed in 18 (31%) patients and electric arc burns in two (3.4%). A total of 17 (29.3%) patients underwent surgical procedures, and eight (13.8%) patients received grafts. Infection was observed in three (5.2%) patients. Among the 29 patients in the HBO_2 group, an average of 9.72 ± 3.41 (range 5 to 16) and median number of nine sessions of therapy were applied. The treatment cost of the whole group was calculated as 2,422.71 ± 1,495.40 TL (Turkish lira).

There were 14 (48.3%) females and 15 (51.7%) males in the HBO_2 group, and 15 (51.7%) females and 14 (48.3%) males in the control group ($p = 1.0$). The mean age was 40.21 ± 13.53 years in the HBO_2 group and 42.31 ± 16.0 years in the control group ($p = 0.591$). The most common burn agent was scalding in both groups (Table 1). Burn etiologies and burned total body surface area (TBSA) did not statistically differ between the two groups (Table 1).

During the treatment process, fewer patients in the HBO_2 group required surgical intervention (10.3 vs. 48.3%) and grafting (3.4 vs. 24.1%) ($p = 0.003$ and $p = 0.03$, respectively) (Table 2). There was no significant difference in the rate of infection between the two groups. When patient satisfaction was evaluated, the results were more positive for the HBO_2 group ($p = 0.03$) (Table 2).

The mean LOHS was 10.52 ± 7.605 days in the HBO_2 group, which was 2.65 ± 1.97 days shorter than the mean value control group. The mean duration of epithelialization was 13.48 ± 4.372 days in the HBO_2 group, which was 8.93 ± 1.28 days shorter compared to the control group ($p < 0.001$) (Table 3). When the treatment cost was evaluated, the mean cost was 2,239 ± 1,384.137 TL ($464.52 ± $287.13 US) for the HBO_2 group, which was 365.75 ± 393.17 TL ($75.8±$81.5 US) lower compared to the control group.

DISCUSSION

In our PubMed and MedLine search on the efficacy of HBO_2 only in partial-thickness dermal burns (deep, minor or moderate second-degree burns), we did not find any study other than animal experiments and a review published in 2019 [14], which shows our study can be considered as the first research in humans.

In the literature, studies have been carried out in patients with full-thickness burns, in which burn area was reported without including information on burn depth. For example, Niezgoda et al. conducted an experimental study on HBO_2 in burns, but they did not evaluate the parameters of cost, surgery frequency, graft requirement, patient satisfaction,

Table 1: Comparison of the patients' parameters among the study and control groups

		HBO_2 group n	(%)	control group n	%	p
gender	female	15	(51.7)	14	(48.3)	1.000
	male	14	(48.3)	15	(51.7)	
age	years (±SD)	40.21	(±13.53)	42.31	(±16.0)	0.60
burn agent	scalding	20	(69.0)	18	(62.1)	0.85
	flame	8	(27.6)	10	(34.5)	
	electric arc	1	(3.4)	1	(3.4)	
burned TBSA	% (±SC)	8.48	(±3.46)	9.97	(±3.30)	0.10

SD = standard deviation; TBSA = total body surface area

Table 2: Evaluation of the patients' treatment parameters

		HBO_2 group n	(%)	control group n	(%)	p
surgery	Yes	3	(10.3)	14	(48.3)	0.003
	No	26	(89.7)	15	(51.7)	
grafting	Yes	1	(3.4)	7	(24.1)	0.03
	No	28	(96.6)	22	(75.9)	
infection	Yes	1	(3.4)	2	(6.9)	1.000
	No	28	(96.6)	27	(93.1)	
patient comfort	unsatisfied	0	(0)	2	(6.9)	*0.14
	partly satisfied	10	(34.5)	14	(48.3)	
	somewhat satisfied	14	(48.3)	12	(41.4)	
	satisfied	5	(17.2)	1	(3.4)	
satisfaction	1 to 4 mean (±SD)	2.83	(±0.711)	2.41	(±0.682)	†0.03

*Since four cells had expected counts less than 5 at Pearson chi-square test and the p-value was found to be 0.029 using the linear-by-linear association test; †Student's t-test was repeated to compare the mean values.

Table 3: Comparison of the treatment parameters and costs of the groups

variables		mean	standard deviation	p
length of hospital stay	HBO_2	10.52	7.605	0.17
	control	13.17	6.903	
epithelialization time	HBO_2	13.48	4.372	< 0.001
	control	22.41	5.329	
cost	HBO_2	2,239.83 TL ($464.52*)	1,384.137 TL ($287.13*)	0.36
	control	2,605.59TL ($540.57*)	1,602.247 TL ($332.41*)	

*2018 USD-TL exchange rate: 1$ = 4.82 TL

and LOHS. In that study, wound size, amount of hyperemia and exudate in the wound site, and epithelialization were evaluated in superficial burns [15]. In the literature, there are also studies investigating various burned TBSA groups, but since the systemic effects and depth of burns in these patients were not evaluated on the basis of subgroups, the direct effects of HBO_2 on burn wound healing could not be discussed [16-18]. In our study, in order to exclude the systemic effects of burn injuries we evaluated only minor and moderate cases of deep second-degree burns that did not require intensive care follow-up. These criteria allowed for the demonstration of the direct effect of HBO_2 on burn healing.

