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The value of blood lactate measurements in ICU: An evaluation of the role in the management of patients on haemofiltration.

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Abstract

In response to clinical demand some point-of-care analysers now provide blood lactate measurements in critical care. Recent literature has raised concerns about the value and interpretation of these measurements. Two particular concerns relate to over-interpretation of lactate rises as equating tissue hypoxia and also the failure to recognise the contribution from inotropic support. We undertook this study to evaluate blood lactate measurements in intensive care unit (ICU) patients in the assessment of response to, and requirements for, haemofiltration (HF) with lactate replacement fluid and to evaluate influences from hepatic failure and from inotropic supportive therapy.

Haemofiltration is a convenient renal replacement therapy widely used in intensive care management as an alternative to haemodialysis. Mainly used for the treatment of acute renal failure the process involves removal by filtration of fluid, electrolytes, metabolites and other substances and simultaneous replacement of essential fluid and electrolytes as well as a buffer, usually in the form of lactate (sodium salt). There is controversy about whether lactate replacement may be harmful to the patient and, if so, when it would be appropriate to use a lactate-free fluid at greater expense.

Serial blood lactate with simultaneous blood gas measurements were recorded in 27 patients requiring HF for acute renal failure. At baseline all patients had base deficits of >5mmol/L and 14 (52%) had blood lactates of >3.5mmol/L. Lactate 'tolerance' was monitored by peak changes in these parameters during the procedure. There was a worsening of base deficit in only three of the patients in whom lactate rises exceeded 10 mmol/L at some stage during HF with one survivor. A further twelve patients with rises of blood lactate greater than 5 mmol/L improved their base deficit (+1 to +17) with 8 (67%) survivors. Of the remaining twelve patients with improved base deficit (+2 to +20), 10(83%) survived. The influence on 'lactate tolerance' in patients with co-incident liver disease and those on inotropic support was studied.

In these groups lactate tolerance was compromised, particularly those on adrenaline support. Patients with initial blood lactate measurements of >10mmol/l and large base deficits were also lactate intolerant.

The data suggest that rises in blood lactate during HF signal harm if accompanied by inadequate improvement in base deficit. Blood lactate and simultaneous acid-base response measurements during HF help to assign correct buffer replacement and should be performed on all patients.

Introduction

Increased metabolic monitoring in intensive care patients has been a key development from new technology in point-of-care testing for critical care and the introduction of parameters to the 'metabolic set' need to match clinical needs and to have a clear role in patient management. The highest mortality rate in intensive care is in patients with multi-system failure associated with severe sepsis, a common complication of which is a degree of lactic acidosis. In recent years much debate has taken place about the mechanisms underlying lactic acidosis in patients with severe sepsis. Traditionally, high blood lactate levels have been regarded as a reflection of cellular hypoxia and hypoperfusion. However many recent experimental and clinical studies have shown that lactate levels do not always correlate with indices such as total oxygen debt, the degree of hypoperfusion or the severity of shock (1). This has led to confusion amongst critical care clinicians concerning the clinical utility of blood lactate measurements. However the lack of correlation between the degree of lactate elevation and the other indices does not necessarily negate the value of lactate determinations but reflects the fact that the changes which take place in sepsis are complex and variable between different tissues (2).

The arterial lactate concentration depends upon the rate of its production and utilisation by various tissues. Net producers of lactate include muscle, brain, skin, red cells and intestine whilst organs which consume lactate include the liver, heart and the kidney. One example of the metabolic complexity is that above a certain lactate level, skeletal muscle is believed to be a net consumer of lactate rather than a producer. Another is the significant reduction in hepatic lactate consumption in hypotensive and acidotic conditions.

Lactate is produced in the cytosol by the action of lactate dehydrogenase on pyruvate as follows:

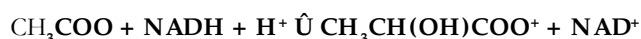
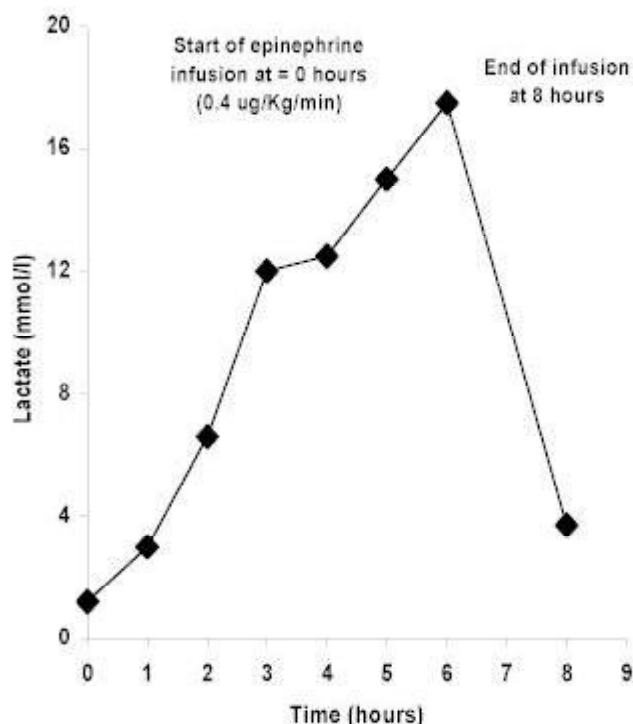


