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Review article

Treatment of Burn Injuries in Children

Vesna Marjanović

University Clinical Centre Niš, Clinic of Anesthesiology and Intensive Care, Niš, Serbia
University of Niš, Faculty of Medicine, Niš, Serbia

SUMMARY

Introduction. Burns represent one of the leading causes of morbidity and mortality in children.
Aim. Aim of this review is to gain better understand of the pathophysiological changes and assessment of the severity of burn injuries in different ages of pediatric patients, which may help in early implementation of appropriate therapeutic procedures and improvement of the outcome of these patients.
Literature review. Children are more likely to develop wider and deeper burns, greater fluid and heat loss in comparison to adults. Therefore, the initial assessment of the TBSA and the depth of the burns in children are crucial for their further treatment. The most important approach in the treatment of children with burn injuries includes the management of airways, effective fluid resuscitation, pain control, and prevention of infection.
Conclusion. In the current review we sought to provide recommendations that might help improve the assessment of the severity of burns in children, which may be important for improving their recovery and reducing mortality rate.

Keywords: **burn injury, children, treatment**

Corresponding author:
Vesna Marjanović
e-mail: drvesnamarjanovic@gmail.com

INTRODUCTION

Burn injury in children is the leading cause of mortality, especially in low- and middle-income countries. According to the World Health Organization, burn injuries are the cause of death in 180,000 cases annually, and the fifth most common cause of non-fatal injuries in childhood (1). With advancement in the treatment of these patients, the mortality has decreased over time by 48.1%, and now amounts to 3.8% (2, 3). Pediatric population is an especially vulnerable group for the development of burn injury due to their natural curiosity, limited understanding of risk, and physical environment. This is why burns at home caused by hot liquids and flame are the most common on the upper limbs (4). Initial accurate assessment of the TBSA in burn injuries of children may be crucial for further decision making about their hospitalization and treatment (5). About 2.5% of children with more than 20% of TBSA burns and second-degree burns required admission to hospital (2, 6). Despite significant progress in the treatment of children with burn injuries, children of younger age, with burns like scalds and inhalation injuries, with over 41% of TBSA, and who are hospitalized in lower volume centers, are still associated with high morbidity and mortality, (1, 3, 6-10). The reason for the high mortality in children lies in the untimely recognition of the severity of burn injury and inadequate treatment of these patients. That can be explained with their greater sensitivity to fluid and heat loss and development of wider and deeper burns even in short-term skin exposure compared to adults (2). Also, the implementation of primary prevention programs would be helpful in reducing the incidence of burn injuries in very young children and teenagers (11, 12).

The focus of this review is on better understanding the pathophysiological processes and accurate assessment of the severity of burn injuries, which can provide the timely implementation of appropriate therapeutic procedures in children. That would improve the initial resuscitation, perioperative care, procedural sedation and pain relief as well as reduce the morbidity and mortality of pediatric patients.

PATHOPHYSIOLOGICAL CHANGES IN CHILDREN WITH BURN INJURIES

Better understanding of pathophysiology of burn injury is very important for effective management of pediatric patients. Burn injuries result in local and systemic responses. Local response involves the zone of coagulation, stasis, and hyperemia. In the zone of coagulation, the strongest damage effect occurs with irreversible tissue loss. The zone of stasis is characterized by vasoconstriction and a decrease of tissue perfusion. The perfusion of this zone may significantly improve with initiation of resuscitation, which would prevent the additional deepening and expansion of the burn wound. In the zone of hyperemia, the tissue perfusion is increased and the tissue's ability to recover is great unless there is severe sepsis or prolonged hypoperfusion of tissue (13). Systemic effects of burn injury are expected in children with TBSA over 30%. Cardiovascular changes involve increased capillary permeability with loss of fluids into the interstitial compartment, peripheral and splanchnic vasoconstriction, and decreased myocardial contractility. These changes lead to systemic hypotension and hypoperfusion of organ systems. Respiratory changes in the form of bronchoconstriction are caused by inflammatory mediators, which may lead to respiratory distress syndrome. In addition, the basal metabolic rate in children with burns may multiple by three. In the setting of splanchnic hypoperfusion, early enteral nutrition may have limited effects on the prevention of catabolism and maintain gut integrity (13).

