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Review

Is lactate an effective clinical marker of outcome for children with major trauma? – A literature review

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ABSTRACT

Introduction: The assessment and treatment of children with major injury is fraught with difficulty – differences in anatomy and physiology mean that children that have suffered trauma can be over or under assessed. In recent years, there has been an increase in the use of biochemical markers, such as haematocrit, to assist the clinician in determining severity of injury. This paper examines the evidence surrounding lactate as a marker in paediatric trauma.
Method: A literature search was completed on Medline, CINAHL, Ovid and Science. 63 papers were initially identified – 41 papers were rejected after reading the abstracts. Of the 22 remaining papers – 6 had a paediatric focus, 16 were adult – of these 12 were rejected as not primary studies. Ten papers were fully critically reviewed – of these only one article related to paediatric patients and trauma.
Results: The literature shows that an elevated lactate in a trauma patient is strongly correlated to severity of injury, length of stay and morbidity and mortality. However, one elevated lactate may be misleading and lactate clearance – that is the time when lactate levels return to normal, is just as important in the assessment of the severely injured. However, from this literature review it is clear that there is very little evidence for the relationship between lactate levels and trauma in children and that more studies are required.

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1. Introduction

Major trauma in children in the United Kingdom is relatively rare. In 2012 4720 children were admitted to Emergency Departments suffering with multiple trauma, of these 737 were severely injured with an injury severity score (ISS) of greater than 15 (TARN, 2012), this number had increased to 1511 in 2014 (TARN, 2015). Major trauma morbidity and mortality surpasses all major diseases in children and young adults. It could be argued that trauma is the most serious public health and health care problem in this population (American College of Surgeons, 2012; TARN, 2015).

The differing physiology in children can pose challenges for the clinician faced with a child suffering major trauma. Children have an increased physiological reserve of blood, which allows for maintenance of systolic blood pressure even when 30% of the circulating blood volume has been lost (American College of Surgeons, 2012). Other vital signs, heart rate, capillary refill and respiratory rate can be altered due to psychological, and environmental factors and not due to blood loss, calling into question their sensitivity. This can lead to the child being incorrectly assessed as to the severity of their injuries, and either be over or under resuscitated, neither an ideal outcome (Shah et al., 2013).

Recent military conflicts led to considerable advances in the care of the severely injured adult. In particular, our understanding of the coagulopathy of haemorrhage, its control and management, and importantly, the use of biochemical markers as an indicator of the severity of shock (Bree et al., 2010; Nordmann et al., 2010).

Lactate is one such biochemical marker and is available in routine arterial and venous blood gases. Kruse et al. (2011) completed a systematic review of the literature surrounding the measurement of lactate, via differing routes. They concluded that a peripheral venous lactate demonstrated a good correlation to arterial lactate, as well as a very high sensitivity and acceptable specificity for hyperlactaemia. There was conflicting evidence surrounding the use of capillary lactate as there is a tendency for a higher lactate to be measured via this route, however the number of studies reviewed were small in nature, but they recommend that a higher lactate level is set for a capillary gas. Lactate is known to be a by-product of anaerobic metabolism and it has been suggested that an increase in the traumatized adult can be an indicator of occult hypoperfusion and occult bleeding (Cheddie et al., 2013). This literature review will firstly discuss the production of lactate in trauma, and the evidence surrounding lactate as a marker of occult bleeding. It will also discuss the application of the evidence to children.

2. The biochemistry of lactate production

Since the 19th Century lactic acid was known to have been formed as a result of lack of oxygen to the cells, and was first discovered with the fermentation of lime beans in anaerobic conditions (Pasteur 1863 cited in Brooks, 2009). Lactate acid is generated in cells under anaerobic glycolysis. Glycolysis is a complex process converting a glucose or glycogen molecule into energy. The process uses different enzymes at differing stages to generate Adenosine Diphosphate (ADP), from Adenosine Triphosphate (ATP). ADP and ATP are the energy molecules required for bodily functions. The end product of glycolysis is pyruvate (Kraut and Madias, 2014).

Pyruvate can have two fates, if there is sufficient oxygen it enters the Kreb's cycle where it is metabolized further and produces more ADP and ATP. If there is insufficient oxygen the pyruvate gets converted into lactate via lactate dehydrogenase (LDH) (Sola-Penna, 2008). This is a reversible process and when there is sufficient oxygen, lactate can be converted back to pyruvate and enter the Kreb's cycle to generate more energy (Agrawal et al., 2004). However, if hypoxia continues this leads to an accumulation of lactate and ultimately lactate acidosis (see Fig. 1).

2.1. Lactate production in children

It is unclear if the biochemistry of lactate production is the same in children. Exercise studies in children (Mocellin et al. 1991 cited by Ramanathan et al., 2015) showed a poor correlation between an increased lactate and anaerobic metabolism. During exercise, children have a higher oxygen transport capacity, thereby, suggesting that they have a differing physiological response to tissue hypoxia (Anderson and Mahon, 2007). It is not clear how this mechanism affects a child's ability to respond to hypoxia due to hypoperfusion.

Aono et al. (1993) suggest that fear and anxiety may also cause an elevated lactate. In a small study ($n = 28$ males aged 2 years), Aono et al. (1993) examined the lactic acid levels between 2 differing sets of children (calm vs. upset) undergoing anaesthesia for circumcision. The study showed a correlation between higher lactic acid and crying ($p < 0.001$). Aono et al., (1993) suggest this rise in lactic acid is due to the release of stress hormones, when the child is crying. However, the authors did not measure the level of stress hormones or when the lactic acid level reduced to normal. Although this study is small, it does raise an interesting point that an increased lactic acid levels in a child with severe trauma may be due to fear and anxiety rather than haemorrhage. What is clear is that there is very little specific knowledge about the production and clearance of lactic acid level in children during trauma, and how their bodies respond to the increase in lactate and the subsequent acidosis.

3. Methodology of literature search

In order to examine this area further, initially a research question was developed using a PICO (Population, Intervention, Control and Outcome) model as a structured approach (Khan et al., 2011). For this literature search the PICO was "Is lactate an effective clinical marker of outcome for children with major trauma?"

From each of the components of the research question a list of keywords was developed including synonyms with spelling variations (see Table 1). These keywords were used in differing computer search engines – for example, Medline, CINAHL, Ovid and Science. Both paediatric and adult populations were included to ensure that as wide a search possible was completed. The literature search was restricted to the English language, peer-reviewed journals and from the 2000–2015, these dates were used to ensure that recent literature pertinent to lactate was reviewed.

The abstracts of the literature were reviewed for their relevance and inclusion. The inclusion criteria, for this review were child and adult trauma, lactate levels, and outcome, both pre-hospital and hospital literature was included. Articles that focused on lactate in sepsis were rejected, due to the differing pathophysiology of disease. The literature was reviewed and categorized according to themes. The themes that emerged were single lactate levels and outcome, and lactate clearance and outcome.

4. Results

Sixty-three papers were identified, and from reviewing the abstracts 27 papers met the inclusion criteria, full text papers were then obtained. Five papers were rejected as opinions, letters and case studies. Of the remaining papers ($n = 22$), 6 were paediatric papers and 16 were adult papers. For this literature review the definition of 'Paediatric' was 16 years and under. Of the 6 paediatric papers, 5 were rejected as not relevant to topic area but added to the body of knowledge. Of the 16 adults papers 7 were rejected