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Research paper

The effect of urinary and arterial blood pH on the progression of acute kidney injury in critically ill patients with systemic inflammatory response syndrome or sepsis and oliguria

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ABSTRACT

Purpose: The aim of this study was to examine the relationship between urinary and arterial blood pH and the progression of acute kidney injury in critically ill patients with sepsis or SIRS and oliguria.
Design and setting: A prospective observational study was performed on critically ill adults in a tertiary intensive care unit in Melbourne, Australia. Urinary and arterial blood pH were measured at 12 hourly intervals for 60 h for patients with sepsis or SIRS, oliguria and who were at high risk of acute kidney injury. Patient RIFLE class at baseline and 60 h were assessed for an association to urinary and arterial blood pH. Secondarily, change in peak serum creatinine from baseline over 5 days was assessed for an association to mean urinary and arterial blood pH in the first 48 h of the study. Finally, relevant patient demographic and physiological variables were assessed for an association to change in peak serum creatinine from baseline over 5 days.
Results: 44 patients were included in the study; 13 did not survive to hospital discharge. Baseline arterial blood pH was associated with baseline RIFLE class but not RIFLE class at 60 h. Urinary pH was not associated with RIFLE class at baseline or 60 h. There was no association between mean urinary or arterial blood pH in the first 48 h and change in peak serum creatinine from baseline over 5 days. None of the patient and demographic and physiological variables showed an association to change in peak serum creatinine from baseline in the 5-day study period.
Conclusion: Urinary and arterial blood pH were not associated with the progression of acute kidney injury in critically ill patients with sepsis or SIRS and at risk of acute kidney injury.

1. Introduction

Acute kidney injury (AKI) is a relatively common occurrence in critically ill patients with sepsis, and accounts for approximately 32% of all acute kidney injury in the critically ill.[1] The beginning and ending supportive therapy (BEST) kidney investigators, in an analysis of critically ill patients in 54 hospitals in 23 countries, revealed that critically ill septic patients with septic acute kidney injury have higher rates of in-hospital mortality than non-septic critically ill patients with acute kidney injury. (70.2% *vs* 51.8%; $p < 0.001$).[2] There is currently no known treatment to prevent the progression of, or to reverse, acute kidney injury in this group of patients. Intermittent dialysis, continuous renal replacement therapies (CRRT) and hybrid therapies, such as Slow Low Efficiency Daily Dialysis (SLEDD) can, where necessary, support patients with acute kidney injury, but these therapies increase cost and workload and come with their

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own potential complications. Even with renal replacement therapy, mortality rates for critically ill septic patients with acute kidney injury remain high.

Urinary alkalinisation by use of bicarbonate infusion is commonly instituted in an attempt to prevent acute kidney injury in critically ill patients who present with rhabdomyolysis. However, research has failed to achieve a genuine consensus on its effectiveness.[3,4] Urinary alkalinisation is also widely used as a treatment to prevent acute kidney injury in patients at risk of contrast nephropathy. However, evidence on the effectiveness of urinary alkalinisation for the prevention of contrast nephropathy is also mixed.[5,6] Recent trials by Haase et al.,[7] and Heringlake et al.[8] have failed to show evidence of a nephroprotective effect of alkalinisation of blood or urine by using sodium bicarbonate infusion perioperatively in open heart surgery patients, despite promising results in a pilot study.[9] There is little known of the effect of urinary or blood pH on the progression of acute kidney injury in adults with sepsis or SIRS and there are no previous studies, to our knowledge, exploring the potential relationship between urinary and/or blood pH and the progression of renal failure in this high risk group of patients. Therefore, we conducted a study to assess the potential association of arterial blood and urinary pH with the development of acute kidney injury in patients with sepsis or SIRS.

