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INFLUENCE OF INHALATION INJURY ON ENERGY EXPENDITURE IN SEVERELY BURNED CHILDREN

Rene Przkora, MD, PhD^{1,2}, Ricki Y. Fram, MD¹, David N. Herndon, MD¹, Oscar E. Suman, PhD¹, and Ronald P. Mlcak, PhD¹

¹Department of Surgery, University of Texas Medical Branch, Galveston, TX and Shriners Hospitals for Children, Galveston, TX

²Department of Anesthesiology, University of Texas Medical Branch, Galveston, TX

Abstract

Objective—Determine the effect of inhalation injury on burn-induced hypermetabolism in children.

Design—Prospective study comparing hypermetabolism (i.e., resting energy expenditure and oxygen consumption) in burned children with and without inhalation injury during acute hospitalization.

Setting—Single pediatric burn center.

Patients—Eighty-six children (1–18 years) with 40% total body surface area burns were stratified to two groups: no inhalation injury and inhalation injury.

Interventions—None.

Main Measurements and Results—Inhalation injury was diagnosed based on bronchoscopic evaluation. At admission, PaO₂:FiO₂ ratios (an index of respiratory distress) were significantly higher in patients with no inhalation injury than in patient with inhalation injury. No differences were detected in resting energy expenditure or percent of the predicted basal metabolic rate between groups. Additionally, oxygen consumption did not significantly differ between groups.

Conclusions—Inhalation injury does not augment the burn-induced hypermetabolic stress response in children, as reflected by resting energy expenditure and oxygen consumption.

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Address correspondence to: Rene Przkora, MD PhD, Shriners Hospitals for Children, 815 Market Street, Galveston, Texas 77555; Tel: (409) 770-6974; Fax: (409) 770-6919; reprzkor@utmb.edu.

Address for Reprints: Ronald P. Mlcak, PhD, Shriners Hospitals for Children, 815 Market Street, Galveston, Texas 77555; Tel: (409) 770-6974; Fax: (409) 770-6919; rmlcak@utmb.edu.

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Keywords

burns; hypermetabolism; indirect calorimetry; inhalation injury; oxygen consumption; resting energy expenditure

INTRODUCTION

The hypermetabolic stress response that occurs following thermal injury is typified by a hyperdynamic state that is associated with elevations in cardiac output (1). The release of catecholamines, cortisol, and glucagon results in a severe catabolic reaction marked by increased energy expenditure (2). Protein is mobilized and used as a major substrate for energy, resulting in muscle wasting and loss of lean body mass (3). As a consequence, immune function is impaired, the incidence of sepsis and pneumonia is increased, wound healing is prolonged, and survival is diminished (4).

Inhalation injury in the presence of a severe burn is a major predictor of mortality and increased morbidity (5). Inhalation injury alone increases oxygen consumption (VO_2) within 2 hours of the injury, leading to increases in metabolic burden (6). Exposure to smoke or other toxic inhalants causes an acute inflammatory response at the injured site. The liberation of reactive oxygen species, lipid peroxides, and neutrophil proteases increases vascular permeability, which results in airway edema. Tissue oxygen demand increases, leading to elevations in VO_2 , and work of breathing becomes more labored (7, 8).

Past work in experimental animals, particularly sheep, demonstrates that the degree of inhalation injury occurring alongside the burn correlates with the severity of lung injury, which is confined to the trachea and large airways (9). Inhalation injury is known to increase resuscitation fluid requirements, metabolic demands, and VO_2 (10-14). Wilmore et al. showed that percent total body surface area (TBSA) burned correlates with metabolic rate (2). At one week post burn, children with > 40% TBSA burned had metabolic rates of 178% of their predicted basal according to the Harris Benedict equation. Fully healed, the same children had 153% of their predicted basal metabolic rate (3). Although it is well established that burn injury increases metabolic rate, no studies have clarified whether additional changes in energy expenditure occur when thermal injury is complicated with inhalation injury.

Indirect calorimetry provides an easy, non-invasive method for measuring caloric energy requirements at the bedside. Saffle and colleagues have shown that resting energy expenditure (REE) measures obtained through indirect calorimetry are valuable in monitoring the nutritional status in burn patients (15) and that this approach is more precise than traditional nutritional calculations, such as the Curreri formula (16).

This study was undertaken to determine the effect of inhalation injury on the metabolic rate in the severely burned pediatric population. We compared energy requirements, as assessed using indirect calorimetry between burned children with and without inhalation injury throughout acute care hospitalization.

