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Hyperbaric Oxygen Therapy: A Must for Trauma Centers?

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Abstract

Background: Wounds that do not heal as expected are a matter of great concern for both the patient and the clinician. These are in turn subjected to variety of adjuvant therapies including Hyperbaric Oxygen Therapy (HBOT), which despite growing evidence, still has debatable indications. We aim to examine and report on the factors determining its applicability in a trauma center.

Methods: A retrospective analysis of all patients subjected to adjunctive HBOT between November 2016 and March 2020 was performed. Patients were given adjunctive HBOT while adhering to wound bed preparation principles and best practices of care. Demographic data, wound characteristics and outcomes of therapy in relation to predefined treatment goal were analyzed.

Results: A total of 268 cases were given therapy with most common indication being surgical wound dehiscence (32.8%). Post-traumatic wounds from road traffic accidents made up 74.2% of the total. 71.9% of individuals who received therapy met their treatment objectives out of which 78.6% post-surgical wounds, 78.3% of post-traumatic wounds and 86.1% of non-healing wounds achieved treatment goals, the results being statistically significant only for non-healing wounds. Wounds that did not meet treatment goals included digital ischemia of hand (72.2%) or Frost Bite (100%) as well as flaps with compromised vascularity (64.2%). HBOT was shown to improve healing rates for all wound ages, whether chronic, subacute, or acute. It was also shown to play a significant role in healing of infected wounds.

Conclusion: In our experience, HBOT service is a must for a busy trauma center. We recommend that the therapy be included in wound healing management algorithms for all kinds of acute or chronic wounds and administered on case-to-case basis.

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Exercise of evidence and study type: Level V, therapeutic/care management.

Keywords: Surgical wound infection; Surgical flaps; Frostbite; Crush injuries; Acute traumatic wounds

Introduction

Wounds, particularly post-surgical complicated wounds, are a matter of great concern for both the patient and the clinician alike. They not only add to morbidity in terms of prolonged healing time but also cause mortality from sepsis and cachexia [1]. In addition, they increased the frequency and duration of hospital admissions and lost time from work [2]. That is why successful and timely healing of wounds significantly improves the quality of life [3]. We know today that it is a complex yet well-orchestrated dynamic process [4].

For achieving proper healing, it is necessary that the wound bed be moist, well vascularized, and free of devitalized tissue and infection [5]. Thus, the wound is subjected to debridement, topical and/or systemic therapy, and most importantly, a suitable dressing. On the other hand, despite optimizing patient and local factors, in some individuals, there can be delayed wound healing that can complicate surgical outcomes.

To close a difficult-to-heal wound, we must explore a variety of adjuvant therapies, one of which is Hyperbaric Oxygen Therapy (HBOT). It is a technique for delivering 100% oxygen at a higher atmospheric pressure. Oxygen plays a pivotal role in the angiogenesis process, in fibroblast function, epithelialization and infection control [6]. Thus, HBOT can be a beneficial treatment for wounds with impaired healing. In recent years, the body of evidence on HBOT has increased. An international consensus conference has issued recommendations on the appropriate use of this technology. It serves as primary or adjunctive therapy for a diverse range of medical conditions namely carbon monoxide poisoning, decompression sickness, air embolism, radiation injury, diabetic foot lesions, open fractures with crush injury, and compromised skin grafts and flaps [7]. Despite reports of the beneficial role of HBOT in wound healing [8-10], its application in routine clinical practice is yet to gain momentum. Frequently, there are situations where HBOT is tried with the hope that it might help but with limited overall confidence in its usefulness.

Therefore, through this study, we aim to examine the impact of HBOT on the management of various types of wounds and clinical situations arising in a busy trauma center and report on its overall clinical outcomes.

Materials and Methods

Patients

This study describes a retrospective audit of pertinent data derived from patient records prospectively maintained by the HBOT nursing therapist in a level 1 Trauma Center. The study was performed in accordance with the principles outlined in the Declaration of Helsinki and Institutional Ethics Committee approval was obtained prior to starting the study. The study involved minimal risk to patients, and the absence of patient identifiers in the data set, hence it was performed under a waiver of consent. All consecutive patients with wounds due to varying etiologies who were given HBOT between November 2016 and March 2020 were included in the analysis.

