


SHORT REPORT

Venous blood for the analysis of acid–base status in a model of septic shock

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Abstract

Objective: To determine the relationship between arterial and venous acid–base status in a model of septic shock.

Methods: Paired samples ($n = 435$) of arterial and femoral venous blood from 57 sheep (47 septic, 10 non-septic) managed with protocol-guided ventilation, sedation, parenteral fluids and inotropic support.

Results: The arterial–venous difference in acid–base parameters was similar with and without sepsis. There was a consistent arterio–venous relationship for metabolic (pH, lactate, bicarbonate, base excess), but not respiratory parameters (partial pressures of oxygen, carbon dioxide, and haemoglobin–oxygen saturation), independent of sepsis.

Conclusions: Venous blood provides a reliable measure of metabolic but not respiratory disturbance.

Key words: animal, blood gas analysis, disease models, lactic acid, sepsis.

Introduction

Assessment of a patient with sepsis includes analysis of acid–base status. This has traditionally relied on pH and blood gas measurement from arterial blood. However, arterial puncture is

uncomfortable and technically more difficult than routine venous blood sampling, especially in patients with cardiovascular instability. Analysis of venous acid–base status may be a suitable alternative in the early assessment of septic patients.

Previous studies investigating the relationship between arterial and venous blood have reported a close correlation, and limits of agreement that many emergency clinicians consider acceptable.^{1,2} However, few have specifically investigated the arterio–venous relationship in sepsis.³ We sought to examine this in a controlled experimental model of septic shock.

Methods

This was a post-hoc study of data obtained from previously published studies of a septic shock model.⁴ The project was approved by the institution's animal ethics committee.

In brief, 57 ewes (60–70 kg) were studied individually for 26 h receiving protocol-guided sedation (midazolam, ketamine), ventilation (via a tracheal tube to maintain end-tidal CO₂ of 30 mmHg, inspired oxygen to maintain pulse O₂ saturation >95%), parenteral fluid (Hartmann's) and noradrenaline infusion to maintain mean arterial pres-

sure 75 mmHg and central venous pressure 5 mmHg.

Sepsis was induced in 47 sheep with intravenous *Escherichia coli* (10⁸ organisms/kg). These animals developed an elevated temperature, increased cardiac index, reduced mean arterial pressure, hyperlactataemia, acute renal dysfunction and a requirement for noradrenaline.⁴ Ten sheep were non-septic controls and remained physiologically stable.

Arterial (carotid) and venous (femoral) blood samples were collected at 0, 2, 4, 8, 12, 16, 20 and 26 h. All samples at time zero were non-septic. Partial pressures of oxygen (pO₂), carbon dioxide (pCO₂), pH, haemoglobin–oxygen saturation (Hb–O₂) and lactate were assayed on a RAPID-Point 405 Blood-gas Analyser (Siemens, Munich, Germany). Actual bicarbonate and base excess were calculated from standard equations.⁵

To account for paired and repeated measures within sheep, a linear mixed effects model was employed with specimen type (arterial, venous) as a fixed effect and random effects for study animal and measurement time. The intra-class correlation coefficient (ICC) was calculated using a variance components approach. Sepsis was then included as an interaction effect with specimen type, and $P < 0.01$ considered significant (Stata v.17; StataCorp LLC, College Station, TX, USA).

Results

There was a total of 435 paired samples; 312 were taken when animals were septic, and 123 non-septic. There was a significant difference between arterial and venous samples for all variables other than lactate. With the

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TABLE 1. Estimated means (95% confidence intervals) for acid–base parameters†

Covariate name	Arterial (A)	Venous (V)	A-V difference	Intra-class correlation	A-V * sepsis P value
pH	7.45 (7.44–7.47)	7.39 (7.37–7.41)	0.066 (0.063–0.069)	0.964 (0.956–0.971)	0.224
pCO ₂ , mmHg	28.9 (28.0–29.7)	37.5 (36.7–38.4)	–8.7 (–9.2 to –8.2)	0.588 (0.518–0.654)	0.214
pO ₂ , mmHg	163 (155–170)	40 (33–48)	123 (117–128)	0.258 (0.181–0.353)	<0.001
HCO ₃ [–] act, mmol/L	20.3 (19.6–21.0)	22.5 (21.7–23.2)	–2.2 (–2.4 to –2.0)	0.935 (0.922–0.946)	0.024
BE(B), mmol/L	–2.6 (–3.6 to –1.7)	–2.2 (–3.1 to –1.3)	–0.5 (–0.6 to –0.3)	0.981 (0.977–0.985)	0.170
Hb-O ₂ , %	99.0 (97.2–100)	63.3 (61.5–65.1)	35.7 (34.2–37.3)	0.191 (0.126–0.279)	0.726
Lactate, mmol/L	3.6 (3.0–4.2)	3.6 (3.0–4.2)	–0.02 (–0.08 to 0.05)	0.995 (0.993–0.997)	0.318

HCO₃[–]act = actual bicarbonate ion = 0.0307 × pCO₂ × 10^(pH[37°C]–6.105). BE(B) = base excess of blood = (1 – 0.014 × tHb) × [(HCO₃[–]act – 24.8) + ((7.7 + 1.43 × tHb) × (pH[37°C] – 7.40))]. Hb-O₂ = haemoglobin-oxygen saturation. †Linear mixed effects regression for arterial and venous blood samples in septic and non-septic sheep. Model estimated means and 95% confidence intervals for the arterial-venous (A-V) fixed effect model, with intra-class correlation coefficient within sheep and time, and interaction model P values for the sepsis by A-V interaction term.