MATERIALS AND METHODS

Patients

This study was performed under a protocol approved by the Institutional Review Board at the University of Texas Medical Branch. Eighty-six severely burned children admitted to Shriners Hospitals for Children (Galveston, TX) during 1998–2002 were enrolled into this prospective study. Children under 18 years old with $\geq 40\%$ TBSA burns were eligible for study participation. Exclusion criteria included anoxic brain injury, severe psychological disorders, quadriplegia, or severe behavioral or cognitive disorders. Before enrollment, each patient's guardian provided written informed consent, with assent from patients aged ≥ 7 years.

All study subjects received identical treatment by the same surgical team. Standard treatment included early excision of the burn wound, systemic antibiotic therapy, and continuous enteral feeding (Age in years: 0–1 Galveston Infant 2100 kcal/m² + 1000 kcal/m² burn; 1–11 Galveston Revised 1800 kcal/m² + 1300 kcal/m² burn; 12–16 Galveston Adolescent 1500 kcal/m² + 1500 kcal/m² burn) (17).

Inhalation Injury Diagnosis

Study subjects were stratified into two groups depending on their diagnosis: no inhalation injury (No Inh) and inhalation injury (Inh). Inhalation injury was documented by bronchoscopy within 24 hours of admission. Inhalation injury was diagnosed based on the presence of infraglottic soot. Alternatively, it was diagnosed based on early inflammatory alterations in the tracheal mucosa such as hyperemia, edema, superficial mucosal sloughing, and ulcerations. Treatment of inhalation injury consisted of bronchial hygiene therapy, heparin (5,000 U) and N-acetylcysteine (3 ml of a 20% solution) aerosolized every 4 hours with albuterol dosed every 4 hours (18), chest physiotherapy, and pressure control mechanical ventilation if indicated.

Indirect Calorimetry

REE measurements were obtained within 1 week of admission and during all subsequent weeks throughout the acute hospitalization. A second metabolic study was conducted at the height of the hypermetabolic state (approximately post burn day 10) to adjust for the ebb and flow stages of the hypermetabolic response. REE measurements were obtained from subjects while they slept (12 am–5 am) using a Sensor-Medics Vmax 29 metabolic cart (Yorba Linda, CA). These measurements coincided with continuous enteral feeding administered at a rate of 1,500 kcal/m² TBSA + 1,500 kcal/m² BSA burned). For testing, patients were in a supine position under a ventilated hood. Measurements were obtained at 30°C, the standard temperature of rooms in our burn ICU. REE was calculated based on CO₂ production and VO₂ using an equation described by Weir (19). REE measures were used to determine the metabolism levels of patients and to guide their nutrition. For surviving study subjects, the REE measurement taken at discharge was used to assess hypermetabolism when the burn wounds were 95% healed. The primary outcome measure was REE (kcal/m²·day), as measured by indirect calorimetry. The secondary outcome measure was VO₂ (ml/min).

Statistics

Demographic and metabolic data were analyzed using a one-way analysis of variance (ANOVA) and a two-way ANOVA, respectively. Chi square analysis was used to compare the incidence of pneumonia among groups. Data are reported as mean+SEM. Significance was set at $p<0.05$.

RESULTS

Demographics

Of the 86 study subjects, 44 had inhalation injury and 42 did not (Table 1). Mean ages were comparable among the survivor groups.

Clinical Measurements

The length of the acute hospital stay did not differ among groups (Table 2). Mean $\text{PaO}_2\text{:FiO}_2$ ratios were calculated upon admission and at the nadir of acute hospital stay. On admission, No Inh patients had a higher $\text{PaO}_2\text{:FiO}_2$ (390.7 ± 34.7) than Inh (281.5 ± 20 ; $p<0.05$). The mean $\text{PaO}_2\text{:FiO}_2$ nadir decreased from admission in all groups ($p<0.05$). The No Inh group had 6 documented cases of pneumonia during the acute stay, whereas Inh group had 16 cases of pneumonia (Table 2).

Indirect Calorimetry

For both groups (patients without inhalation injury and patients recovering from inhalation injury), REE, percent predicted REE, and VO_2 were measured at admission, at post burn day 10, and when patients were 95% healed. The REE (normalized for body surface area) was comparable between groups at admission (No Inh, $1,494 \pm 68$ vs. Inh, $1,416 \pm 82$ kcal/m²·day), at post burn day 10 (No Inh, $1,524 \pm 83$ vs. Inh, $1,631 \pm 88$ kcal/m²·day), and at 95% healed (No Inh, $1,431 \pm 55$ vs. Inh, $1,469 \pm 63$ kcal/m²·day; $p>0.05$ for all). See Figure 1.