HBOT was either introduced in the acute care setting, such as for acute traumatic wounds or on an outpatient basis for those with chronic non-healing wounds as a bridge to surgery. The duration of therapy was decided as per the institution's protocol and was tailored on a case-to-case basis and tolerance by the patients. Patients with chronic obstructive pulmonary disease, previous spontaneous pneumothorax, chronic sinusitis, chronic otitis media, unstable angina, severe congestive heart failure, claustrophobia, severe dementia, and a history of seizures were excluded from HBOT administration. Hemodynamically unstable patients were also deferred until stable. The wound bed preparation principles were properly followed [5]. Wound debridement was performed as and when necessary. Patients receiving HBOT were encouraged to follow best-practice wound-care principles [11], such as limb elevation for acute traumatic wounds, compression for venous leg ulcers, off-loading for neurotrophic ulcers, blood glucose control for diabetic foot ulcers (where the wounds began following trauma) and general nutritional guidance. The type of dressing and other adjuvant therapies, such as negative pressure wound therapy, were selected based on clinical discretion. For example, in wounds that were highly exudative and had a high bacterial burden, twice-daily wound dressing was done and an antimicrobial agent was selected according to departmental protocols.

Hyperbaric oxygen therapy procedure

A standard HBOT treatment for a wound at our center consisted of placing the patient in a Monoplace chamber (Figure 1). In ten minutes, the pressure in the chamber was raised to 2.5 Atmospheres Absolute (ATA). When the pressure reached 2.5 ATA, 100% oxygen was administered in three 20-min sessions using a face mask, followed by five minutes of room air and a final 15-min session of oxygen therapy. After that, the pressure was reduced in 10 minutes, with oxygen decompression up to 1.3 ATA. This resulted in a total treatment time of 110 min, with patients receiving 90 min of hyperbaric oxygen therapy at 2.5 ATA.

Data collection

At the beginning of therapy, the demographic data, wound characteristics, and the original treatment goal was recorded, and whether the treatment goal was met or not was a key outcome assessed. Treatment goals for open wounds were: Healing in the form of granulation tissue formation, reduction in wound exudate, reduction in surrounding tissue edema/redness, and preparedness for surgical closure. The treatment goal for ischemic or congested flaps was the arrest of or reduction in discoloration present at the time of instituting the therapy. The treatment goal for post-traumatic vascular compromise of digits of hand/feet as well as frostbite injuries was the cessation of progression of tissue necrosis or improvement in the viability of doubtful tissue. Data on wound status was gathered at baseline, as well as on days 3, 7, and 10 after HBOT treatment. Only those who received more than 10 sessions were subjected to additional weekly evaluations. Readiness for definitive surgical treatment was judged by three clinicians at separate times to avoid observer bias. The proportion of patients who achieve their predetermined treatment goal was one of the performance criteria. Additional information on HBOT-related adverse events was gathered.

Data analysis

The data was maintained in a Microsoft Excel spreadsheet. The following data elements were documented in this study: Patient age at the time of therapy, patient sex, primary and/or secondary diagnosis, wound(s) location(s), wound(s) age(s), wound(s) dimensions, and wound(s) character before and after HBOT, indication for starting and stopping HBOT, and the definitive surgical outcome. The statistical analysis was carried out using STATA Corp. LP, College Station, Texas, USA. Qualitative data were expressed as frequency and percentage. Quantitative data was expressed as mean \pm SD, and median (min-max) for normally distributed and skewed data, respectively. A p-value of less than 0.05 was considered significant.

Results

Patient demographics and clinical variables

From November 2016 to March 2020, the departments of plastic surgery and trauma surgery of the hospital referred 297 patients to the hyperbaric facility (a mean of 87 cases per year).

A total of 268 cases were subjected to at least one session of therapy and were analyzed in this study. They ranged in age at the time of treatment from 6 to 87 years, with a mean age of 34.5 ± 16.1 years. Patient demographics and clinical variables are summarized in Table 1. The most common indication for referral for HBOT was surgical wound dehiscence (32.8%), such as amputation stump dehiscence or laparotomy wound dehiscence. Other major indications were posttraumatic raw areas (31.0%) and non-healing wounds (14.9%). The distribution of patients, prescribed HBOT for other indications is listed in Table 1.

