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# Adjunctive hyperbaric oxygen therapy in severe burns: Experience in Taiwan Formosa Water Park dust explosion disaster

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## ABSTRACT

**Background:** Despite major advances in therapeutic strategies for the management of patients with severe burns, significant morbidity and mortality is observed. Hyperbaric oxygen therapy (HBOT) increases the supply of oxygen to burn areas. The aim of this study was to determine whether HBOT is effective in the treatment of major thermal burns.

**Methods:** On June 27, 2015 in New Taipei, Taiwan, a mass casualty disaster occurred as fire erupted over a large crowd, injuring 499 people. Fifty-three victims (20 women and 33 men) were admitted to Tri-Service General Hospital. Thirty-eight patients underwent adjunctive HBOT (HBOT group), and 15 patients received routine burn therapy (control group). Serum procalcitonin (PCT) level, a sepsis biomarker, was measured until it reached normal levels ( $<0.5 \mu\text{g/L}$ ). The records of all patients from June 2015 to March 2016 were analyzed retrospectively. Outcome measures that were compared between the groups included the use of tracheostomy and hemodialysis, total body surface area (TBSA) and the number of skin graft operations, length of hospital stay, infection status, and mortality.

**Results:** The mean age of the patients was 22.4 years, and the mean TBSA was 43%. All the patients survived and were discharged without requiring limb amputation or being permanently disabled. Patient characteristics did not differ significantly between the groups. PCT levels returned to normal significantly faster ( $p = 0.007$ ) in the HBOT group.

**Conclusion:** Multidisciplinary burn care combined with adjunctive HBOT improves sepsis control compared with standard treatment without HBOT. Prospective studies are required to define the role of HBOT in extensive burns.

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## 1. Introduction

Burn accidents in large-scale events can be a devastating public health crisis. Burn is often a devastating event for the patient because of the physical and psychosocial trauma, and severe burns can lead to significant morbidity and mortality [1]. The revised Baux score developed by Osler et al. [2] to predict mortality after burn is calculated as the sum of age and the total body surface area (TBSA) burned plus 17 points for inhalation injury. The treatment of acute burns includes fluid resuscitation and the maintenance of hemodynamic stability, escharotomy, nutritional support, topical and intravenous antimicrobials, wound dressing, surgical debridement, and skin graft [3].

The pathophysiology of acute burn proceeds in a time-dependent manner. Therefore, proper and timely intervention and control of the pathogenic mechanisms involved in thermal injury are critical to a successful clinical outcome. Oxygen can stimulate wound healing because the enzymes involved in bacterial killing, collagen synthesis, angiogenesis, and epithelialization require a plasma oxygen level of >25 mmHg in the wound tissue [4–6]. Hyperbaric oxygen therapy (HBOT) is a treatment designed to increase the supply of oxygen to the burn area and thus improve healing. However, the results of a systematic review and a randomized prospective trial did not find sufficient evidence to support or refute the effectiveness of HBOT in the management of thermal burns [7,8].

On June 27, 2015, flammable starch-based powder exploded at Formosa Fun Coast, a recreational water park in New Taipei City, Taiwan. This was one of Taiwan's worst mass burn casualty incidents in which 499 people were injured and 15 died [9]. Fifty-three patients were sent to Tri-Service General Hospital for burn management. The aim of this research was to study the effects of HBOT in these patients who suffered from starch-based powder explosive burns.

## 2. Materials and methods

On June 27, 2015, 53 patients with explosive burn were sent to Tri-Service General Hospital, Taipei, Taiwan. The patients were immediately assessed by plastic surgeons to determine the TBSA and burn depth. The patients were randomly and equally assigned to seven plastic surgeons. The members of the burn teams included respiratory therapists, pharmacists, psychiatrists, physical therapists, nephrologists, and infectious disease experts, who were all immediately involved in the treatment of these patients.

All the patients received the same treatment according to the burn treatment protocol of our hospital that included fluid resuscitation, nutritional support, topical and intravenous antimicrobials, wound dressing, and surgical treatment. Patients with inhalation injury proven by bronchoscopy were intubated and transported to the intensive care unit. All the burn patients were immediately given broad-spectrum antibiotic therapy, and this was later adjusted according to the culture reports. Serum procalcitonin (PCT) is a sepsis biomarker whose level is used to guide antibacterial therapy

and its duration [10,11]. PCT levels were measured daily until they reached normal levels (<0.5 µg/L).

