Egyptian Journal of Anaesthesia (2016) xxx, xxx–xxx

HOSTED BY

ELSEVIER

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Disturbed fluid responsiveness and lactate/pyruvate ratio as predictors for mortality of septic shock patients

Ahmed Abdalla Mohamed [a,*], **Ahmed Essam** [b]

[a] *Department of Anesthesiology & ICU, Faculty of Medicine, Cairo University, Egypt*
[b] *Department of Anesthesiology & ICU, Faculty of Medicine, Tanta University, Egypt*

Received 19 November 2015; revised 3 April 2016; accepted 3 April 2016

KEYWORDS

Septic shock;
Shock index;
Pleth variability index;
Blood lactate;
ICU mortality

Abstract *Objectives:* Evaluation of fluid responsiveness of septic shock patients admitted to surgical ICU and the predictability of non-invasive monitoring and estimated lactate/pyruvate (L/P) ratio for survival of these patients.

Patients and methods: The study included 58 septic shocked patients admitted and managed at surgical ICU. After non-invasive determination of baseline hemodynamic data and calculation of shock index (SI-0) and Pleth variability index (PVI-0), all patients received intravenous colloid infusion followed 15-min later by non-invasive re-evaluation for SI-15 and PVI-15. Blood samples were obtained for estimation of blood lactate and pyruvate levels at admission (BLL-0 and BPL-0) and 12-h after fluid resuscitation (BLL-12 and BPL-12) and L/P ratio was calculated. All patients were managed according to the Surviving Sepsis Campaign guidelines and followed up for ICU mortality rate (MR).

Results: ICU stay MR was 20.7%. Survival showed negative significant correlation with PVI, L/P ratio and BLL, while it showed positive significant correlation with BPL. Receiver Operating Characteristic (ROC) curve analysis defined baseline and persistently low PVI, high BLL and L/P ratio as significant sensitive predictors for MR, while elevated BPL-12 as significant specific predictor for survival. Regression analysis defined persistently elevated L/P ratio as the highly significant specific predictor, while persistently disturbed SI and PVI could predict mortality as screening tests. Odds ratio for mortality at BLL-0 of >2 mmol/L was 0.0321 (95% CI: 0.0037–0.2755), while it was 4.1111 (95% CI: 1.0702–15.792) at BLL-0 >4 mmol/L.

Conclusion: After fluid resuscitation and hemodynamic stability, persistently elevated BLL could predict mortality, while elevated BPL could predict survival of septic shock patients. Continuous non-invasive evaluation of fluid responsiveness judged by PVI and SI could provide sensitive

* Corresponding author at: Department of Anesthesiology & ICU, Faculty of Medicine, Cairo University, Egypt. Tel.: +20 1002598952.
E-mail address: abdalla2011125@hotmail.com (A.A. Mohamed).

Peer review under responsibility of Egyptian Society of Anesthesiologists.

http://dx.doi.org/10.1016/j.egja.2016.04.009

Please cite this article in press as: Mohamed AA, Essam A Disturbed fluid responsiveness and lactate/pyruvate ratio as predictors for mortality of septic shock patients, Egypt J Anaesth (2016), http://dx.doi.org/10.1016/j.egja.2016.04.009

screening for survival outcome of shocked patients. Wider scale comparative studies are mandatory for establishment of discriminative PVI and BLL cutoff points for prediction of survival of shocked patients.

1. Introduction

Shock is a life-threatening syndrome of acute circulatory failure. It can be caused by loss of intravascular volume, obstruction of flow through the vascular compartment, or a generalized state of vasodilation [1]. Shock leads to decreased organ perfusion, with inadequate delivery of oxygenated blood to tissues and resultant end-organ dysfunction [2].

Sepsis is a systemic response to infection, which may progress to severe sepsis and septic shock [3]. Septic shock causes vascular dysregulation making tissue perfusion dependent on blood pressure. Furthermore, microvascular perfusion could be disrupted by circulating inflammatory mediators that directly damage the peripheral vascular bed [4]. Microcirculatory dysfunction has been documented in the early phase of sepsis and its severity has been related to poor outcome [5].

In critically ill septic patients, early hemodynamic resuscitation was effective to restore macro-hemodynamia and myocardial contractility. Fluid responsiveness is defined by a cardiac preload challenge by fluid infusion resulting in augmented stroke volume and cardiac output [6]. Currently, both static and dynamic parameters are utilized for prediction of fluid responsiveness [7].