Less than half of the patients, 116 (43.3%), had never smoked before. Eighty patients (30.0%) had quit smoking more than six months before starting HBOT, and 18 patients (6.7%) had quit smoking within six months of starting HBOT. At the start of HBOT, 54 patients (16.7%) were still smoking. Diabetes Mellitus (DM) was Table 1: Patient demographics and wound characteristics.

	N	%
No. of patients	268	-
Patient Age (Mean, SD)	34.5 ± 16.1	-
<21 years	54	20.1%
21-64 years	200	74.6%
65+ years	14	5.2%
Gender		
Male	220	82.1%
Female	48	17.9%
Etiology		
1. Surgical wound dehiscence	86	32.1%
2. Post traumatic raw area	83	31.0%
3. Non-healing wound	40	14.9%
4. Flap Compromise	20	7.5%
Vascular compromise (digits of hand/feet)	15	5.6%
6. Frost Bite	7	2.6%
7. Diabetic Foot ulcer	6	2.2%
8. Post Burn wound	5	1.9%
9. Soft tissue infection	5	1.9%
10. Pressure ulcer	1	0.4%
Reasons for ending treatment		
Wound fit for definitive intervention	159	59.3%
Patient denied	8	2.9%
Adverse event	12	4.5%
Discontinued due to unintended result	63	23.5%
Lost to follow-up	12	4.4%
Patient expired	14	5.2%

	N	%
Wound Age		
Range (weeks)	4-574	-
<3 weeks (Acute)	132	49.2%
3-12 weeks (Subacute)	95	35.4%
>12 weeks (Chronic)	41	15.2%
Median Wound area (cm2) (range)	123 (4-2492)	
Total no. of wounds	238	
Total no. of ischemic digits	22	
Total no. of compromised flaps	20	
Wound location		^
Foot	53	19.8%
Leg	76	28.4%
Knee & Thigh	40	14.9%
Trunk	29	10.8%
Hand	28	10.5%
Rest of upper limb	25	9.3%
Others*	17	6.4%
Key Clinical outcomes		
Patients meeting their treatment objective	193	71 96 %
Median time in days to achieve treatment objective	15 3 (4-41)	-
(range)	10.0 (+ +1)	
Infection		
Non-infected	139	51.9%
Infected	129	48.1%

found in 37 (13.8%) of the patients.

Wound characteristics

The wounds ranged in age from 4 to 574 days. The leg was the most common wound location (27.8%), followed by the foot (21.7%). Patients with post-traumatic wounds from road traffic injuries made up 74.2% of the total. Hand wounds constituted 10% and were associated with industrial accidents, frostbite and road traffic injuries. The percentage of infected wounds analyzed was 49.6% (139). Non-traumatic and traumatic non-healing wounds (12.6% and

Table 3: Wound characteristics impacting wound healing.

	Treati	ment Goal m	et?
	Yes	No	P value
Wound Etiology			
Surgical wound dehiscence	59 (78.6%)	16 (21.3%)	0.113
Post traumatic raw area	58 (78.3%)	16 (21.6%)	0.132
Non-healing wounds	31 (86.1%)	5 (13.8%)	0.039
Vascular compromise (digits of hand/feet)	5 (27.7%)	13 (72.2%)	0.000
Flap Compromise	5 (35.7%)	9 (64.2%)	0.002
Frost Bite	0 (0%)	7 (100%)	0.000
Diabetic Foot ulcer	3 (75%)	1 (25%)	0.888
Post Burn	5 (100%)	0 (0%)	0.326
Soft tissue infection	4 (100%)	0 (0%)	0.579
Pressure ulcer	1 (100%)	0 (0%)	0.530
Wound Age			
<3 weeks (Acute)	79 (66.9%)	39 (33.0%)	
3-12 weeks (Subacute)	61 (73.4%)	22 (26.5%)	0.128
>12 weeks (Chronic)	31 (83.7%)	6 (16.2%)	
Wound location			
Foot	36 (72%)	14 (28%)	0.979
Leg	55 (79.7%)	14 (20.3%)	0.085
Knee & Thigh	30 (83.3%)	6 16.67	0.096
Trunk	15 (71.4%)	6 (28.5%)	0.964
Hand	10 (37.0%)	17 (63.0%)	0.000
Rest of upper limb	14 (63.6%)	8 (36.3%)	0.369
Groin, Hip	8 (80.0%)	2 (20.0%)	0.730
Head & Neck	1 (25.0%)	3 (75.0%)	0.036
Perineum	2 (100%)	0 (0%)	1.000
Patient Age			
<21 years	25 (75.8%)	8 (24.2%)	
21-64 years	91 (74.0%)	32 (26.0%)	0.31
65+ years	4 (50.0%)	4 (50.0%)	
Infection			
Infected	93 (80.2%)	23 (19.8%)	0.005
Non infected	78 (63.9%)	44 (36.1%)	0.005
Trauma			
Yes	96 (73.8%)	34 (26.2%)	0.702
No	24 (70.6%)	10 (29.4%)	0.703