The ischemic area specified in the stasis zone, one of the Jackson burn zones, either deepens over time or the damage can be reversed [19]. In the damage reversal process, the treatment applied to the patient is vital. In deep second-degree partial-thickness burns, the progression of the ischemic zone to the necrosis zone may require grafting. However, if the damage is reversed, spontaneous healing can be achieved. HBO_2 has been shown to be beneficial in relieving capillary obstruction in ischemic skin, increasing capillary revascularization, resolving edema, and controlling infection by increasing the bactericidal effect of leukocytes [8,9]. In our study, 10.3% of the patients in the HBO_2 group and 48.3% of those in the control group required surgery. Thus, HBO_2 was

determined to reduce the need for surgery in partial-thickness burns ($p = 0.003$). Although various studies in the literature have presented the results of graft requirement or graft loss, none provided patient standardization based on a certain burn area or depth [16,17,20-22]. In this sense, this study can be considered as the first to be conducted with a patient group that does not have systemic effects, since we evaluated only partial-thickness burns of minor and moderate nature, which represents the group that is most discussed in terms of the surgical or conservative approach. HBO_2 promotes oxygen diffusion for Jackson ischemic burn areas (ischemic/intermediate zone) and increases cell-based nutrition with its edema-reducing effect. It is also known that HBO_2 increases neovascularization, stopping the progression of the ischemia zone to the necrosis zone in partial-thickness burns and preventing the conversion of partial- to full-thickness burns. The results of our study indicate that HBO_2 is a treatment modality that reduces the need for surgery, debridement and subsequent grafting by minimizing the development of full-thickness burns.

In our evaluation of the effect of HBO_2 on graft requirement we determined that grafting was performed in 3.4% (1/29) patients in the HBO_2 group and in 24.1% (7/29) patients in the control group. Thus, HBO_2 reduced the need for grafting in partial-thickness dermal burns ($p = 0.026$). In a 1974 study conducted by Hart et al. without standardization of burn depth or area in a very small patient group, grafts were placed in three of the eight patients in the HBO_2 group and two of the eight patients in the control group. While all three grafts placed in the HBO_2 group were intact, one of the two grafts placed in the control group was lost. According to the same study, HBO_2 did not reduce the need for grafting, but it did provide benefits in terms of the preservation of grafts [20]. In a study by Chiang et al. conducted in 2017 after an explosion in Taiwan, the mean number of required grafts was 4.37 ± 0.67 for the HBO2 group and 3.87 ± 1.29 for the control group ($p = 0.710$) [23]. However, the authors did not distinguish between major and other burns, and they only discussed the effect of HBO_2 on mortality and sepsis. Unlike our study, neither of these studies applied a limitation on burn depth in their patient selection, and many of the patients included in these studies had major burns and were under the systemic catabolic effect. HBO_2 reduces the need for grafting by increasing oxygen diffusion into the tissue and preventing the increase in burn depth [20,23]. These effects of HBO_2 statistically significantly reduced the need for grafting in our sample. In the study, hospitalized treatment was terminated when the patients were evaluated to be suitable for outpatient follow-up. LOHS was significantly shorter in the HBO_2 group. We consider this shorter hospital stay to be the most important reason why the patients in the HBO_2 group were also more satisfied with treatment.

The epithelialization time of burn wounds was also significantly shorter in the HBO_2 group (8.93 ± 1.28 days shorter compared to the control group), independent of the length of hospitalized or outpatient treatment. Early healing of wounds not only contributes to patient comfort but also reduces treatment costs. In the 1974 prospective randomized study of Hart et al., the epithelialization time was 19.7 days in the HBO_2 group and 43.8 days in the control group. Despite the limitation of not considering burn depth, the authors showed that HBO_2 reduced the epithelialization time ($p < 0.001$) [20].

It is inevitable that HBO_2 adds to the cost of standard burn wound dressing. However, according to the results of our study, the addition of HBO_2 to conventional treatment reduced the total cost of burn treatment by shortening LOHS, reducing the need for surgery and grafting, and decreasing the epithelialization time. All the studies in the literature are two to three decades old. In our more recent study, no significant difference was observed between the two groups. However, while the patients in the HBO_2 group were successfully treated with non-invasive techniques, surgery and grafts were required at a significant rate in the control group. Considering that as a result of grafting, donor site injury is added to burn wounds, the cost of treatment without surgery

and grafting is similar to the group receiving conventional treatment alone, which means that HBO_2 is also cost-effective [16,17,21].