Because of the limited availability of hyperbaric chamber space, it was not possible for all patients to receive HBOT. Moreover, the effectiveness of HBOT in burn treatment is controversial. Therefore, 38 patients under the care of five plastic surgeons received adjunctive routine burn management and adjuvant HBOT (HBOT group), and 15 patients under the care of two plastic surgeons were treated with routine burn management as described above (control group). The decision to receive HBOT or not was according to the preference of the surgeons. All the patients were older than 18 years. The exclusion criteria for the HBOT group were pregnancy, pneumothorax, severe chronic obstructive pulmonary disease, recent chest surgery, upper- or lower-airway infection, psychiatric conditions (particularly claustrophobia), concussion or head injury, convulsions, epilepsy, or heart disease (ejection fraction < 35%). The patients in the HBOT group received HBOT as soon as their hemodynamic variables were stable. The number of HBOT sessions was decided by the plastic surgeons and doctors administering the HBOT according to the wound condition.

The clinical and demographic data (mean age, sex, degree of burn, presence or absence of inhalation injury, and admission lab data) of the two groups are summarized in Table 1. The patient outcomes, such as the need for tracheostomy and hemodialysis, TBSA and number of skin graft operations, TBSA of re-graft, length of hospital stay, days required for the normalization of PCT levels, and number of sessions and complications of HBOT from June 2015 to March 2016 were recorded and analyzed retrospectively (Table 2).

The study was approved by the Tri-Service Hospital Institutional Review Board Committee before the initiation of the data analysis.

### 2.1. HBOT protocol

Each patient in the HBOT group was positioned in the hyperbaric chamber and received 90 min of 100% oxygen at 2.5 atmosphere absolute (ATA) while inside the chamber. Patients used the chamber 5 days per week except on the day of an operation or if their hemodynamics were unstable.

### 2.2. Statistical analysis

Statistical analyses were performed using SPSS for Windows (version 16.0; SPSS, Inc., Chicago, IL, USA). The chi-square test was used to analyze the treatment efficacy. Fisher's exact test was used instead of the chi-square test when any expected frequency was <1 or when 20% of the expected frequencies were ≤5. Results are expressed as the mean ± standard deviation (SD). A p-value of <0.05 was considered to indicate significance.

## 3. Results

The mean age of the 53 admitted patients (20 women and 33 men) was 22.43 years, and their mean TBSA was 42.97%. All the patients were healthy with no medical problems except for the

**Table 1 – Patient characteristics.**

	Control (n = 15)	HBOT (n = 38)	t or $\chi^2$	p-value <sup>a</sup>
Age, mean $\pm$ SD	23.40 $\pm$ 0.96 years	22.05 $\pm$ 0.61 years	1.185	0.242
Sex, n (%)			0.010	0.920
Female	5 (33.33)	15 (39.47)		
Male	10 (66.67)	23 (60.53)		
TBSA, n (%)			–	0.451 <sup>b</sup>
<23%	5 (33.33)	8 (21.05)		
23–39%	1 (6.67)	9 (23.68)		
40–59%	4 (26.67)	12 (31.58)		
$\geq$ 60%	5 (33.33)	9 (23.68)		
Total TBSA	40.45 $\pm$ 6.72%	43.96 $\pm$ 2.92%	0.561	0.577
Third degree TBSA	23.39 $\pm$ 6.50%	26.59 $\pm$ 3.14%	0.498	0.621
Inhalation injury, n (%)			0	1.000
No	8 (53.33)	20 (52.63)		
Yes	7 (46.67)	18 (47.37)		
<b>Biochemical data on admission</b>				
Albumin (g/dL)	2.54 $\pm$ 0.25	2.47 $\pm$ 0.13	0.263	0.794
WBC (/mm <sup>3</sup> )	19,945.00 $\pm$ 3952.30	22,299.72 $\pm$ 1467.44	0.559	0.584
Hb (g/dL)	15.58 $\pm$ 0.84	16.82 $\pm$ 0.42	1.459	0.151
PLT $\times 10^3$ (/mm <sup>3</sup> )	210.43 $\pm$ 18.72	245.11 $\pm$ 8.46	1.944	0.058
Na (mEq/L)	134.31 $\pm$ 0.92	134.28 $\pm$ 0.51	0.030	0.976
K (mEq/L)	3.93 $\pm$ 0.18	3.60 $\pm$ 0.10	1.630	0.110
PT (second)	12.16 $\pm$ 0.30	12.07 $\pm$ 0.31	0.162	0.872
PTT (second)	34.67 $\pm$ 1.63	33.23 $\pm$ 1.55	0.521	0.605
Cr (mg/dL)	0.80 $\pm$ 0.05	0.81 $\pm$ 0.04	0.121	0.904