Immunological changes occur in damaged cells with the release of inflammatory mediators (histamine, bradykinin, vasoactive amines, prostaglandins, leukotrienes, etc.). Thus, histamine released from mast cells increases membrane and vascular permeability, while serotonin and thromboxane A2 increase pulmonary vascular resistance and mesenteric vasoconstriction (14). Due to vasodilatation and increased permeability of blood vessels, there is a significant loss of intravascular fluid, protein into the interstitial space and the development of hyperemia and edema. Thus, tissues that are in the immediate vicinity of the necrosis zone can be additionally damaged in conditions of hypotension, hypoxia and infection, which may additionally increase the necrosis zone after burn injury (13). In addition to inflammatory mediators, hormones such as catecholamines, cortisol and glucagon are also released. These hormones lead to proteolysis, lipolysis, gluconeogenesis, glycogenolysis, and loss of lean body mass and body fat. Catecholamines increase gluconeogenesis, glycogenolysis, lipolysis, production of acute phase reactants, thermogenesis, and cardiac output. Released cortisol leads to hyperglycemia in the first 24 hours of burns as well as proteolysis with simultaneous reduction of protein synthesis (15). All this leads to a negative nitrogen balance, loss of muscle mass up to 50% and slow rehabilitation of children with burns (16). Because of the profound immunological and metabolic changes in severely burned children, complications such as infection, growth arrest, and loss of lean body mass may develop (17).

Released inflammatory mediators, as well as physiological characteristics of children, make these patients more sensitive to fluid and heat loss compared to adults. This is due to an almost 3-fold higher TBSA to body mass ratio, as well as thinner layers of skin and insulating subcutaneous tissue in younger children compared to older children and adults. Because of that, younger children are at greater risk of developing a wider and deeper burn even with short-term skin exposure to heat compared to older children and adults (2). On the other side, temperature regulation in very young children is based in part on non-shivering thermogenesis, which further increases their metabolic rate, oxygen consumption, and lactate production. Therefore, these patients require more intensive fluid replacement and maintenance of normothermia than adult patients. When replacing fluids, it should be taken into account that children younger than one year are more prone to developing hyponatremia due to their larger blood volume, greater loss of sodium through urine, and the inability to concentrate urine (18). These patients are also prone to airway obstruction due to their anatomical features such as smaller relative diameter, shorter mandible and trachea, larger tongue and adenoid, and anteriorly displaced pharynx. Due to anatomical features of the airway and released inflammatory mediators, pediatric patients with inhalation burns may be at greater risk for bronchospasm (19-21).

FIRST AID IN CHILDREN WITH BURN INJURIES

Providing first aid in the form of cooling may be useful in children with TBSA of burns less than 10% and in the absence of shock (22). This type of first aid was implemented in 86.1% of patients, while in others it was not implemented or information about it was missing. Short-term cooling with water was done in 80.2% of patients, while recommended cooling longer than 20 minutes was applied only in 12% of patients (23). This long-term cooling of the burned surface was associated with a reduction in the depth of the burn, as well as in the time required for re-epithelialization of those burned surfaces (24, 25). However, the final outcome of these patients did not depend on the length of cooling of the burned surface, but on the surface and depth of the burns, as well as the mechanism of their injury (26). In chemical burns with corrosive agents, it is necessary to remove contaminated clothing from the surface of the skin and dilute the chemical agent by irrigating it with water (27).