Figure 1. Effects of adrenaline (norepinephrine) infusion on blood lactate concentration in the normal sheep. During the same time period the systemic oxygen delivery approximately doubled indicating that rise in lactate cannot be due to cellular hypoxia.



At a cellular level the determinants of the lactate concentration include: the pyruvate concentration, the cytosolic redox state or NADH/NAD ratio and the rate of transmembrane transport of lactate. From the above equation it will be appreciated that an increased pyruvate concentration will therefore lead to increased lactate concentration by mass action. As mentioned previously, there is little evidence to support the view that increased lactate levels stem from impaired metabolism of pyruvate due to lack of oxygen. However evidence in septic patients does exist for increased pyruvate concentrations as a result of excessive glycolysis, producing more pyruvate than can be metabolised oxidatively, consequently leading to high blood lactate levels. Similarly catecholamines that are administered in often high doses as cardiac inotropes in severe shock can also increase glycolysis and reduce hepatic gluconeogenesis. The effects of such drugs on lactate levels has been convincingly demonstrated in animals (**Figure 1**) and similar effects are believed to be the cause of high lactate levels seen in patients receiving catecholamine infusions and particularly when given to septic patients (3). There is no convincing evidence of the role of lactate transporters in determining cellular lactate levels.

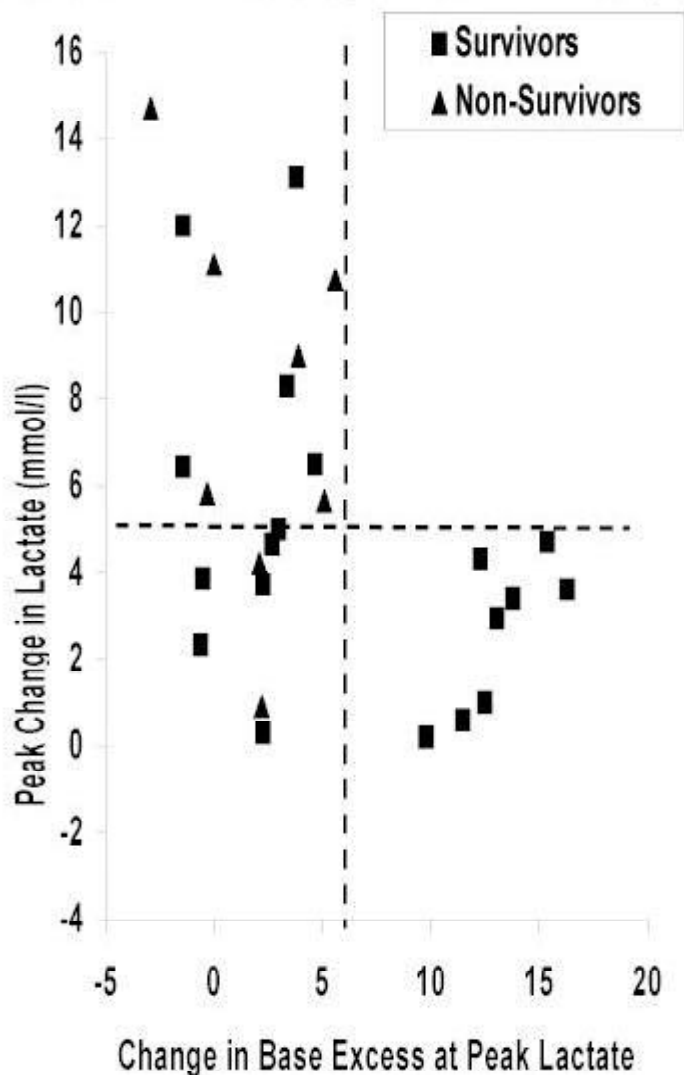
Another possible cause for high lactate levels in sepsis is reduced oxidation of lactate via the TCA cycle as a result of inhibition of activity of the pyruvate dehydrogenase complex by endotoxin and cytokines with subsequent unavailability of pyruvate for mitochondrial oxidation. In addition several studies have documented hyperlactataemia in patients with sepsis and lung injury which has been attributed to lactate release predominantly from the lungs, a sizeable proportion originating from activated

lymphocytes (4,5). Finally, impairment of kidney and liver function are common abnormalities in septic patients and hyperlactataemia is a common feature of both and can predict poor outcome.