HBOT, hyperbaric oxygen therapy; SD, standard deviation; n, number of patients; TBSA, total body surface area; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time; Cr, creatinine.

<sup>a</sup> Independent t test or chi-square test for all analyses except where noted.

<sup>b</sup> Fisher's exact test.

**Table 2 – Patient outcomes.**

	Control (n = 15)	HBOT (n = 38)	t or $\chi^2$	p-value <sup>a</sup>
Needing tracheostomy, n (%)			–	0.064 <sup>b</sup>
No	12 (80.00)	37 (97.37)		
Yes	3 (20.00)	1 (2.63)		
Needing hemodialysis, n (%)			–	0.568 <sup>b</sup>
No	13 (86.67)	36 (94.74)		
Yes	2 (13.33)	2 (5.26)		
TBSA of skin graft (%)	22.38 $\pm$ 6.54	25.91 $\pm$ 3.14	0.546	0.587
TBSA of skin re-graft (%)	5.87 $\pm$ 3.13	4.50 $\pm$ 1.18	0.504	0.616
Number of skin graft (times)	3.87 $\pm$ 1.29	4.37 $\pm$ 0.67	0.374	0.710
ICU (days)	33.33 $\pm$ 14.13	18.11 $\pm$ 4.41	1.029	0.318
Length of hospital stay (days)	70.21 $\pm$ 16.23	77.92 $\pm$ 6.61	0.527	0.600
Time until normalization of PCT level (days)	136.25 $\pm$ 23.01	83.63 $\pm$ 6.72	3.045	0.007
Number of HBOT (sessions)	0.00 $\pm$ 0.00	8.74 $\pm$ 0.66	13.142	<0.001
HBOT side effects			–	1.000 <sup>b</sup>
None, n (%)	15 (100.00)	36 (94.74)		
Chest tightness, n (%)	0 (0)	2 (5.26)		

HBOT, hyperbaric oxygen therapy; n, number of patients; TBSA, total body surface area; ICU, intensive care unit; PCT, procalcitonin.

<sup>a</sup> Independent t test or chi-square test for all analyses except where noted.

<sup>b</sup> Fisher's exact test.

burns noted during admission. All the patients survived and were discharged. No patient required limb amputation or was permanently disabled. The patients who received tracheostomy and hemodialysis were successfully weaned before discharge. The patient characteristics did not differ significantly between the HBOT and control groups (Table 1).

The HBOT group comprised 15 women and 23 men with a mean age of 22.05  $\pm$  0.61 years and mean TBSA of 43.96  $\pm$  2.92%. Of the 38 patients, 18 suffered inhalation injury.

All the patients completed HBOT, and the mean number of sessions was 8.74  $\pm$  0.66. The control group comprised 5 women and 10 men with a mean age of 23.40  $\pm$  0.96 years and mean TBSA of 40.45  $\pm$  6.72%. In this group, seven of the 15 patients suffered inhalation injury.