Percent predicted REE values were calculated using the Harris Benedict equation. An analysis of percent predicted values from survivors revealed that these values did not change during hospitalization in either the No Inh group ($136 \pm 8\%$ at admission; $137 \pm 7\%$ at post burn day 10; $122 \pm 4\%$ at 95% healed) or the Inh group ($130 \pm 8\%$ at admission; $149 \pm 9\%$ at post burn day 10; and $136.5 \pm 5\%$ at 95% healed), see Figure 2.

Similar to predicted REE, VO_2 measured in l/kg·min (normalized to body weight) did not change during hospitalization for the No Inh group (0.0074 ± 0.00055 at admission; 0.0076 ± 0.00059 at post burn day 10; 0.0073 ± 0.00048 at 95% healed) or the Inh group (0.0070 ± 0.00055 at admission; 0.0082 ± 0.00059 at post burn day 10; 0.0075 ± 0.00051 at 95% healed; $p>0.05$). No significant differences in VO_2 were detected between these groups.

DISCUSSION

The catabolic stress response is a recognized phenomenon that occurs secondary to traumatic events, such as a severe burn. Increases in energy expenditure lead to the

breakdown of protein (20). The free amino acids act as a source of energy, but the breakdown of protein leads to severe muscle wasting and increases in morbidity during the acute hospitalization (21). As illustrated in our study, REE rises above the expected basal value by 20–50% after a severe burn and persists throughout hospitalization. Previous studies at our institution have shown that this severe catabolic state can persist for 12 months post injury (3). Although burn injury alone is known to increase the metabolic rate (2, 3), whether the addition of an inhalation injury influences the metabolic response in burn patients remains undocumented. In an animal model, inhalation injury has been shown to increase VO_2 and work of breathing (12), however, these models are limited by their short observation periods. In combination with a thermal injury, an inhalation injury leads to greater ventilation-perfusion mismatch, soft tissue vascular permeability secondary to increases in tissue oxidant stress, and profound hemodynamic instability (22, 23). We postulated that the presence of an inhalation injury would affect hypermetabolism induced by severe burns in pediatric patients.

Here, the hypermetabolic stress response was quantified through indirect calorimetry, which is part of routine care in the acute setting to monitor the nutritional requirements of severely burned patients. REE determined through indirect calorimetry has been shown to be an accurate measure of total energy expenditure (15). Using this approach, we detected no differences in REE, percent predicted REE, or VO_2 among patients with or without inhalation injury throughout the acute hospitalization. A number of clinical factors could affect these results. As already stated, patients in the Inh group spent more days on a ventilator than patients in the other group. In addition, Inh displayed a trend towards more days on a ventilator than No Inh patients. Patients who required mechanical ventilation also needed adequate sedation medications and in some cases, muscle paralytics to tolerate the ventilator modes. These medications have been shown to artificially affect energy expenditure as well as VO_2 by lessening the work of breathing (24–28). Barton et al. found that ventilated patients who require chemical muscle paralysis with vecuronium have significantly lower REEs (29). If patients were not adequately sedated, one would expect to see a higher VO_2 as patients fight to breathe over the ventilator settings and work of breathing becomes more labored.

Patients with inhalation injury had $\text{PaO}_2:\text{FiO}_2$ nadir ratios that were below 200. A ratio below 200 is considered indicative of adult respiratory distress syndrome. Among patients, the incidence of pneumonia during the acute hospitalization was significantly greater in those with inhalation injury. Although we showed that inhalation injury does not augment the hypermetabolic response in our population, one would expect to see greater oxygen demands and work of breathing as a result of lower $\text{PaO}_2:\text{FiO}_2$ ratios, longer times on the ventilator, and the presence of pneumonia. Further evaluation of the effects of sedatives and types of ventilator settings on our unique population is necessary.

Fluid resuscitation is a critical and challenging aspect of treating burn patients. Inhalation injury increases the amount of fluid needed for resuscitation. Yet, previous studies have shown that inadequate fluid resuscitation, whether too much or not enough, can worsen the effects of an inhalation injury and lead to greater complications (12, 14). We did not assess

the amount of fluids and blood products that each group of patients received and whether these measures had an effect on REE or VO_2 .

Aside from the considerations discussed above, one could speculate that the addition of an inhalational injury to an already severe burn plays only a minor contribution to the already massively increased energy expenditure. On the other hand, in smaller burns (e.g., <40% TBSA burns), inhalation injury may contribute independently to the overall energy expenditure. This should be evaluated in further studies.

