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Evaluation of end-tidal carbon dioxide role in predicting elevated SOFA scores and lactic acidosis

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Abstract The development of organ dysfunction is a key contributor to morbidity and mortality in sepsis. End-tidal carbon dioxide levels measured by non-invasive end-tidal capnography (ETCO2) may provide a rapid assessment of a patient's underlying metabolic status. The objective of this study was to explore the association between ETCO2 and (1) organ dysfunction [sequential organ failure assessment (SOFA) score], and (2) serum lactate levels in febrile emergency department (ED) patients. Prospective, observational cohort study of a convenience sample of 97 adult (age 18 years or older) patients presented to an academic urban ED with a fever and suspected infection. The outcomes were ED SOFA score and serum lactate level. Based on prior studies, we categorized an ETCO2 <35 mmHg, a priori, as abnormal for the exposure. We defined clinically significant organ failure as a SOFA score of >2, and an abnormal lactate as >4 mmol/L. The correlation of ETCO2 with SOFA and lactate level was analyzed using Pearson correlation coefficient. Operating characteristics were calculated with 95% confidence intervals, along with the area under the curve (AUC). Among 97 patients enrolled, 5 (5%) had an abnormal lactate and 34 (35%) had a SOFA score >2. A significant correlation was found between ETCO2 and SOFA score ($r = -0.35$, $p < 0.01$), and ETCO2 and lactate level ($r = -0.35$, $p < 0.01$). A receiver operator curve for ETCO2 and SOFA >2 had an AUC of 0.69. ETCO2 of <35 has a sensitivity of 0.73 (95% CI 0.56–0.85) and specificity 0.50 (0.38–0.62) in predicting SOFA scores >2. ETCO2 <35 has a sensitivity of 0.60 (0.22–0.88) and specificity 0.42 (0.32–0.52) in predicting lactate >4 with an AUC of 0.62. We found a small, but statistically significant correlation, between ETCO2 and SOFA scores; however, based on questionable operating characteristics, the test seems to have limited ability to meaningfully impact clinical decision making. Larger confirmatory studies are required before final assessment.

Keywords SOFA · Capnography · Lactic Acidosis · End-tidal carbon dioxide level

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Introduction

Bacteremia and severe sepsis are responsible for significant morbidity, mortality, and costs to the health care system. Approximately 2.8 million emergency department (ED) visits over 10 years were related to sepsis [1]. Early identification of these patients is essential in reducing their mortality. Furthermore, the presence and extent of end organ dysfunction predicts mortality in this patient population [2]. The severity of lactic acidosis is an accepted marker of disease severity in patients with sepsis [3]. The normal physiological response to metabolic acidosis is a compensatory respiratory alkalosis in an attempt to maintain homeostasis. Capnography is a non-invasive measure of exhaled end-tidal carbon dioxide (ETCO2) that is a function of basal metabolic rate, cardiac output, and

ventilation status. Capnography is regularly used in the pre-hospital and ED settings to monitor respiratory status during procedural sedation and to confirm proper endotracheal tube placement. Novel uses of ETCO2 in trauma have shown that ETCO2 is low in patients with hypovolemic shock, and that ETCO2 can be used as a marker in injury severity and prediction of mortality [4]. Capnometry appears to be a feasible method to identify patients with acidosis, leading us to postulate utility in another disease state where acidosis is well-established marker of poor outcome, severe sepsis

Early identification of patients at risk for end-organ damage is a challenge for the clinician [1, 5]. Others have demonstrated the potential mortality benefit of early identification and treatment with aggressive resuscitation protocols [6]. Thus, end-tidal carbon dioxide monitoring may allow for early identification of those patients who are acidotic from their infection, whose mortality may be reduced with aggressive resuscitation. Therefore, the objective of this investigation is to study the utility of initial ETCO2 measurements in identifying patients with occult hypoperfusion or end-organ dysfunction. To study this, we will determine the association between ETCO2 and (1) organ dysfunction [assessed by sequential organ failure assessment (SOFA) score], and (2) serum lactate levels in febrile emergency department (ED) patients.