The HBOT and control groups did not differ significantly in the percentage of patients receiving tracheostomy (HBOT vs. control: 2.63% vs. 20.0%,  $p = 0.064$ ) or hemodialysis (5.26% vs. 13.33%,  $p = 0.568$ ) (Table 2). The groups also did not differ in the

**Table 3 – Analysis of patient outcomes according to TBSA.**

	<23% (n = 13)	23–39% (n = 10)	40–59% (n = 16)	≥60% (n = 14)	F or $\chi^2$	p-value <sup>a</sup>
Age, mean ± SD	23.31 ± 1.31 years	20.60 ± 0.58 years	22.94 ± 1.05 years	22.36 ± 0.80 years	1.143	0.341
Sex, n (%)					–	0.487 <sup>b</sup>
Female	3 (23.08)	3 (30.00)	8 (50.00)	6 (42.86)		
Male	10 (76.92)	7 (70.00)	8 (50.00)	8 (57.14)		
Third degree TBSA	2.06 ± 1.09%	18.16 ± 2.68%	29.63 ± 3.16%	48.51 ± 4.81%	33.700	<0.001
HBOT, n (%)					–	0.451 <sup>b</sup>
No	5 (38.46)	1 (10.00)	4 (25.00)	5 (35.71)		
Yes	8 (61.54)	9 (90.00)	12 (75.00)	9 (64.29)		
Inhalation injury, n (%)					–	<0.001 <sup>b</sup>
No	13 (100.00)	9 (90.00)	6 (37.50)	0 (0)		
Yes	0 (0)	1 (10.00)	10 (62.50)	14 (100.00)		
Needing tracheostomy, n (%)					–	0.181 <sup>b</sup>
No	13 (100.00)	10 (100.00)	15 (93.75)	11 (78.57)		
Yes	0 (0)	0 (0)	1 (6.25)	3 (21.43)		
Needing hemodialysis, n (%)					–	0.181 <sup>b</sup>
No	13 (100.00)	10 (100.00)	15 (93.75)	11 (78.57)		
Yes	0 (0)	0 (0)	1 (6.25)	3 (21.43)		
TBSA of skin graft (%)	1.46 ± 1.00	16.84 ± 2.69	28.48 ± 3.12	48.36 ± 4.76	35.311	<0.001
TBSA of skin re-graft (%)	0.00 ± 0.00	0.00 ± 0.00	4.31 ± 1.30	13.57 ± 3.35	10.768	<0.001
<b>Biochemical data on admission</b>						
Albumin (g/dL)	3.47 ± 0.30	2.28 ± 0.14	2.62 ± 0.16	1.99 ± 0.14	10.837	<0.001
WBC (/mm <sup>3</sup> )	14,181.82 ± 1604.79	18,964.00 ± 2545.39	22,826.67 ± 2359.30	28,141.43 ± 3539.73	4.606	0.007
Hb (g/dL)	14.12 ± 0.57	16.43 ± 0.84	16.33 ± 0.61	18.49 ± 0.61	7.404	<0.001
PLT × 10 <sup>3</sup> (/mm <sup>3</sup> )	240.36 ± 12.62	222.80 ± 20.54	239.47 ± 12.31	236.14 ± 20.52	0.198	0.897
Na (mEq/L)	137.40 ± 0.73	133.80 ± 0.83	133.13 ± 0.79	133.64 ± 0.72	5.634	0.002
K (mEq/L)	3.51 ± 0.06	3.77 ± 0.12	3.73 ± 0.14	3.71 ± 0.27	0.330	0.804
PT (second)	11.04 ± 0.20	12.01 ± 0.41	11.87 ± 0.22	13.05 ± 0.67	3.174	0.033
PTT (second)	28.05 ± 1.07	33.27 ± 2.32	33.26 ± 2.52	38.21 ± 2.25	3.214	0.032
Cr (mg/dL)	0.77 ± 0.06	0.78 ± 0.06	0.80 ± 0.07	0.86 ± 0.04	0.412	0.745
Number of skin graft (times)	0.31 ± 0.24	2.00 ± 0.26	4.63 ± 0.69	9.00 ± 1.25	22.382	<0.001
ICU stay (days)	0.00 ± 0.00	1.60 ± 1.60	20.19 ± 5.41	60.64 ± 13.48	12.724	<0.001
Length of hospital stay (days)	28.46 ± 5.70	51.10 ± 4.32	90.69 ± 7.91	124.00 ± 11.08	26.976	<0.001

TBSA, total body surface area; SE, standard deviation; HBOT, hyperbaric oxygen therapy; n, number of patients; WBC, white blood cell; Hb, hemoglobin; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time; Cr, creatinine; ICU, intensive care unit.

<sup>a</sup> Independent t test or chi-square test for all analyses except where noted.

<sup>b</sup> Fisher's exact test.