ASSESSMENT OF BURN INJURIES IN CHILDREN

Initial assessment of burn injury in children is crucial for further treatment of these patients. Thus, in the case of minor burns, after dressing the burn wound with dry sterile gauze with the goal of reducing the risk of hypothermia and infection, the patient can be referred for home treatment. However, 2.5% of pediatric patients with burn injury require admission to specialized centers which are intended for the hospital treatment of burns (6). The indication for direct admission to the hospital is based on the following criteria: burns with partial involvement of the skin thickness and TBSA greater than 10%, with complete involvement of the skin thickness greater than 2% of TBSA, burns of the face, hands, genitals, perineum or major joints, circumferential burns of the extremities, all electrical burns caused by high voltage of electric current or low voltage in selected cases, chemical and inhalation burns, burns in patients with already existing comorbidities (diabetes, immunosuppression), which can complicate treatment and increase mortality, suspected abused children, as well as children whose parents are unable to take care of them (22, 28).

During the initial examination, detailed anamnestic data on the mechanism of injury and assessment of the depth and TBSA of the burn should be obtained. The measurement of the TBSA of burns is crucial for initial management, particularly for fluid resuscitation in the first hours after injury. There are several methods of measuring the TBSA of burns in use. The most accurate method for the assessment of TBSA of burns in children is achieved using the Lund and Browder table, which takes into account the age of children (29, 30). The Wallace rule of nines is used for the rapid assessment of TBSA of burns in adult patients. However, this method is not suitable for children, due to significant overestimates of TBSA burns (31). An alternative rule of thumb for rapid assessment of the burned area is the palm of the patient, which represents 1% of the body surface (13). Despite various methods of assessing TBSA, the problem of estimating burn size in children still persists. Overestimating the burn size is present in 70% of cases, underestimating in 15%, while a correct estimation is present only in 15% of children (29). Overestimating may lead to inappropriate resuscitation and administration of fluids over what's required (30). Also, it should be kept in mind that a definitive assessment of the burn depth may only be obtained after 48 to 72 hours from the occurrence of burn injury to children, due to the dynamic nature of the damage and the possibility of the burn deepening during this period. Thus, the assessment of burn depth in children appears to require continued training and education of initial burn providers (29, 32).

TREATMENT OF BURN INJURIES IN CHILDREN

The initial approach in the treatment of children with burn injury involves the management, of airways, fluid resuscitation, and pain control (5). Assessment of airways and possible intubation is especially important in children with burns of the face or neck, symptoms of airway obstruction as well as in children with greater TBSA burn. The intubation process should be considered in patients with deeper and circular burn on the neck, signs of inhalation injury to the airways (stridor, hoarseness, black sputum, respiratory distress, damage to the hairs in the nose, swelling of the face) and oropharyngeal region (soot in the mouth, intraoral edema, and erythema), and burns over 40% of TBSA (22, 33), due to their tendency to develop airway obstruction. The reason for that are anatomical and physiological characteristics of airways and rapid developing of secondary edema after inhalation injury or after intensive fluid resuscitation in the first 48 hours after burn injury in children. The size of the endotracheal tube in children can be determined using the formula, tube size = 4 + (age in years/4) or based on the diameter of the patient's little finger. In case of difficult intubation, it is necessary to provide a video laryngoscope and equipment for emergency tracheotomy (12, 20, 22). Children with smoke injuries, besides airway obstruction may also develop pulmonary edema, decreased pulmonary compliance, ventilation-perfusion mismatch as well as carbon monoxide or cyanide intoxication. The diagnosis of smoke injury may be confirmed through anamnestic data, physical exam, and bronchoscopy. Therefore, these patients often require supportive measures, treatment of pulmonary infection and ventilatory support (20, 33). In case of children with carbon monoxide and cyanide intoxication, the administration of high-flow oxygen and hydroxocobalamin are recommended (22).