Experimental design

Design

This was a pilot, prospective, observational cohort study. The patients were identified from a total pool of adult (age 18 years or older) patients who presented to the ED of Beth Israel Deaconess Medical Center during the study period of July 2006 to January 2007. This urban academic ED sees over 50,000 patient visits per year. This was a non-consecutive convenience sampling based on researcher or research assistant availability. Inclusion criteria were: (a) age of 18 years or older and, (b) temperature of 38°C or greater in the ED, or a history of fever prior to presentation. Exclusion criteria were: patient refusal or inability to give consent, those with cranial facial abnormalities that prevent measurement of end tidal carbon dioxide, a history of asthma or chronic obstructive disease, an environmental cause leading to hyperthermia, patients unable to cooperate with ETCO2 measurements or patients intubated prior to hospital arrival. Institutional Research Board approval was obtained for this study. Baseline demographic information including age, sex, co-morbidities, vital signs, current medications, laboratory information, and imaging data obtained in the ED were collected. The data collection was performed by trained research assistants employed by the Department of Emergency Medicine. Data were collected on a pre-printed data collection form, and were entered into an electronic database (Microsoft Access). A Nelcor NBP-70 microstream capnometer that provides both a capnogram and capnometry for respiratory rate was used for ETCO2 data collection.

Exposures

The exposure of interest was the initial end-tidal carbon dioxide level obtained at triage, or on initial evaluation.

Outcomes

The outcomes of interest were organ dysfunction as assessed by the sequential organ failure assessment (SOFA) score and illness severity as assessed by lactic acid level. Based on prior work, we defined a SOFA score of >2 and a serum lactate level of >4 mmol/L as abnormal. We used the initial end-tidal carbon dioxide measurements to assess for the relationship and predictive value of ETCO2 related to SOFA scores and lactate level.

Data analysis

Descriptive statistics were used to summarize the demographics and characteristics of the eligible patients. Continuous variables such as age are reported with the mean and standard deviation when appropriate. The correlation of ETCO2 with SOFA and lactate level was analyzed using Pearson correlation coefficient. Operating characteristics were calculated with 95% confidence intervals, along with the area under the curve (AUC). Data were analyzed using SAS statistical software (version 9.1, SAS Institute, Care, NC).

Results

We enrolled a convenience sample of 97 patients in our study. The mean age of enrolled patients was 51.8 years (SD ± 19 years) of whom 57 (59%) were men. The mean SOFA score for patients with ETCO2 <35 was 2.0 (95% CI 1.5–2.6) compared to 1.0 (0.4–1.5) for ETCO2 ≥35 ($P < 0.02$). The mean lactate level for patients with ETCO2 <35 was 2.1 mmol/L (1.6–2.5) compared to 1.8 mmol/L (1.3–2.2) in those with a normal ETCO2 ($p = 0.36$).

Among the 97 patients enrolled, 5 (5%) had a lactate >4 mmol/L and 34 (35%) had a SOFA score >2. A significant correlation was found between ETCO2 and SOFA score ($r = -0.35$ $p < 0.01$), and ETCO2 and lactate

ETCO2 and Lactate:

Decision Rule	Lactate ≥ 4	Lactate < 4	
ETCO2 < 35	3	53	56
ETCO2 ≥ 35	2	39	41
	5	92	

Sensitivity	73% (95% CI: 56-85%)
Specificity	50% (38-62%)
Negative Predictive Value	95% (82-99%)
Positive Predictive Value	5% (1-15%)

ETCO2 and Lactate:

Decision Rule	SOFA ≥ 2	SOFA < 2	
ETCO2 < 35	25	31	56
ETCO2 ≥ 35	9	32	41
	34	63	

Sensitivity	73% (95% CI: 56-85%)
Specificity	50% (38-62%)
Negative Predictive Value	78% (63-88%)
Positive Predictive Value	44% (32-57%)

Fig. 1 This figure represents the operating characteristics for ETCO2 at a threshold of 35 for predicting a lactate ≥4 mmol/L

($r = -0.35$ $p < 0.01$). A receiver operator curve for ETCO2 and SOFA >2 had an AUC of 0.69 and ETCO2 and lactate >4 mmol/L had an AUC of 0.62. ETCO2 of <35 has a sensitivity of 0.73 (95% CI 0.56–0.85) and specificity 0.50 (0.38–0.62) in predicting SOFA scores ≥2 (Fig. 1). ETCO2 <35 had a sensitivity of 0.60 (0.22–0.88) and specificity of 0.42 (0.32–0.52) in predicting lactate >4 mmol/L (Fig. 1).