TBSA of skin graft (HBOT vs. control: 25.91 ± 3.14% vs. 22.38 ± 6.54%, *p* = 0.587), TBSA of skin re-graft (4.50 ± 1.18% vs. 5.87 ± 3.13%, *p* = 0.616), and the number of skin graft operations (4.37 ± 0.67 vs. 3.87 ± 1.29 times, *p* = 0.710). The time spent in the intensive care unit (HBOT vs. control: 18.11 ± 4.41 vs. 33.33 ± 14.13 days, *p* = 0.318) and length of hospital stay (77.92 ± 6.61 vs. 70.21 ± 16.23 days, *p* = 0.600) also did not differ between the groups.

The number of days required for the normalization of PCT levels was significantly shorter in the HBOT group (83.63 ± 6.72

vs. 136.25 ± 23.01 days, *p* = 0.007) (Table 2). Two of the 38 patients (5.26%) experienced chest tightness during their first HBOT session, but they tolerated all subsequent HBOT sessions.

Table 3 shows the patients divided by quartile according to the TBSA of the burns. Patients with greater burn were more likely to have inhalation injury, higher graft failure rate, or longer hospital stay and more likely to need a tracheostomy, hemodialysis, or skin re-graft. These data are consistent with those of previous studies [3,12].

Statistical analysis of the relationship between HBOT and the time required for the normalization of PCT levels was performed using a two-stage stepwise regression. The first stage included the possible covariates known to influence the time required for the normalization of PCT levels. Following the determination of covariates in the first model, indicator variables were added to the model as the second stage. The results of the regression models are shown in Table 4. Analysis of covariance showed that the time required for the normalization of PCT levels was strongly related to the TBSA of skin re-graft and the use of HBOT. Taken together, these two variables accounted for 77.6% of the variance. The time required for the normalization of PCT levels increased with the percentage of TBSA of skin re-graft and decreased with the use of HBOT.

**Table 4 – Regression estimates for the time required for the normalization of PCT levels (days).**

Variable	$\beta$	SE	t	p-value
(Constant)	89.22	12.35	7.22	<0.001
TBSA of skin re-graft (%)	2.38	0.41	5.76	<0.001
HBOT <sup>a</sup>	-29.41	11.11	-2.65	0.017
R <sup>2</sup>	0.776			<0.001

$\beta$ , regression coefficient; SE, standard error; HBOT, hyperbaric oxygen therapy.

<sup>a</sup> HBOT: 0 = no, 1 = yes.

#### 4. Discussion

Burn causes coagulation necrosis of the cellular elements of the epidermis and dermis and encompasses a dynamic response to the initial insult. The depth of the injury is determined by the intensity and duration of heat exposure [3,12]. Secondary interstitial edema and organ dysfunction caused by bacterial overgrowth within the eschar can lead to systemic infection [3]. Thus, quantifying the degree of injury is an important initial step in the treatment of the burn.

Escharotomy or fasciotomy is performed in the case of circumferential burns or compartment syndrome. Aggressive diagnosis of inhalation injury and early prophylactic intubation are lifesaving. The goal of resuscitation is to achieve sufficient blood volume to ensure end-organ perfusion and avoid abdominal compartment syndrome. Topical and intravenous antibiotics are used to inhibit bacterial overgrowth and burn wound sepsis. Early identification and surgical debridement of full-thickness burn wounds, skin grafting, early enteral feeding, and wound closure using advanced techniques (skin substitutes) help to avoid wound sepsis and decrease the severity of systemic inflammation [3,12]. Patients with severe burns are at risk of organ dysfunction, particularly multiple organ dysfunction syndrome, possibly as a result of under-resuscitation, exacerbation of underlying medical comorbidities, or sepsis [3,13,14].