Figure 1: An HBOT monoplace chamber.

2.2% respectively) were observed. Non-traumatic causes included neurological diseases such as peripheral neuropathy and spinal diseases such as meningomyelocele. Table 2 summarizes the most important clinical outcomes.

Reasons for terminating HBOT & adverse events

Twelve patients (4.4%) were lost to follow-up. Readiness of the wound for intervention was the most frequent reason for ending HBOT, followed by premature termination of therapy by the clinician owing to unintended outcomes such as failure to prevent the progression of flap ischemia or digital gangrene or worsening



Figure 2: This is a case of post road traffic accident left side hip disarticulation with extensive soft tissue infection. The wound was managed with three debridement spaced 72 h apart, wound wash and twice daily dressings with nanocrystalline silver hydrogel with adjunctive HBOT. Day 0 (A), Day 5 (B), Day 9 (C) and Day 21 images show gradual readiness of wound bed with reduction in slough and appearance of granulation tissue.



Figure 3: This is a case of post-traumatic raw area which was managed with debridement, twice daily saline wound wash and dressings with nanocrystalline silver hydrogel with adjunctive HBOT. Day 0 (A) image shows highly exudative wound with slough. It was subjected to re-debridement 72 h later. Day 7 (B) and Day 13 (C) images show marked reduction in infected tissue and improvement in granulation tissue and its readiness of the wound bed for cover.

of wound inflammation and exudate. Adverse events were noted in only 12 (4.4%) patients. Most reported earaches, and one patient developed a tympanic membrane perforation. In one other patient, therapy had to be discontinued due to claustrophobia. Eight (2.9%) patients refused to continue therapy, seeking definitive treatment.

Wound healing

Overall, 71.9% of individuals who received therapy met their treatment objectives. The median (range) number of sessions (one/ day) for those who met their goal, as well as those who didn't, was 7 (3-29). Depending on the indication, it was given either during the preoperative period (31.3%) or during the postoperative period (25.3%). It was given to some (17.5%) during both periods.

Wound etiology, patient age, wound age, wound location; traumatic vs. non-traumatic etiology, and the presence or absence of infection were all factors that influenced wound healing. Amongst various etiological causes of wounds, more than 50% of wounds were those with surgical wound dehiscence such as amputation stump dehiscence or post-traumatic raw areas and non-healing wounds such as neurotrophic ulcers showed healing after HBOT. Although 78.6% of post-surgical wounds, 78.3% of post-traumatic wounds (Figure 2, 3) and 86.1% of non-healing wounds achieved treatment goals, the result was statistically significant only for non-healing wounds (p-value: 0.03). The majority of wounds that did not meet treatment goals following HBOT were those related to vascular compromise such as digital ischemia following crush injuries to the hand (72.2%) or Frost Bite (100%) as well as flaps with compromised vascularity (64.2%) (Distal arterial insufficiency/partial or complete venous congestion). The results are statistically significant (p-value <0.05) for all three categories.



Figure 4: This is a case of Grade 4 frostbite of toes, which showed no improvement from Day 0 (A) to Day 7 (B). HBOT was terminated on day 7 for debridement of obviously necrotic tissue. This is a case of Reverse sural artery flap reconstruction supercharged to great saphenous vein done for post-traumatic composite soft tissue defect over dorsum of foot. Discoloration was noted in the peripheries from post operative day one. HBOT was administered but no improvement was observed from Day 3 (A) to Day 7 (B). HBOT was terminated on day 7. Necrotic flap was debrided, and raw area was grafted.