Discussion

In our study we attempted to define the role of ETCO2 in predicting end-organ dysfunction and lactic acidosis in patients with temperatures 38°C or higher. We were able to show that it was feasible to measure ETCO2 in febrile ED patients, and that there was an association between ETCO2 and both SOFA score and serum lactate level; however, the association may not be strong enough for reliable clinical decision making. Our hypothesis was centered on the pathophysiological mechanism of respiratory compensation for metabolic acidosis, and end-organ hypoperfusion as shown by elevated SOFA scores.

Prior studies have examined the utility of ETCO2 to assess acidosis [7–9], pre-hospital trauma [4], and ventilation during procedural sedation [10]. Given our limited sample size, we did not search for the optimal thresholds, instead we relied upon previously defined cut-offs. Capnography is a non-invasive measure of exhaled end-tidal carbon dioxide ($ETCO_2$) that is a function of basal metabolic rate, cardiac output, and ventilation status. Thus, while it makes intuitive sense that it may be useful in sepsis, we are unaware of any prior investigations testing this. However, it is also possible that the combination of factors that determine the composite ETCO2 may make interpreting the final ETCO2 difficult in febrile patients.

Limitations

This was a convenience sample so patients who were eligible for enrollment were missed, leading to a potential selection bias. Our low prevalence of patients with elevated lactate levels is another limitation. The sickest patients were potentially less likely to be enrolled as they may have been intubated earlier, or were more difficult to obtain consent from. Another limitation of this study is using surrogate outcomes of lactic acidosis and SOFA scores as markers of mortality. It was not feasible to achieve the necessary power to detect difference in mortality in this single center pilot study. Finally, given our limited sample size we did not search for optimal threshold, instead we relied upon previously defined cut-offs.

Conclusion

We were able to demonstrate that it is possible to enroll and measure ETCO2 levels in febrile adult ED patients. We found a statistically significant correlation between ETCO2 and (a) SOFA score, and (b) serum lactate levels; however, operating characteristics of ETCO2 in predicting a lactic acidosis or end-organ dysfunction in this specific patient population might not be reliable enough for clinical decision making. Future studies may enroll larger, more critically ill patients and looking for new ETC02 testing thresholds are warranted before final determination of ETCO2 utility.

References

1. Strehlow MC, Emond SD, Shapiro NI, Pelletier AJ, Camargo CA Jr (2006) National study of emergency department visits for sepsis, 1992 to 2001. Ann Emerg Med 48(3):326–331, 331 e321–323
2. Ferreira FL, Bota DP, Bross A, Melot C, Vincent JL (2001) Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 286(14):1754–1758
3. Shapiro NI, Howell MD, Talmor D et al (2005) Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med 45(5):524–528
4. Deakin CD, Sado DM, Coats TJ, Davies G (2004) Prehospital end-tidal carbon dioxide concentration and outcome in major trauma. J Trauma 57(1):65–68

5. Shapiro NI, Wolfe RE, Moore RB, Smith E, Burdick E, Bates DW (2003) Mortality in Emergency Department Sepsis (MEDS) score: a prospectively derived and validated clinical prediction rule. Crit Care Med 31(3):670–675
6. Rivers E, Nguyen B, Havstad S et al (2001) Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 345:1368–1377
7. Garcia E, Abramo TJ, Okada P, Guzman DD, Reisch JS, Wiebe RA (2003) Capnometry for noninvasive continuous monitoring of metabolic status in pediatric diabetic ketoacidosis. Crit Care Med 31(10):2539–2543
8. Fearon DM, Steele DW (2002) End-tidal carbon dioxide predicts the presence and severity of acidosis in children with diabetes. Acad Emerg Med 9(12):1373–1378
9. Nagler J, Wright RO, Krauss B (2006) End-tidal carbon dioxide as a measure of acidosis among children with gastroenteritis. Pediatrics 118(1):260–267
10. Santos LJ, Varon J, Pic-Aluas L, Combs AH (1994) Practical uses of end-tidal carbon dioxide monitoring in the emergency department. J Emerg Med 12(5):633–644