These recent investigations provide some understanding of the complex biochemical and cellular events involved in lactate metabolism. They show that in patients with sepsis, increasing lactate levels do not necessarily correlate with hypoxia, the magnitude of the hypoperfusion or the severity of the shock. However hyperlactatemia during critical illness can serve as a metabolic marker of cellular stress and in intensive care regular monitoring of blood lactate levels provides a guide to diagnosis and treatment in certain patients. It is recognised that hyperlactataemia occurs relatively late in patients with ischaemic bowel when the balance of overproduction of lactate is no longer matched by its utilisation. In patients at risk of this complication, and when methods of assessment of local ischaemia such as gastric tonometry are unavailable or unvalidated, regular monitoring to detect an increasing blood lactate should serve to alert the clinicians. Most importantly, in this and many other contexts, units that measure lactate consistently with each blood gas analysis recognise the value to their patient management of the 'normal lactate'.

An example of the importance of this regular metabolic monitoring is in-patients undergoing continuous veno-venous haemofiltration (CVVH or HF) for the treatment of acute renal failure and metabolic acidosis. Haemofiltration is a convenient renal replacement therapy widely used in intensive care management as an alternative to haemodialysis because it can be sustained over a 24-hour

Figure 2. Survival from haemofiltration using lactate buffer. Relationship between lactate tolerance and changes in base excess at peak lactate value.



period with better control of the pH and less disturbance of homeostasis in very sick patients. The process of HF involves removal by filtration of fluid, electrolytes, metabolites and other substances and simultaneous replacement of essential fluid and electrolytes as well as a buffer, usually in the form of lactate (sodium salt). There is controversy about when lactate replacement may be harmful to the patient and, if so, when it would be appropriate to use a lactate-free fluid at greater expense (6,7,8,9,10,11). Apart from cost other advantages of lactate over bicarbonate buffer include ease of use and lesser volume replacement.

Methods

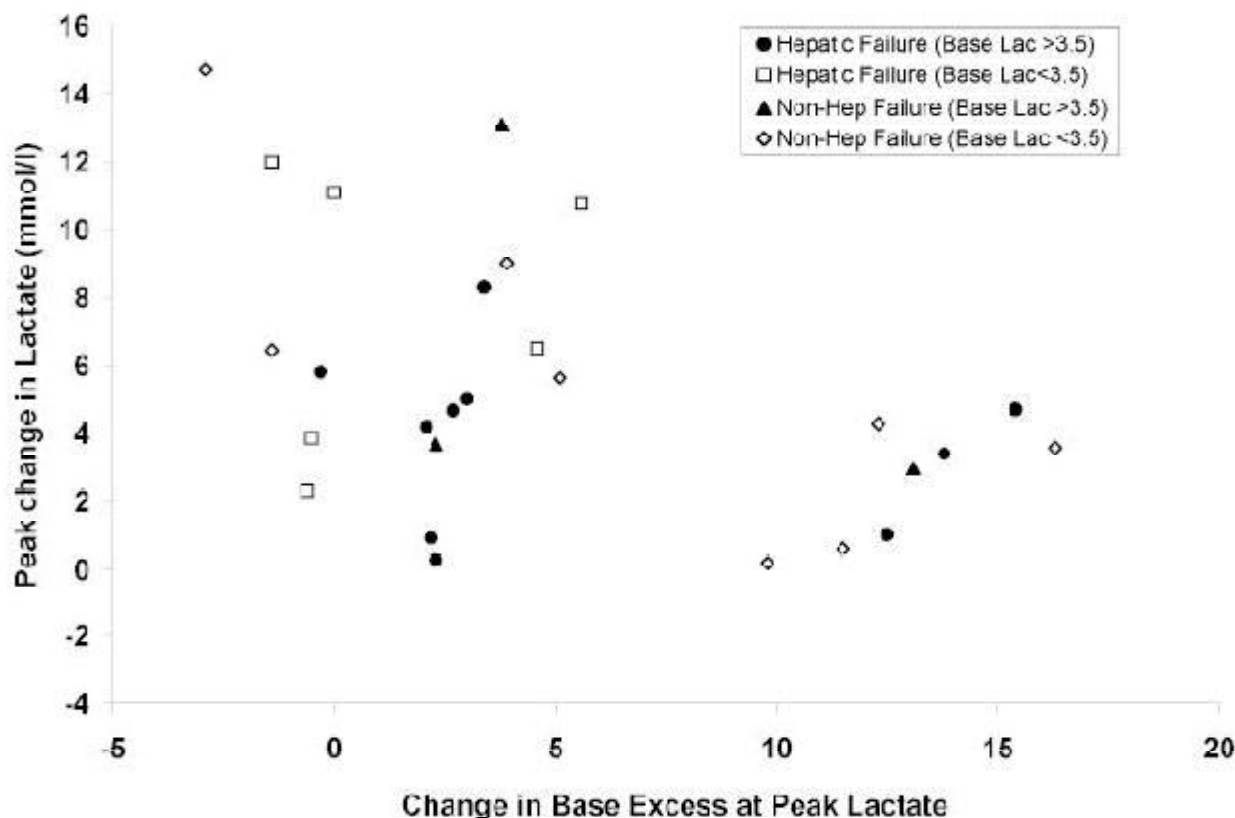
To investigate the metabolic effects of using lactate buffer in-patients undergoing HF we carried out an observational study of 27 patients undergoing this procedure for treatment of acute renal failure in the ICU. The 'lactate tolerance' in these patients was monitored by measuring the peak changes in acid-base parameters including base excess and blood lactate levels during the HF procedure. All acid-base and lactate measurements were performed on a Roche OMNI 9 Critical Care Analyser (Roche Diagnostics,