Static parameters as central venous pressure and pulmonary artery occlusion pressure are much less reliable than dynamic parameters, which are based on respirophasic variation in stroke volume as pulse pressure variation and changes in aortic blood flow. However, most common dynamic parameters are invasive and expensive [8]. Klijn et al. [9] demonstrated that in critically ill septic patients, non-invasively assessed tissue perfusion and oxygenation is not inferior to invasive hemodynamic measurements in monitoring fluid responsiveness.

Mitochondrial function is thought to play a role in sepsis-induced multiple organ failure [10]. In septic patients, inflammatory signaling leads to changes in the phosphorylation state of mitochondrial proteins resulting in a reduction of the mitochondrial membrane potential, and consequently a lack of energy, which can cause organ failure and death [11]. Septic shock induced a severe hypotension in association with metabolic acidosis and significantly decreased rates of mitochondrial oxygen consumption, activity and content of cytochrome c oxidase [12].

The blood lactate-to-pyruvate (L/P) molar ratio reflects the equilibrium between product and substrate of the reaction catalyzed by lactate dehydrogenase that favors lactate production and normally maintains a constant L/P ratio of about 10:1 [13]. The L/P ratio is correlated with the cytoplasmic ratio between the reduced and oxidized forms of nicotinamide adenine dinucleotide ($NADH:NAD^+$) and is used as a surrogate measure of the cytosolic oxido-reduction state. Impaired cellular respiration, as in hypoxia, causes reduced pyruvate oxidation, resulting in lactic acidosis and increased L/P ratio [14]. Romijn et al. [15] using isotopic tracer found pyruvate and lactate tracer-to-tracer ratios equilibrated almost completely within 3–4 min in whole blood, thus indicating a very rapid lactate clearance.

The current study aimed to evaluate fluid responsiveness of septic shock patients admitted to surgical ICU and the predictability of non-invasive monitoring and estimated lactate/pyruvate (L/P) ratio for survival of these patients.

2. Patients and methods

The current prospective multi-center study was conducted at surgical ICU centers at Cairo University Hospitals, Naser Institute, Al-Marwa and Demascus private centers since January 2014 till June 2015. The study protocol was approved by the Local Ethical Committee of Cairo University Hospitals and written fully informed consents were signed by near patients' relatives.

Patients inclusion relied on shock definition as hypoperfusion of tissues and/or organs manifested as systolic blood pressure (SBP) of $\leqslant$90 mmHg, heart rate (HR) increased by $\geqslant$10% from baseline, urine output (UOP) of $<$0.5 ml/kg/min for $>$2 h, presence of skin mottling; and/or blood lactate level of $>$2 mmol/L [16]. Sepsis was diagnosed depending on the presence of at least two of the four systemic inflammatory response syndrome (SIRS) criteria and fulfilled the requirements for either severe sepsis or septic shock. SIRS criteria include body temperature $<$36 °C or $>$38 °C, heart rate (HR) $>$ 90 beats/min, respiratory rate $>$20 breaths/min or, an arterial partial pressure of CO_2 $<$32 mmHg and/or white blood cell count $<$4000 cells/mm^3 or $>$12,000 cells/mm^3, or the presence of greater than 10% immature neutrophil band forms. Requirements for severe sepsis patients included the following: (i) fulfilling at least 2 or more of SIRS criteria, (ii) an associated or suspected source of infection, and (iii) it has one or more of the following: evidence of end organ damage, serum lactate levels of $\geqslant$4 mg/dL, and episode of hypotension ($<$90/60 mmHg), which responds to initial fluid resuscitation. Septic shock patients must have the diagnostic criteria for severe sepsis but blood pressure was persistently $<$90/60 mmHg and did not respond to adequate fluid resuscitation [17].

Clinical evaluations entail collection of demographic data including age, gender, and body mass index data. Body injury severity was assessed using scoring on the anatomical abbreviated injury scale and the scores of the three most severely injured body regions were squared and added together to produce the injury severity scale (ISS) score ranking from 0 to 75 indicating unsurvivable injury [18]. Acute physiology and chronic health evaluation II (APACHE II) [19] and Glasgow Coma Scale (GCS) [20] scores were also determined.

Patients were continuously non-invasively monitored for electrocardiogram, blood pressures (SBP, DBP and MAP), HR and temperature. Severity of hemodynamic compromise

Please cite this article in press as: Mohamed AA, Essam A Disturbed fluid responsiveness and lactate/pyruvate ratio as predictors for mortality of septic shock patients, Egypt J Anaesth (2016), http://dx.doi.org/10.1016/j.egja.2016.04.009