HBO_2 is a treatment modality that affects patient satisfaction in burn treatment. In our study the number of satisfied patients was higher and that of unsatisfied patients was lower in the HBO_2 group compared to the control group. In the literature, there is a retrospective study evaluating satisfaction with HBO_2 in burn cases [24], but we found no prospective study. In this regard our study is the first publication to evaluate satisfaction in patients with burn injuries undergoing HBO_2, and we found this treatment to be of significant benefit.

In our study, the mean LOHS was shorter in the HBO_2 group. There is no consensus regarding LOHS in the literature [16,17,21-25]. If we had continued the conventional treatment of patients who underwent surgery, we could have detected longer hospital stays and later recovery, as was reported by Hart et al. [20]. In light of current medical information, since the risk of hypertrophic scarring and contracture increases in late-healing wounds, we considered it to be unethical to wait for epithelialization without grafting, and therefore performed this procedure. Although the difference in LOHS between the two groups was not significant in our study, HBO_2 shortened the mean LOHS by 2.65 ± 1.97 days compared to the control group. Since full-thickness burns and major burns were not included in our study, mortality was not investigated. In the literature, mortality is among the parameters investigated in studies without burn depth and burn area restrictions. While Brannen et al, Chiang et al, and Waisbren et al. found no statistical difference in mortality with HBO_2 [22,23,26], Grossman et al. reported the mortality rate to be lower in the HBO_2 group [25].

Study limitations

This study was prospective but not randomized and not blinded. Patients received HBO_2 five days a week, but it would have been better to evaluate them every day of the week. Lastly, results should be evaluated over a longer period in order to more clearly reveal the long-term effects of HBO_2 on hypertrophic scar and keloid formation. There is a need for randomized controlled studies to address the beneficial effects of HBO_2 and also to reinforce our findings.

CONCLUSION

With deep second-degree dermal burns there is no consensus regarding whether to perform early surgery and grafting or to wait for spontaneous epithelialization with dressings. In this study, we compared conventional treatment alone to conventional treatment plus HBO_2 in a selected patient group with only deep second-degree burns to prevent comorbidities affecting wound healing in the presence of minor and moderate burns; therefore, this is the first human study in the literature evaluating the direct wound healing effects of HBO_2. According to the results, HBO_2 reduced the need for surgery and grafting and shortened LOHS and hospitalization time, which all contributed to increased patient satisfaction. Despite the additional cost of HBO_2, the reduction in the need for surgery and LOHS decreased the overall treatment cost. Therefore, the addition of HBO_2 to conventional treatment should be evaluated as an option in the management of burn cases that are eligible for this therapy since it not only shortens the epithelization time and reduces the need for surgery but also positively affects overall patient outcomes. ■

Acknowledgment

We would like to thank Selcen Abayli, MD, for her effort during the application of HBO_2 during the study.

Availability of data and materials

Original data not included in the manuscript can be obtained from the authors. Please contact the corresponding author via email.

Authors' contributions

All authors have substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; drafting the article, responsibility for the integrity of the work as a whole, revising the article critically for important intellectual content and final approval of the version to be published,

REFERENCES

1. Rawlins JM. Management of burns. Surgery - Oxford International Edition, 2011. 29(10): 523-528.

2. Burns, 2018; WHO Fact Sheets; https://www.who.int/news-room/fact-sheets/detail/burns (Accessed July 2021)

3. Singer AJ, Toussaint J, Chung WT, McClain SA, Raut V, Rosenberg L. Early versus delayed excision and grafting of full-thickness burns in a porcine model: a randomized study. Plast Reconstr Surg. 2016 Jun;137(6):972e-979e. doi: 10.1097/PRS.0000000000002161. PMID: 27219266.

4. Omar MT, Hassan AA. Evaluation of hand function after early excision and skin grafting of burns versus delayed skin grafting: a randomized clinical trial. Burns. 2011 Jun;37(4):707-713. doi: 10.1016/j.burns.2010.12.012. Epub 2011 Jan 26. PMID: 21276660.

5. Monstrey S, Hoeksema H, Verbelen J, Pirayesh A, Blondeel P. Assessment of burn depth and burn wound healing potential. Burns. 2008;34(6):761.

6. Shin JY, Yi HS. Diagnostic accuracy of laser Doppler imaging in burn depth assessment: Systematic review and meta-analysis. Burns. 2016;42(7):1369-1376.

7. Hettiaratchy S, Papini R. Initial management of a major burn: II—assessment and resuscitation. BMJ, 2004; 329: 101-103.

8. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. N Engl J Med. 1996 Jun 20;334(25):1642-1648. doi: 10.1056/NEJM199606203342506. PMID: 8628361.