2. Method

We conducted a prospective observational study, with all inpatients in the Royal Melbourne Hospital Intensive Care Unit eligible to be screened for the study. The project was approved by the Melbourne Health Human Research Ethics Committee (HREC 2010.254). Our study used a convenience sample of inpatients at the Royal Melbourne Hospital over a 12-month period from January 21, 2010 to January 21, 2011. Data collection was ceased after 12 months in order to comply with study funding guidelines. The screening was undertaken by the study investigators and took place at any time during the 12-month study period. Patients who were oliguric (urine < .5 ml/kg/h for two consecutive hours) were screened initially for evidence of two SIRS criteria. Patients meeting the SIRS inclusion criteria were then tested for serum neutrophil gelatinase-associated lipocalin (NGAL) (Biosite Triage Meter Pro (San Diego, USA)). If the NGAL was greater than 150 ng/ml patients were then enrolled in the study if all other inclusion criteria and no exclusion criteria were met. NGAL was used in the inclusion criteria in order to predict and include those patients who were at risk of acute kidney injury but who may not yet have increased serum creatinine or urea. Previous studies assessing the accuracy of serum NGAL as an early predictor of acute kidney injury have shown this measurement to be an accurate and valid early predictor of risk of acute kidney injury.[10,11]

Tables 1 and 2 outline the inclusion and exclusion criteria for patient enrolment in the study.

Table 3 outlines the criteria for diagnosis of SIRS.[12]

Table 1
Inclusion criteria.

Critically ill patients over the age of 18, who exhibit at least two SIRS criteria (see Table 3)
Oliguria (<0.5 ml/kg/h urine for 2 h) at any point in the ICU stay
Plasma NGAL level > 150 ng/ml
Presence of an arterial line for clinical care
Presence of a urinary catheter
Patient expected to remain in ICU for at least 60 h

Table 2
Exclusion criteria.

Known chronic renal failure or end-stage renal failure with creatinine > 350 and/or receiving renal replacement therapy
Confirmed or suspected acute glomerulonephritis, acute interstitial nephritis, renal vasculitis or post renal aetiology for kidney dysfunction
Already receiving or about to start CRRT at time of enrolment
Expected death within 24 h

Table 3
SIRS criteria.[12]

Patients were required to meet any two of the following:
Temperature > 38 C or <35 C
Heart rate > 90 beats/min
Respiratory rate ≥ 20/min
$PaCO_2$ < 32 mmHg
Alteration in white blood cell count > 12,000 cells/mm^3 or < 4000 cells/mm^3

2.1. Measurement

To be included in the study patients had to demonstrate a high risk of progression of acute kidney injury and therefore a serum NGAL greater than 150 ng/ml was required. At study commencement a baseline arterial blood gas analysis (ABG) (Radiometer ABL 800 Flex (Copenhagen)) and urinalysis were performed by the bedside nurse. Urine was sampled from the burette attached to the main urine drainage bag. Urinary pH was measured by bedside nurses using SIEMENS Multistix 10 SG reagent strips. The ABG and urinalysis were subsequently recorded at 12 h intervals (±1 h) for 60 h. Creatinine was recorded at least once a day, as part of routine unit procedure, for the five day study period. If patients were transferred out of the intensive care unit, a urinalysis was performed on the ward, where possible, but no further ABGs were taken where arterial lines were not available. Demographic data and illness severity scores were derived from the AORTIC (Australasian Outcomes Research Tool for Intensive Care) database, a departmental support database that routinely records data on all patients admitted to the ICU. Relevant clinical indices were derived from the ICU observation and medication charts. RIFLE class was determined according to established criteria (Table 4) and recorded at study commencement, 60 h, ICU discharge and hospital discharge. Classification of acute kidney injury according to RIFLE criteria[13] has been a widely accepted tool for the detection and classification of severity of acute kidney injury in patients since its creation by the Acute Dialysis Quality Initiative Working Group.[14,15]

Statistical analysis was performed primarily to determine the potential correlation at baseline and 60 h between RIFLE class and

Table 4
RIFLE Criteria.[13]

Class	Glomerular filtration rate and creatinine Criteria	Urine output criteria
Risk	Increased serum creatinine × 1.5 or decreased Glomerular filtration rate (GFR) > 25%	Urine output < 0.5 ml/kg/h × 6h
Injury	Increased serum creatinine × 2 or GFR decrease > 50%	Urine output < 0.5 ml/kg/h × 12 h
Failure	Increased serum creatinine × 3 or GFR decrease 75% or serum creatinine ≥ 4 mg/dL (354 μmol/L)	Urine output < 0.3 ml/kg/h × 24 h or anuria × 12 h
Loss	Persistent acute renal failure – complete loss of renal function > 4 weeks	
ESKD	End stage kidney disease > 3 months	