Historically, inhalation injury has been found to be the chief burn-associated injury contributing to burn mortality. At our institution, the presence of an inhalation injury with larger burn sizes has been found to be an early indicator of death (30, 31). Barrow et al. found that severely burned pediatric patients who had a concomitant inhalation injury and who were between the ages of 0 to 3 years presented with higher rates of mortality than children without an inhalation injury (32). Looking at overall mortalities in 1998–2002, we did find that an associated inhalation injury led to a significant number of deaths prior to discharge. Nevertheless, it is important to mention that mortality rates after burn injury have generally declined due to progress in areas such as early fluid resuscitation, prompt excision and grafting, implementation of aggressive enteral feeding regimens early in the acute course, and identification and treatment of inhalation injuries with inhaled medications (30, 33–35). Based on our findings, an inhalational injury in pediatric burn patients is not automatically associated with higher energy requirements. This information will help to design the nutritional support for these patients.

CONCLUSIONS

In severely burned children, inhalation injury does not potentiate the hypermetabolic stress response to thermal injury during acute hospitalization as measured by REE. Although inhalation injury lowers $\text{PaO}_2:\text{FiO}_2$ ratio and leads to a greater incidence of pneumonia and more days requiring ventilator support, it does not affect VO_2 .

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References

1. Wolfe RR. Review: acute versus chronic response to burn injury. *Circ Shock*. 1981; 8:105–115. [PubMed: 7016359]
2. Wilmore DW, Long JM, Mason AD Jr, et al. Catecholamines: mediator of the hypermetabolic response to thermal injury. *Ann Surg*. 1974; 180:653–669. [PubMed: 4412350]
3. Hart DW, Wolf SE, Mlcak R, et al. Persistence of muscle catabolism after severe burn. *Surgery*. 2000; 128:312–319. [PubMed: 10923010]
4. Chang DW, DeSanti L, Demling RH. Anticatabolic and anabolic strategies in critical illness: a review of current treatment modalities. *Shock*. 1998; 10:155–160. [PubMed: 9744642]
5. Wolf SE, Rose JK, Desai MH, et al. Mortality determinants in massive pediatric burns. An analysis of 103 children with $\geq 80\%$ TBSA burns ($\geq 70\%$ full-thickness). *Ann Surg*. 1997; 225:554–565. [PubMed: 9193183]

6. Demling R, LaLonde C, Heron P. Initial effect of smoke inhalation injury on oxygen consumption (response to positive pressure ventilation). *Surgery*. 1994; 115:563–570. [PubMed: 8178255]
7. Enkhbaatar P, Traber DL. Pathophysiology of acute lung injury in combined burn and smoke inhalation injury. *Clin Sci (Lond)*. 2004; 107:137–143. [PubMed: 15151496]
8. Demling RH. Pulmonary problems in the burn patient (a leading cause of morbidity and mortality in the burn patient). *Journal of Burns and Surgical Wound Care*. 2004; 3:5–55.
9. Demling RH, LaLonde C. Moderate smoke inhalation produces decreased oxygen delivery, increased oxygen demands, and systemic but not lung parenchymal lipid peroxidation. *Surgery*. 1990; 108:544–552. [PubMed: 2396198]
10. Demling R, Lalonde C, Youn YK, et al. Effect of graded increases in smoke inhalation injury on the early systemic response to a body burn. *Crit Care Med*. 1995; 23:171–178. [PubMed: 8001368]
11. Demling RH, Knox J, Youn YK, et al. Oxygen consumption early postburn becomes oxygen delivery dependent with the addition of smoke inhalation injury. *J Trauma*. 1992; 32:593–598. [PubMed: 1588648]
12. Lalonde C, Picard L, Youn YK, et al. Increased early postburn fluid requirements and oxygen demands are predictive of the degree of airways injury by smoke inhalation. *J Trauma*. 1995; 38:175–184. [PubMed: 7869432]
13. Herndon DN, Traber DL, Traber LD. The effect of resuscitation on inhalation injury. *Surgery*. 1986; 100:248–251. [PubMed: 3738753]
14. Navar PD, Saffle JR, Warden GD. Effect of inhalation injury on fluid resuscitation requirements after thermal injury. *Am J Surg*. 1985; 150:716–720. [PubMed: 4073365]
15. Saffle JR, Medina E, Raymond J, et al. Use of indirect calorimetry in the nutritional management of burned patients. *J Trauma*. 1985; 25, 32–39.
16. Saffle JR, Larson CM, Sullivan J. A randomized trial of indirect calorimetry-based feedings in thermal injury. *J Trauma*. 1990; 30:776–782. [PubMed: 2116532]
17. Pereira C, Murphy K, Jeschke M, et al. Post burn muscle wasting and the effects of treatments. *Int J Biochem Cell Biol*. 2005; 37:1948–1961.
18. Desai MH, Mlcak R, Richardson J, et al. Reduction in mortality in pediatric patients with inhalation injury with aerosolized heparin/N-acetylcystine [correction of acetylcystine] therapy. *J Burn Care Rehabil*. 1998; 19:210–212. [PubMed: 9622463]
19. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. 1949. *Nutrition*. 1990; 6:213–221. [PubMed: 2136000]
20. Wolfe RR, Shaw JH, Durkot MJ. Energy metabolism in trauma and sepsis: the role of fat. *Prog Clin Biol Res*. 1983; 111:89–109. [PubMed: 6867023]
21. Reiss E, Pearson E, Artz CP. The metabolic response to burns. *J Clin Invest*. 1956; 35:62–77. [PubMed: 13278402]
22. Demling R, Lalonde C, Picard L, et al. Changes in lung and systemic oxidant and antioxidant activity after smoke inhalation. *Shock*. 1994; 1:101–107. [PubMed: 7749927]
23. Shimazu T, Yukioka T, Ikeuchi H, et al. Ventilation-perfusion alterations after smoke inhalation injury in an ovine model. *J Appl Physiol*. 1996; 81:2250–2259. [PubMed: 8941552]
24. Theye RA, Tuohy GF. Oxygen Uptake During Light Halothane Anesthesia in Man. *Anesthesiology*. 1964; 25:627–633. [PubMed: 14211489]
25. Theye RA, Tuohy GF. Oxygen Uptake During Ether Anesthesia in Man. *Anesth Analg*. 1964; 43:483–489. [PubMed: 14209301]
26. Swinamer DL, Phang PT, Jones RL, et al. Effect of routine administration of analgesia on energy expenditure in critically ill patients. *Chest*. 1988; 93:4–10. [PubMed: 3335166]
27. Dempsey DT, Guenter P, Mullen JL, et al. Energy expenditure in acute trauma to the head with and without barbiturate therapy. *Surg Gynecol Obstet*. 1985; 160:128–134. [PubMed: 3918351]
28. Christensen KJ, Andersen AP, Jorgensen S. Energy expenditure on breathing during anaesthesia. *Acta Anaesthesiol Scand*. 1985; 29:280–282. [PubMed: 3922196]