Mannheim, Germany). Survival, defined as those patients alive five days after completion of the course of haemofiltration, was used as an arbitrary endpoint recognising its limitation in these sick patients

Results

At baseline all the patients had base deficits of >5mmol/L and 14 (52%) had blood lactates of >3.5mmol/L. During the HF there was a worsening of base deficit in only three of the patients, in whom lactate rises exceeded 10 mmol/L at some stage during the procedure with one survivor. A further twelve patients with rises of blood lactate greater than 5 mmol/L improved their base deficit, from +1 to +17: 8 (67%) of these patients were survivors. Of the remaining twelve patients with improved base deficit (+2 to +20), 10(83%) survived (Figure 2). The influence on 'lactate tolerance' in patients with coincidental liver disease was studied. In these groups lactate tolerance was compromised although the baseline lactate did not predict either the rate of lactate tolerance or the outcome. However patients with initial blood lactate measurements of

Figure 3. Influence of hepatic failure and baseline arterial lactate on lactate tolerance and changes in base excess at the peak lactate concentration during haemofiltration using lactate replacement fluid buffer.



>10mmol/l and large base deficits were also lactate intolerant (Figure 3). Patients on inotropic support at least at the commencement of HF were also less lactate tolerant with less improvement in base deficit.

Discussion

The data suggest that rises in blood lactate during HF signal harm if accompanied by inadequate improvement in base deficit. Blood lactate and simultaneous acid-base response measurements during HF help to assign correct buffer replacement and should be performed on all patients. The data from this study suggest good outcome where peak base excess exceeds 6.0 mmol/l at peak lactate and worse outcome if the peak lactate exceeds 5.0 mmol/l. This study is continuing with monitoring of the metabolic effects of changing replacement buffer to lactate-free in lactate intolerant patients.

The controversy in this area extends to the actual mechanism of how acidosis is corrected by haemofiltration with lactate and how it could be might be exacerbated in certain patients. On the basis of conventional acid-base theory, the lactate anions are eventually converted into CO₂ which is removed by ventilation, thereby correcting the acidosis. This relies to a large extent upon the liver metabolising the lactate as part of the Cory cycle, carrying out the appropriate conversion to glucose with simultaneous consumption of hydrogen ions. In patients with compromised liver function, this conversion does not take place with development of an acidosis from free unmetabolised CO₂

However an alternative theory is that the removal of lactate from the plasma by the liver maintains the Strong Ion Difference (SID), calculated from the equation $(Na + K + Ca(i) + Mg - Cl + lactate)$, at a normal level (40-42 mmol/l) thereby reducing the dissociation of water to produce hydrogen ions (12). In cases of severe liver failure or when the metabolic pathway for lactate metabolism is compromised for reasons discussed earlier, then lactate accumulates in plasma, SID is lowered and more water dissociates to maintain electroneutrality leading to more hydrogen ions and an acidosis. This theory is not easy to evaluate in patients entirely on lactate replacement but may be studied in those where the buffer is changed and in those on lactate-free replacement from the onset of HF.

The unravelling of this system in intensive care patients with multi-system failure requiring complex and continuous manipulation of physiological processes, is critical not only for prognosis but also management. Point-of-Care testing in the ICU is now able to help provide more continuous and precise metabolic monitoring of acid-base disturbances in the critically ill and should allow real progress in this unravelling process.

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