9. Leach RM, Rees PJ, Wilmshurst P. Hyperbaric oxygen therapy. BMJ. 1998 Oct 24;317(7166):1140-1143. doi: 10.1136/bmj.317.7166.1140. PMID: 9784458; PMCID: PMC1114115.

10. Gill AL, Bell CN. Hyperbaric oxygen: its uses, mechanisms of action and outcomes. QJM. 2004 Jul;97(7):385-395. doi: 10.1093/qjmed/hch074. PMID: 15208426.

11. Nguyen TT, Gilpin DA, Meyer NA, Herndon DN. Current treatment of severely burned patients. Ann Surg. 1996 Jan;223(1):14-25. doi: 10.1097/00000658-199601000-00004. PMID: 8554414; PMCID: PMC1235059.

12. Wolf SE, Debroy M, Herndon DN. The cornerstones and directions of pediatric burn care. Pediatr Surg Int. 1997 Jul;12(5-6):312-320. doi: 10.1007/BF01076929. PMID: 9244089.

13. Villanueva E, Bennett MH, Wasiak J, Lehm JP. Hyperbaric oxygen therapy for thermal burns. Cochrane Database Syst Rev. 2004;(3):CD004727. doi: 10.1002/14651858.CD004727.pub2. PMID: 15266540.

14. Weitgasser L, Ihra G, Schäfer B, Markstaller K, Radtke C. Update on hyperbaric oxygen therapy in burn treatment. Wien Klin Wochenschr. 2021 Feb;133(3-4):137-143. doi: 10.1007/s00508-019-01569-w. Epub 2019 Nov 7. PMID: 31701218.

15. Niezgoda JA, Cianci P, Folden BW, Ortega RL, et al. The effect of hyperbaric oxygen therapy on a burn wound model in human volunteers. Plast Reconstr Surg. 1997 May;99(6):1620-1625. PMID: 9145132.

16. Cianci P, Lueders HW, Lee H, Shapiro RL, et al. Adjunctive hyperbaric oxygen therapy reduces length of hospitalization in thermal burns. J Burn Care Rehabil. 1989 Sep-Oct;10(5):432-435. doi: 10.1097/00004630-198909000-00012. PMID: 2793923.

17. Cianci P, Williams C, Lueders H, Lee H, et al. Adjunctive hyperbaric oxygen in the treatment of thermal burns. An economic analysis. J Burn Care Rehabil. 1990 Mar-Apr;11(2):140-143. doi: 10.1097/00004630-199003000-00009. PMID: 2110567.

18. Chong SJ, Kan EM, Song C, Soh CR, Lu J. Characterization of early thermal burns and the effects of hyperbaric oxygen treatment: a pilot study. Diving Hyperb Med. 2013 Sep;43(3):157-161. PMID: 24122191.

19. Jackson DM. [The diagnosis of the depth of burning]. Br J Surg. 1953 May;40(164):588-96. Undetermined Language. doi: 10.1002/bjs.18004016413. PMID: 13059343.

20. Hart GB, O'Reilly RR, Broussard ND, Cave RH, Goodman DB, Yanda RL. Treatment of burns with hyperbaric oxygen. Surg Gynecol Obstet. 1974 Nov;139(5):693-6. PMID: 4610853.

21. Cianci P, Slade JB Jr, Sato RM, Faulkner J. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns. Undersea Hyperb Med. 2013 Jan-Feb;40(1):89-108. PMID: 23397872.

22. Brannen AL, Still J, Haynes M, Orlet H, et al. A randomized prospective trial of hyperbaric oxygen in a referral burn center population. Am Surg. 1997 Mar;63(3):205-208. PMID: 9036884.

23. Chiang IH, Chen SG, Huang KL, Chou YC, et al. Adjunctive hyperbaric oxygen therapy in severe burns: Experience in Taiwan Formosa Water Park dust explosion disaster. Burns. 2017 Jun;43(4):852-857. doi: 10.1016/j.burns.2016.10.016. Epub 2016 Dec 27. PMID: 28034667.

24. Chen KL, Wu CJ, Tseng WS, Lee HC, et al. Improvement of satisfaction in burn patients receiving adjuvant hyperbaric oxygen therapy. Formos J Surg 2018;51:184-191.

25. Grossman AR. Hyperbaric oxygen in the treatment of burns. Ann Plast Surg. 1978 Mar;1(2):163-171. doi: 10.1097/00000637-197803000-00006. PMID: 365048.

26. Waisbren BA, Schutz D, Collentine G, Banaszak E, Stern M. Hyperbaric oxygen in severe burns. Burns Incl Therm Inj. 1982 Jan;8(3):176-179. doi: 10.1016/0305-4179(82)90084-5. PMID: 7059858.