29. Barton RG, Craft WB, Mone MC, et al. Chemical paralysis reduces energy expenditure in patients with burns and severe respiratory failure treated with mechanical ventilation. *J Burn Care Rehabil.* 1997; 18:461–468. [PubMed: 9313131]
30. Herndon DN, Gore D, Cole M, et al. Determinants of mortality in pediatric patients with greater than 70% full-thickness total body surface area thermal injury treated by early total excision and grafting. *J Trauma.* 1987; 27:208–212. [PubMed: 3546714]
31. Milner EA, Cioffi WG, Mason AD, et al. A longitudinal study of resting energy expenditure in thermally injured patients. *J Trauma.* 1994; 37:167–170. [PubMed: 8064909]
32. Barrow RE, Spies M, Barrow LN, et al. Influence of demographics and inhalation injury on burn mortality in children. *Burns.* 2004; 30:72–77. [PubMed: 14693089]
33. Hart DW, Wolf SE, Herndon DN, et al. Energy expenditure and caloric balance after burn: increased feeding leads to fat rather than lean mass accretion. *Ann Surg.* 2002; 235:152–161. [PubMed: 11753055]
34. Hart DW, Wolf SE, Zhang XJ, et al. Efficacy of a high-carbohydrate diet in catabolic illness. *Crit Care Med.* 2001; 29:1318–1324. [PubMed: 11445678]
35. Hart DW, Wolf SE, Chinkes DL, et al. Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. *J Trauma.* 2003; 54:755–761. [PubMed: 12707540]

Figure 1.

Data are means $\pm$ SEM. Resting energy expenditure is normalized for body surface area and is expressed in units of kcal/m²/day. There was no significant difference in REE between groups at admission, post burn day 10 and 95% healed ($p > 0.05$).

Figure 2.
Percent of predicted basal energy expenditure in patients with and without inhalation injury through acute hospitalization.

Table 1

Patient Demographics

Measurement	No Inh	Inh
Subject (n)	42	44
Age (years)	8±1	8±1
Gender (M:F)	25:17	27:17
TBSA burn (%)	55±2	58±2
3 rd Degree Burn (%)	43±3	49±3

Table 2

Clinical Measurements

Measurement	No Inh	Inh
Length of Stay (days)	29±3	35±2
Length of Ventilation (days)	2±1	5±1
Pneumonia	13% (6/42)	27% (16/44)