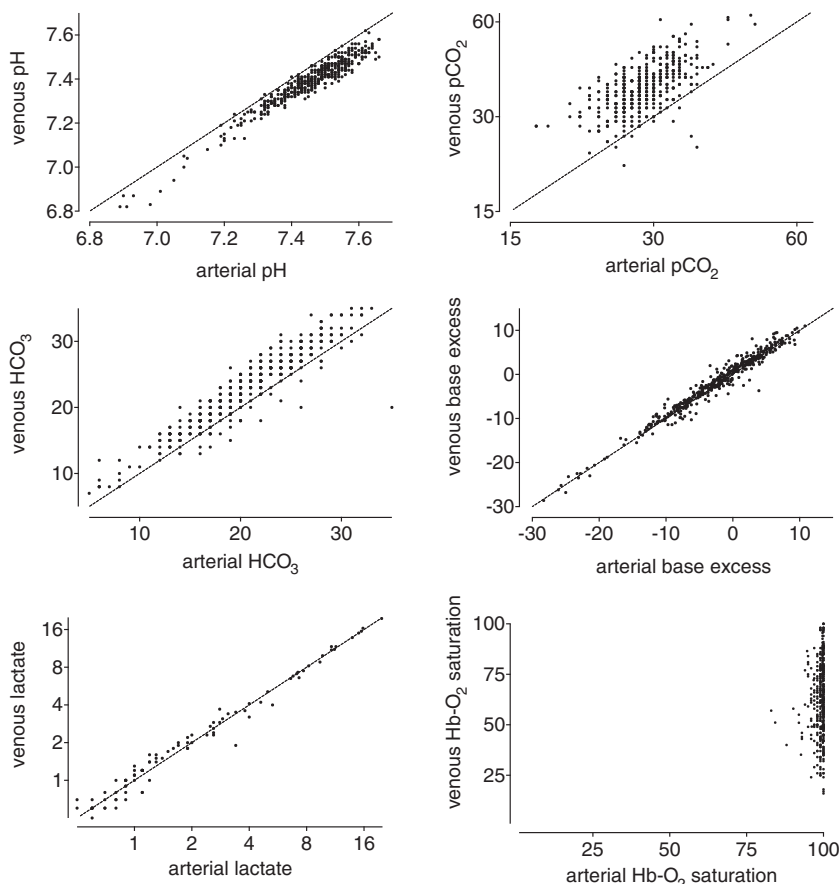


Figure 1. Scatter plots with the line of identity of paired arterial and venous blood samples for pH, pCO₂ (mmHg), HCO₃[–] (mmol/L), base excess (mmol/L), lactate (mmol/L) and haemoglobin-oxygen saturation (%). Samples were taken from 57 sheep (47 septic, 10 non-septic) receiving protocol-guided ventilation, sedation, parenteral fluids and inotropic support for 26 h. pCO₂ and lactate are plotted on a log-scale.

exception of pO₂, the extent of arterio-venous difference did not differ in the presence of sepsis (Table 1). For any given sheep, correlation between arterial and venous samples was almost perfect for lactate (ICC >0.99), substantial for pH and base excess (ICC >0.95), moderate for bicarbonate (ICC >0.90) and poor for pCO₂, pO₂, and Hb-O₂ (ICC <0.6; Fig. 1).

Discussion

In a controlled experimental setting, venous blood provided a reliable assessment of metabolic but not respiratory acid–base status in non-septic and septic sheep. Venous blood lactate was almost equivalent to arterial concentrations, and there was a consistent arterial–venous relationship for pH, BE and bicarbonate. These observations were independent of sepsis.

In contrast, the relationship between arterial and venous pO₂, pCO₂ and Hb-O₂ is wide and inconsistent. This is despite controlling ventilation to maintain a fixed end-tidal CO₂ and pulse Hb-O₂ saturation. The poor relationship is consistent with a meta-analysis concluding venous pCO₂ is an unpredictable substitute for arterial pCO₂,¹ and precludes reliable analysis of the respiratory contribution to acid–base disturbances.

Strengths of this experimental study are that it was specific for sepsis, had

non-septic controls, standardised timing of blood samples, replicated many features seen in the clinical setting, applied protocol-guided supports, and analysis accounted for paired and repeated measures.

Limitations include it being an experimental model of sepsis, and translation from non-human models to the clinical environment must be done with caution. The model incorporated supportive treatments, and the arterio-venous relationship may differ in the un-resuscitated state. Finally, this is a post-hoc study, and the model was not designed to specifically assess arterio-venous relationship. It does, however, ensure the principles of animal research ethics to utilise information available from non-human models of disease.

Conclusion

In an ovine model of sepsis, venous blood reliably predicts arterial pH, lactate, bicarbonate, and base excess. However, venous pCO₂, pO₂ and Hb-O₂ has a poor relationship with arterial blood. The present study supports data from previous uncontrolled clinical

studies, and suggests that venous blood can be a reliable measure of metabolic acid-base status in septic shock.

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Competing interests

None declared.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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