Loss of circulating volume is proportional to the severity of the burn. Thus, in case of children with minor burns, oral hydration may be sufficient. However, in children with TBSA of burns greater than 10%, initial fluid resuscitation with 20 mL/kg of intravenous crystalloid solution is needed (5, 22). In early hypovolemic phase, within the first hour of burn injury occurrence, balanced solution such as Ringer's lactate is used for all age groups of children. Its overall amount is calculated based on the Parkland formula (volume mL = 4 × body weight (kg) × % TBSA of burns) (34) and the Galveston formula (volume mL = 5000 mL/m^2 TBSA burns + 2000 mL/m^2 TBSA of Ringer-lactate + Albumin and 5% dextrose). Modified Parkland formula is used in children with a body mass below 20 kg, according to which, in addition to the calculated amount of fluid in keeping with the percentage of burned surface, a certain amount of maintenance fluid should be added. Maintenance of fluid involves the administration of Ringer's lactate solution and 5% dextrose in a volume of 4 mL/kg/h for patients up to 10 kg body weight, plus 2 mL/kg/h for children with body weight between 10 and 20 kg, plus 1 mL/kg/h for every kg above 20 kg of body weight. The reason for that are reduced glycogen storages in younger children and their tendency towards hypoglycemia.

Also, glucose solutions can compensate for the initial hypermetabolic response to burn, characterized by increased energy expenditure, stroke volume, cardiac output, and hyperthermia (14). Of the total amount of calculated fluids, half should be given in the first eight hours after the burn injury, and the remaining half in the next 16 hours. This concept shows its ineffectiveness in patients with greater fluid loss than the ones that are calculated for a given time period, thus emphasizing the importance of hourly titration of fluids to provide satisfactory amount of urine output in the burn patient (22). Therefore, reassessment of fluid status, every 1-2 hours, within the first 24 hours after burn injury is needed.

Administration of colloids can significantly reduce crystalloid overuse, tissue edema, and length of hospitalization in patients with severe burns (35, 36). Therefore, human albumins are recommended in patients with TBSA burns of 15-45% by Legard et al. (22) or over 30% by Dittrich et al. (35) after the first six hours of fluid resuscitation. Other solutions reducing fluid volume have been largely abandoned, such as dextran due to coagulopathy, fresh frozen plasma because of transmissible diseases, and hypertonic saline because of increased mortality and renal failure (22, 37). Until now, different formulas have been used to replace hypertonic solutions or colloids, with different results in the treatment of these patients. This indicates that it is difficult to develop a standardized method of fluid replacement in children with burns because of its dynamic nature and the need to titrate fluids based on evidence of end-organ perfusion.

The effectiveness of fluid resuscitation in children with burns is evaluated based on the achievement of satisfactory end-organ perfusion. Resuscitation fluids should be titrated to provide a urine output of 0.5–1 mL/kg/h, which is in contrast to the previous practice of 1–2 mL/kg/h (15, 36, 38). Depending on the urine output, the amount of fluids should be increased by 10-20% in case of lower target value, or decreased by 10-20% in case of higher target value. Any delay in fluid replacement may increase the risk of acute renal failure, multiorgan dysfunction, prolonged hospitalization, and increase mortality of these patients (10). Pediatric burn patients are also prone to developing acute kidney injury (AKI) not only in the setting of insufficient fluid replacement but also in the setting of rhabdomyolysis or drug-induced kidney injury. AKI occurs in 30 to 50% of burn patients. There are identified risk factors for AKI development such as age, wider and full-thickness of TBSA of burns, flame burn, inhalation injury, burn severity index on admission, organ failure assessment score on admission, baseline level of urea and creatinine, multiple surgeries, sepsis, compartment syndrome, and prolonged PICU hospitalization (39-41). Moreover, the occurrence of AKI in patients with burns can increase mortality by six times compared to patients who did not develop this injury (42-44). Also, a burn in the first 24 hours after the injury can cause a hypermetabolic inflammatory response, the release of catecholamines and other stress hormones and the consequent occurrence of refractory tachycardia, increased cardiac output and increased oxygen consumption. When these patients are anesthetized, catecholamine depletion and cardiovascular collapse may occur. In these clinical settings, the selection of the induction agent for anesthesia should be considered carefully, and inotropic and vasoactive drugs should be administered additionally. Children with burns greater than 10% of TBSA are more prone to greater heat loss due to a higher ratio of TBSA to body mass as well as thinner skin and insulating subcutaneous tissue, compared to adults. Therefore, constant measurement of body temperature, maintaining of environmental temperature at 30-32 ºC, administration of warm intravenous fluids and the use of heating mattresses for parts of the body that are not covered with gauze and bandages is needed to avoid hypothermia (45). In children with TBSA burn over 25% TBSA, systemic edema may be expected within the first 4 to 36 hours of injury, leading to circulatory shock, reduced cardiac output, and organ hypoperfusion. Thus, hemodynamic monitoring such as pulse oximetry, ECG, non-invasive blood pressure measurement can be necessary and at the same time difficult, especially in children with greater burns. In these cases, monitoring of invasive blood pressure and cardiac output via esophageal Doppler is recommended. The placement of a urinary catheter is mandatory in children with burns greater than 15% TBSA to assess hourly diuresis. In addition, continuous monitoring of laboratory parameters such as blood counts, electrolytes, and lactate may be useful in the assessment of burn severity and determination of resuscitation endpoints during the treatment of burn shock (46).