HBOT includes intermittent administration of 100% oxygen at pressures >1 ATA in a pressure vessel [7]. HBOT improves tissue oxygen and phagocytosis, impairs bacterial metabolism, and inhibits exotoxin production; moreover, oxygen has a synergistic effect with antibiotics [4–6]. In animal and clinical studies, HBOT for burn has yielded contradictory results in terms of preventing dermal ischemia, reducing edema, modulating the zone of stasis, preventing partial- to full-thickness conversion, preserving cellular metabolism, and promoting healing [7,8,14–18]. Brannen et al. performed a randomized study of the effects of HBOT in 125 burn patients and were unable to demonstrate any significant benefit of HBOT in burn patients in terms of mortality, the number of operations required, and length of hospital stay [8]. Hart et al. reported that the mean healing time was significantly shorter and fluid requirements were smaller in patients given HBOT [16]. In a study of split-thickness skin grafts, Perrins et al. showed a significantly higher graft-survival percentage in patients treated with HBOT [15]. Cianci et al. retrospectively analyzed the effects of adjunctive HBOT on treating burns to 19–50% of the TBSA in their center and found that the HBOT group had a shorter hospital stay, fewer number of surgical procedures, and lower hospital costs [17].

We found no significant difference between the groups in the percentage of TBSA of skin grafts, percentage of TBSA of skin re-grafts, and length of hospital stay. Our findings show a higher survival rate in skin grafts (lesser skin to re-graft) than those of Perrins et al. in 1967, who reported 91.7% for graft survival in the HBOT group and 62.7% in the control group [15]. The percentage of TBSA of skin re-graft (4.5% in the HBOT group and 5.8% in the control group) may have been affected by the use of early skin grafts, improvements in skin graft methods, and use of antibiotics. In addition, the total number

of hospital days in our study may have been influenced by our government's policy for critical national disasters and the patients' expectations.

In burn treatments, the widespread use of antibiotics for all burn patients is likely to increase antibiotic resistance and costs. A meta-analysis by Ren et al. suggested that serum PCT level is a useful biomarker for the early diagnosis of sepsis in burn patients [13]. A study by Lavrentieva et al. and meta-analysis by Prkno et al. showed that use of a PCT-guided algorithm for antibiotic therapy in the burn intensive care unit may reduce antibiotic exposure without adversely affecting the clinical outcomes such as mortality rate, percentage of patients with relapse or superinfection, and length of intensive care unit and hospital stays [10,19]. Therefore, we used serum PCT level as an early marker of sepsis and guide for antibiotic use. In our study, the HBOT group required fewer days for the normalization of PCT levels. From Table 4, it can be seen that the time required for the normalization of PCT levels increased with increase in the percentage of TBSA of skin re-graft and decreased with the use of HBOT. This suggests that although adjunctive HBOT in burn patients improves sepsis control and shortens the duration of antibiotic treatment, PCT levels would not return to normal until most of the infection of burned skin was under control.

Hyperbaric chambers are safe and are even used routinely for treating critically ill patients with appropriate monitoring precautions and careful patient selection. Hadanny et al. retrospectively analyzed 2334 patients and reported that the main side effects related to HBOT were barotrauma in 9.2% of patients, and other effects such as hypoglycemia, oxygen toxicity, dizziness, anxiety reactions, dyspnea, or chest pain occurred in 0.5–1.5% of the patients [20]. Complications of HBOT are rare and are usually self-limiting [4]. Irreversible nuclear cataracts have been described after HBOT exceeding 150–200 h [21]. In our patients, all patients received 2.5 ATA for 90 min for a mean of  $8.74 \pm 0.66$  sessions, and only two patients experienced chest tightness in their first HBOT session.

To the best of our knowledge, this is the first report of the use of adjuvant HBOT for patients who suffered burns in a major flammable starch-based powder explosion. Fifty-three young and healthy patients were injured at the same time and were treated similarly in one center. All the 53 patients survived, and no patients required amputation or were permanently disabled. The excellent results in all the patients were due to the rapid transfer (within hours) to our burn center, appropriate triage, organized chains of communication, designation of team members, and treatment experience in our hospital. The multidisciplinary approach that includes HBOT can improve the outcome in this type of mass burn casualty incident.

Although these results should be confirmed in a study with a larger number of patients and further research is needed to clearly define the role of HBOT in the treatment of thermal burns, our study indicates that adjunctive HBOT can reduce the risk of sepsis and antibiotic exposure.

#### 5. Conclusion

Burn patients require interdisciplinary team care with intensive fluid resuscitation, early surgical intervention, and

nutritional support. We found that the use of HBOT in conjunction with comprehensive burn management led to significant control of sepsis in burn patients.

### Conflicts of interest and sources of funding

None declared.

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