Wound age did not seem to determine the possibility of positive outcome with HBOT as all three categories of wounds- acute (66.9%), subacute (73.4%) and chronic (83.7%) wounds achieved treatment goals and the association wasn't statistically significant. The age of the patient also did not have an impact on the achievement of treatment goals (Table 3).

The location of the wound did not affect the attainment of treatment goals either. More than 50% of wounds located over the foot, leg, thigh and knees, hip and groin, trunk, and upper limb (other





than the hand) met their treatment goals. This was not so in the case of wounds located over the hands (37%) and head & neck wounds (25%).

Lastly, both traumatic (73.8%) and non-traumatic (70.6%) wounds achieved treatment goals. However, a statistically significant (p-value: 0.005) percentage of infected wounds (80.2%) attained treatment goals compared with non-infected wounds (63.9%).

Discussion

It is being increasingly recognized that HBOT and wound healing are tightly linked. The current clinical studies continue to provide strong and convincing evidence favoring HBOT for diabetic wounds in reducing the risk of major amputation and improving wound healing results significantly [12-14]. It has also been suggested to augment the healing of acute surgical and traumatic wounds [15-17]. However, a 2013 Cochrane review determined that there was insufficient high-quality data to support its use in the treatment of acute wounds [18]. Acute traumatic wounds constituted the majority of referrals to the HBOT service at our center. Through this study, which is one of the largest case series, we explore the potential benefit of HBOT in the management of acute wounds commonly seen in a trauma center.

In our case series, HBOT was shown to improve healing rates with more than 50% of patients meeting their treatment goals. However, our adverse event rate was 4.5%, which was quite high compared to a very low rate of 0.68% in the published literature [19]. Our relatively high rate can be explained by our low threshold for discontinuing therapy at even the slightest suspicion of barotrauma. Overall, HBOT is considered to be safe and well-tolerated. The majority of adverse effects are minor and reversible [20].

Loss to follow-up was mostly observed for outpatients. This may reflect the inconvenience of daily visits to healthcare facilities. The patients who expired while on HBOT therapy were due to various causes such as septic shock and co-existing polytrauma. The general response of those who requested premature termination of therapy was that there wasn't much improvement and they desired definitive treatment.

We also evaluated various wound characteristics (wound etiology, patient's age, age of the wound, wound location, traumatic *vs.* non-traumatic origin, and the presence or absence of infection) and their relation with clinical outcomes in patients undergoing HBOT. Based on our results, we found that HBOT not only significantly aids the healing of long-standing non-healing wounds, but it also shows a tendency to expedite the healing of immediate post-traumatic and surgical wounds, although not statistically significant. This can be

explained because oxygen is a critical modulator of normal wound healing and plays a key nutritional and "cell signal" role, thereby promoting angiogenesis, collagen deposition, fibroplasia, and epithelization [21].

On the other hand, it failed to aid in the salvage of acute traumatic ischemic digits and those with frostbite. A review of clinical notes of patients with ischemic digits was done, and it was noted that patients (n=5) who had positive outcomes had undergone microsurgical revascularization. The rest (n=13) had mutilating injuries to their hands not amenable to revascularization. These findings are supported by another study [22] which showed that a combination of microsurgery and early intervention using adjunctive HBOT was effective in preserving partially viable tissue and restoring hand function in patients with a mutilated hand injury.

The detailed review of the charts of patients with frostbite showed that patients had poor prognoses at the time of enrolment and were subjected to empirical HBOT but with little hope. Except for one, all of the patients were army personnel who were airlifted from a high altitude. That one other patient was a mountain climber who was airlifted from Mt. Everest base camp (Figure 4). For these patients (n=7) by the time treatment was started, permanent damage had probably already set in. Although the literature on the subject is limited, a number of case studies have shown that HBOT can be used to effectively treat frostbite [23,24]. We, therefore, advise that for such indications, case selection needs to be very specific and any surgically treatable causes of ischemia should be remedied simultaneously with HBOT.

HBOT was also employed as a non-operative attempt to salvage compromised flaps or after the re-exploration of compromised free flaps. HBOT can enhance the salvage of compromised flaps, decreasing the need for additional flap surgeries [25]. However, in our series of 14 patients, we did not see similar results.