Treatment of burns in children requires adequate pain management. Inadequate treatment of pain can increase stress, anxiety and fear in patients, which will further intensify the pain. Acute pain can interfere not only with a child's physical activity, but also with their recovery process. Chronic pain can lead to long-term physical dysfunction and impairment of children's quality of life, as well as psychological consequences after the end of burn treatment. This leads to constant emotional stress, disturbed mood, sleep and appetite, school failure and fear of further medical services. In the essence of inadequate treatment of pain lies a poor understanding of pain pathophysiology and its complex nature. Therefore, the treatment of pain remains one of the most challenging medical issues (17, 47). It is believed that multimodal pain management can be effective in eliminating pain in children with burn injury. In addition, analgesic medications have to be titrated on the basis of validated comfort and analgesia assessment scales (22). Opioids represent a key analgetic for pain control in children with burns. However, individual use of opioids can cause some side effects such as nausea, constipation, drowsiness, pharmacological tolerance, addiction during short-term or long-term use. Therefore, combining opioids with non-steroidal anti-inflammatory drugs (NSAIDs) can reduce the need for opioids. The most often used combination is paracetamol and morphine, which can be substituted for oxycodone in case of tolerance (48, 49). Although the use of NSAIDs can reduce the need for opioids, they should be used with caution in severe burns because of their side effects (renal toxicity, gastric ulceration, and antiplatelet effects). Recent data indicates that the use of ketamine in combination with other analgesics may be more effective in pain treatment than a single administration of opioids (22). In addition, ketamine-dexmedetomidine, ketamine-propofol, propofol-remifentanil, propofol-fentanyl, and ketamine-midazolam may be useful in reducing procedural pain and anxiety during wound care procedures in children (50). Other drugs that may be useful in relieving pain are gabapentin and alpha 2 agonists (clonidine and dexmedetomidine). However, despite this, a high intensity of pain (7 out of 10) was recorded during the treatment of patients with burns (51). Thus, combining non-pharmacological techniques such as hypnosis, distraction techniques, relaxation and distraction with analgesics reduced the intensity of pain significantly in stabile burn patients who require frequent wound care procedures (52-56).

Infection is the leading cause of morbidity and mortality in children with severe burns. With the progression of the wound infection to sepsis, death occurs in about 55% of patients (57). The reason for that is an impaired protective function of the skin as the first line of defense for pediatric patients against infection. Risk factors that increase the susceptibility of these patients for infections are: burns with greater TBSA and depth, as well as inhalation injuries (58, 59). Simultaneously, these patients have an altered thermoregulation and metabolic homeostasis, which, along with local capillary damage, local and systemic vasodilatation, makes them more sensitive to fluid loss, tissue edema, invasion of infectious microbes and infection (57, 60, 61). Dysregulation of the immune response in these patients makes them susceptible also to urinary tract infections, pneumonia, and central venous catheter infections (59). If sepsis occurs in the early phase of treatment, gram-positive bacteria should be considered as a cause of infection. Late sepsis is predominantly caused by gram-negative drug-resistant bacteria such as multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. With the identification of the source of infection, treatment should be started as soon as possible with a de-escalation antibiotic in order to reduce the degree of antibiotic resistance (61, 62). In addition to antibiotics in the treatment of burn children with sepsis, vasopressors can also be used. This is due to pediatric patients normally having a higher cardiac output compared to adults, as well as a limited ability to modulate contractility, therefore an increase in stroke volume is often impossible when needed, especially in sepsis. The vasopressor epinephrine proved to be more useful in the treatment of septic shock in children due to improving cardiac output and tissue oxygen delivery, compared to norepinephrine (63). In addition, thromboprophylaxis should be routinely prescribed in the initial phase of severe burn patients and in the patients with placed central venous catheter (22).

