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Biological markers of stress in pediatric acute burn injury

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ABSTRACT

Background: Burns and their associated wound care procedures evoke significant stress and anxiety, particularly for children. Little is known about the body's physiological stress reactions throughout the stages of re-epithelialization following an acute burn injury. Previously, serum and urinary cortisol have been used to measure stress in burn patients, however these measures are not suitable for a pediatric burn outpatient setting.

Aim: To assess the sensitivity of salivary cortisol and sAA in detecting stress during acute burn wound care procedures and to investigate the body's physiological stress reactions throughout burn re-epithelialization.

Methods: Seventy-seven participants aged four to thirteen years who presented with an acute burn injury to the burn center at the Royal Children's Hospital, Brisbane, Australia, were recruited between August 2011 and August 2012.

Results: Both biomarkers were responsive to the stress of burn wound care procedures. sAA levels were on average 50.2 U/ml higher ($p < 0.001$) at 10 min post-dressing removal compared to baseline levels. Salivary cortisol levels showed a blunted effect with average levels at ten minutes post dressing removal decreasing by 0.54 nmol/L ($p < 0.001$) compared to baseline levels. sAA levels were associated with pain ($p = 0.021$), no medication ($p = 0.047$) and Child Trauma Screening Questionnaire scores at three months post re-epithelialization

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($p = 0.008$). Similarly, salivary cortisol was associated with no medication ($p < 0.001$), pain scores ($p = 0.045$) and total body surface area of the burn ($p = 0.010$).
Conclusion: Factors which support the use of sAA over salivary cortisol to assess stress during morning acute burn wound care procedures include; sensitivity, morning clinic times relative to cortisol's diurnal peaks, and relative cost.

1. Background

Burns are a traumatic event and both the injury itself and the associated wound care procedures evoke high levels of stress and anxiety [1]. Despite this, there are very few studies which measure biological markers of stress in patients with acute burns. Catecholamines and cortisol are the two most commonly used biomarkers of stress [2]. The hypothalamus is alerted to both physical and emotional threats and controls the stress response by activating the central hypothalamic–pituitary–adrenal (HPA) axis which secretes glucocorticoids, and the peripheral locus ceruleus–norepinephrine (LC–NE) stress systems which secrete epinephrine/norepinephrine (E/NE) [3]. The degree of activation is proportional to the stress experienced.

The steroid hormone cortisol (also known as hydrocortisone), is the primary glucocorticoid in humans. Cortisol is historically used in research as a substantiated physiological measure of stress and anxiety. Several studies in severe burns of large total body surface area (TBSA) have measured serum cortisol [4–7] and urinary cortisol [5,8,9]. Salivary cortisol is often considered as a better measure of adrenocortical function than serum cortisol, as it is not only a less invasive measure, but also free cortisol (the predominant form in saliva) is the biologically active fraction of the hormone rather than bound cortisol [10–12]. To the best of our knowledge, there is only one study that has measured salivary cortisol [13] for acute burn injury patients, however, this study had high attrition rates, highlighting the need for further studies.

Plasma blood analysis of catecholamines (E/NE), is not only an invasive measure, but also requires immediate processing following blood draw. These challenges make it almost impossible to include as a measure in clinical trials [14]. Furthermore, difficulty in maintaining stability of salivary catecholamines due to oxidative decay [2,15], together with their delayed appearance rate (peaks occur 60 min post stress) [16], highlight the need for alternate measures of sympathetic nervous system (SNS) activity.

Growing literature supports salivary alpha-amylase (sAA) as a surrogate marker of SNS activity, providing evidence that sAA is responsive to stress and reflects the fast activation pattern of the SNS [17–21]. sAA is one of the major proteins in saliva and accounts for 40–50% of protein produced by the salivary glands [18,22]. Activation of the autonomic nervous system has a strong influence over the salivary glands and controls the secretion of sAA [22]. Mastication activates salivary production, however salivary flow is not the primary determinant of stress-induced increases in sAA and therefore unlikely to significantly confound results [23]. Additionally age, medication, food, caffeine, alcohol, smoking, medical drugs, exercise and somatic or psychiatric diseases can alter sAA activity [18]. No studies of burn injury have been published which measure sAA as a biomarker of SNS activity. The aim of this study was to establish if salivary cortisol and sAA were sensitive to detecting stress during acute burn wound care procedures. Furthermore, this study compared the utility of the biomarkers and identified wound management factors or patient/wound demographics associated with salivary cortisol and sAA levels.

1.1. Design

This is a prospective longitudinal study assessing salivary cortisol and sAA as biological markers of stress, based on data collected from a randomized controlled trial (RCT) on burn re-epithelialization [24–26]. The Queensland Children's Health Services (Royal Children's Hospital) Human Research Ethics Committee and The University of Queensland Ethics Committee approved this RCT and it was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12611000913976).

2. Methods

2.1. Setting & participants

Data were collected from August 2011 to August 2012 at the Stuart Pegg Pediatric Burns Center (SPPBC) at the Royal Children's Hospital (RCH), Brisbane, Australia. The RCH is a tertiary pediatric burn referral center servicing approximately 800 new burn patients per year. Inclusion criteria were; (1) children aged 4–13 years, (2) acute burn injury, and (3) burn total body surface area (TBSA) less than 15%. Exclusion criteria were; (1) non-English speaking, (2) a diagnosed condition/illness/developmental delay/psychological condition in addition to a burns injury, (3) prior history of suspected child abuse and (4) grafting of burns. Data collection did not alter the standard medical treatment received.

Participants were recruited and consented at the first change of dressing (COD), with data repeatedly collected at every dressing change until discharge from the outpatient burns clinic. Demographic questionnaires were completed by caregivers and charts were reviewed to obtain pertinent clinical characteristics about the patient and their burn injury.

2.2. Sample & data collection

Prior to the administration of pharmacological pain relief pre-procedurally, Saliva Sample 1 was obtained in the waiting