During careful chart review of those patients (n=9) with unsuccessful outcomes (Figure 5), non-response to HBOT was attributable to errors in planning (n=4), flap harvested larger than the territory of its vascular supply (n=3), and pedicle injury (n=2). We, therefore, recommend HBOT is not a substitute for mechanical causes of interruption in the vascular supply of flaps (either arterial or venous) and that all surgically correctable conditions causing flap compromise should be reversed as soon as they are discovered.

Infection continues to be a key barrier in the treatment of acute traumatic wounds. Our wound practice guidelines for infected wounds include meticulous debridement; wound washing with nanocrystalline silver-based solutions, as well as the use of silver impregnated dressings, in addition to the use of adjunctive. **HBOT** in our case series, we found statistically significant results favoring the use of HBOT in infected wounds. In our series, all four patients with necrotizing fasciitis following trivial trauma had limb salvage and successful wound healing. HBOT is believed to promote the efficiency of leukocytes to kill pathogens by phagocytosis, which may help in controlling infection. To inactivate pathogens within phagosomes, phagocytosis necessitates a substantial amount of oxygen to create reactive species such as free radicals. HBOT causes an increase in the production of oxygen free radicals, which oxidize proteins and membrane lipids, damage DNA, and prevent bacteria from performing their metabolic processes. The efficacy of antibiotics like aminoglycosides has also been reported to improve after administration of hyperbaric oxygen [26]. HBOT also controls anaerobic organisms by suppressing clostridial-toxin generation in gas gangrene [27,28].

Oedema develops in all acute traumatic wounds, which can inhibit wound healing [29]. HBOT lowers wound inflammation by reducing the ability of circulating neutrophils to attach to target tissues, protecting the endothelium, lowering its porosity, and thereby lowering interstitial edema. Although the findings in our case series were not statistically significant, we obtained results favoring HBOT as an add-on therapy for traumatic wounds, which can be explained by the mechanism described above.

In our case series, patients >65 years of age had a limited representation (5.2%) and an equivocal result of 50% each was observed for those meeting or not meeting their treatment goals. Although the sample size is small and because of equivocal results, we suggest a guarded decision to enroll geriatric patients for HBOT because of the higher prevalence of conditions like chronic obstructive pulmonary disease, unstable angina, and congestive heart failure, which are contraindications for HBOT.

Depending upon the location of the wounds, we found that HBOT didn't prove useful for the hand, head and neck. Hand injuries with acute ischemia, especially those with a severe crush component, are not suitable for HBOT as there is a mechanical disruption to peripheral vascular supply, which unless restored, will not let the elevated oxygen in the blood reach the ischemic tissues and reverse the damage. Similarly, the head and neck are highly vascular regions, wounds in this region are usually not hypoxic, and instituting HBOT may not make any difference.

Limitations of the Study

It is evident that demonstrating hypoxia in wounds is essential if HBO treatment is to be beneficial. If this sophisticated and expensive treatment is to be performed cost-effectively, a therapeutic endpoint must be determined. Transcutaneous oxygen technology is used for peri-wound oxygen mapping and can detect underlying hypoxia, determine whether regional perfusion is present in sufficient volumes to transfer centrally delivered hyperbaric oxygenation to the wound margin, assess for early angiogenic response, and assess for "normalized" tissue transcutaneous oxygen [30]. This facility is not available at our center and its absence may have resulted in overuse as well as underuse of HBOT. Secondly, this technology will allow us to tailor the compression protocols based on the type of wound and its level of hypoxia, rather than using one standard protocol for a variety of wounds. We, therefore, recommend further studies where this technology is employed to assess starting and ending points of HBOT. Finally, having a control group would have strengthened the evidence, but this study lacked one because it would be unethical not to administer HBOT to patients with complicated wounds.

Conclusion

HBOT and wound healing are tightly connected. It accelerates the healing of acute traumatic wounds by reducing inflammation and edema. In our experience, HBOT service is a must for a busy trauma center. We recommend that the therapy be included in wound healing management algorithms for all kinds of acute or chronic wounds and administered on a case-to-case basis because only in appropriately selected cases HBOT can play a significant adjunctive role. Finally, without appropriate surgical and medical wound management, HBOT cannot be expected to be a miraculous solution and efforts should be made to integrate best practices into wound management.

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