During the surgical treatment of children with burns, significant blood loss is possible. Therefore, these patients often require more intensive restitution of blood and blood products, which may amount to more than one estimated circulating blood volume. Sometimes, blood loss can be difficult to assess, especially in children with a large TBSA burn (64). The formula that can be used to calculate the percentage of blood loss during surgical intervention is as follows: 3 x body weight (kg) x % TBSA in burns. In case of patients with anemia, it is recommended to correct the hemoglobin level below 7 mg/dL. With the use of restrictive strategy, blood replacement was reduced by 50% in the operating room and by 25% outside the operating room or by one third in another study (65, 66). With the application of this strategy, the duration of mechanical ventilation and blood utilization of these patients was significantly reduced, but without affecting mortality, organ dysfunction, wound healing or the occurrence of infectious complications (66).

Other types of treatment include nutritional support, which should be started 12 hours after burn injury occurrence. In addition, oral and enteral nutrition have advantages over parenteral nutrition. With high carbohydrate, low fat enteral nutrition together with pharmacological agents such as growth factors, insulin, propranolol and oxandrolone, and increased nutrient intake is ensured, catabolism and malnutrition are prevented, reparative processes are stimulated, which overall shortens hospitalization, ensures successful recovery and rehabilitation of these patients (67, 68).

CONCLUSION

Burn injury in children is associated with high mortality. With better understanding of pathophysiology and assessment of the severity of burns, especially at younger age, effective management and treatment of pediatric patients may be achieved. Therefore, adequate management of airways, fluid replacement, multidisciplinary approach in pain relief, and prevention of infection may provide the best possible chance for quick and successful recovery of pediatric patients as well as an optimal quality of life afterwards.

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Human and animal rights and informed consent

This paper is a review article, so it was not research involving human participants and/or animals nor there was a need of an informed consent.

Conflict of interest

The authors declare no competing interests.

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Lečenje opekotina kod dece

Vesna Marjanović

Univerzitetski klinički centar Niš, Klinika za anesteziju, reanimatologiju i intenzivnu negu, Niš, Srbija
Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija

SAŽETAK

Uvod. Opekotine predstavljaju jedan od vodećih uzroka morbiditeta i mortaliteta kod dece. Cilj. Cilj ovog preglednog rada bio je da omogući bolje razumevanje patofizioloških promena i procene težinu opekotina kod dece različitog uzrasta, što može pomoći u ranoj primeni odgovarajućih terapijskih procedura i poboljšanju ishoda lečenja ovih pacijenata.
Pregled literature. Verovatnoća da će doći do razvoja širih i dubljih opekotina, većeg gubitka tečnosti i toplote veća je kod dece nego kod odraslih. Stoga, početna procena površine i dubine opekotina kod dece ključna je za njihovo dalje lečenje. Najvažniji pristup u lečenju dece sa opekotinama obuhvata upravljanje disajnim putevima, efikasnu reanimaciju tečnostima, kontrolu bola i prevenciju infekcije.
Zaključak. U ovom preglednom radu nastojali smo dati preporuke koje bi mogle pomoći u poboljšanju procene težine opekotina kod dece, budući da bi to moglo biti važno za poboljšanje procesa njihovog oporavka i smanjenje stope mortaliteta.

***Ključne reči*: opekotine, deca, lečenje**