

PROGNOSTIC VALUE OF BLOOD LACTATE AND APACHE II IN SEPTIC PATIENTS

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INTRODUCTION

Septic patients in ICU have high risk of developing multiple organ failure (MOF) and high mortality rates, in spite of modern technologies used nowadays. Various prognostic methods have been suggested in order to evaluate patient's state and possible evolution, such as APACHE, SAPS, SOFA, blood lactate levels, intragastric mucosal pH etc.

OBJECTIVE

The objective of our study is to evaluate prognostic value of blood lactate and APACHE II in septic patients.

PATIENTS AND METHODS

We performed a retrospective analysis of 54 septic patients out of 249 critically ill patients admitted to the ICU of our University Hospital in 4 months period during 1999. There were 37 men and 17 women with age ranging from 15 to 81 years. Twenty four patients were clinical, 9 had elective surgery and 21 emergency surgery. APACHE II was calculated at admission to the ICU. Blood lactate values were taken for the first five days of the stay at the ICU. MOF and mortality were also recorded. Sepsis was diagnosed according to ACCP/SCCM criteria, while MOF was diagnosed according to Marshall and Meakings criteria. Blood lactate was measured by gasometric method (Radiometer-Kopenhagen BL3, normal value $< 2,4$ mmol/l). Statistical methods used: Spearman's correlation coefficient, Mann-Whitney and Student t-test, p value $< 0,05$ were considered significant.

RESULTS

Twenty four patients survived and thirty died (total mortality 55,5%). The mean value $\pm$ SD of APACHE II for survivors was $21,11 \pm 18,49$, while for non-survivors it was $41,70 \pm 25,81$ ($p < 0,001$). Blood lactate on the first day (BL1): survivors $3,72 \pm 3,35$ mmol/l; non-survivors $5,81 \pm 4,75$ mmol/l ($p < 0,031$). Blood lactate on the second day (BL2): survivors $2,39 \pm 1,55$ mmol/l; non-survivors $4,45 \pm 3,83$ mmol/l ($p < 0,009$). Blood lactate on the third day (BL3): survivors $1,86 \pm 1,03$ mmol/l; non-survivors $4,37 \pm 3,46$ mmol/l ($p < 0,001$). Blood lactate on the fourth day (BL4): survivors $1,76 \pm 0,82$ mmol/l; non-survivors $4,73 \pm 4,76$ mmol/l ($p < 0,002$). Blood lactate on the fifth day (BL5): survivors $1,86 \pm 0,82$ mmol/l; non-survivors $3,03 \pm 2,20$ mmol/l ($p < 0,014$). MOF on the first day (MOF1): survivors $1,96 \pm 1,10$; non-survivors $2,96 \pm 1,48$ ($p < 0,008$). MOF on the second day (MOF2): survivors $1,96 \pm 1,34$; non-survivors $3,18 \pm 1,44$ ($p < 0,003$). MOF on the third day (MOF3): survivors $1,88 \pm 1,33$; non-survivors $3,12 \pm 1,15$ ($p < 0,001$). MOF on the fourth day (MOF4): survivors $1,79 \pm 1,35$; non-survivors $3,31 \pm$

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1,46 ($p < 0,001$). MOF on the fifth day (MOF5): survivors $1,65 \pm 1,23$; non-survivors $3,35 \pm 1,50$ ($p < 0,003$).

CONCLUSION

There was significant statistical correlation in daily values of APACHE II, blood lactate and MOF between survivors and non-survivors, so we conclude that APACHE II and blood lactate have a good prognostic value in ICU patients with sepsis.

Sepsis remains an important cause of morbidity and mortality in ICUs [1,7,8,9,11]. Septic patients present high risk of developing multiple organ failure (MOF), possibly due to tissue hypoxia. In ischaemic tissues, lactate is produced by anaerobic metabolism and it is believed that levels of blood lactate could have prognostic value in septic patients [26]. However, it is not yet clear whether occult tissue hypoxia or some other mechanisms related to sepsis, such as direct cell alterations, result in lactic acidosis observed in critically ill patients [3,4,6,22,23,24].

It has also been suggested that persistent mild hyperlactatemia in stable septic patients is a sign of altered lactate clearance rather than evidence of lactate overproduction and, therefore, should not be considered a reliable indicator of anaerobic metabolism [14,15,17].

Whichever the case, in sepsis, a high lactate concentration should be interpreted as a marker of disease and a prolonged acidemia should predict a poor outcome according to different authors [10,12,13,16,18,191].

Several methods have been suggested in order to evaluate patient's state and predict the outcome, such as APACHE I, II and III, SAPS I and II, SOFA, gastric intramucosal pH (pHi), blood lactate etc. They should help the physician to recognise patients with higher risk of developing MOF and also give the insight in physiological alterations that might lead to such condition.

In this study, we examine the prognostic value of blood lactate and APACHE II in septic patients.

PATIENTS AND METHODS

We performed a retrospective analysis of 54 septic patients out of 249 critically ill patients admitted to ICU in our university teaching hospital during January, February, July and August 1999. There were 37 men and 17 women with age ranging from 15 to 81 years. Twenty four patients were clinical, 9 had elective surgery and 21 emergency surgery. APACHE II [21,30] was calculated on admission to the ICU. Blood lactate values were taken for the first five days of the stay at the ICU. MOF and mortality were

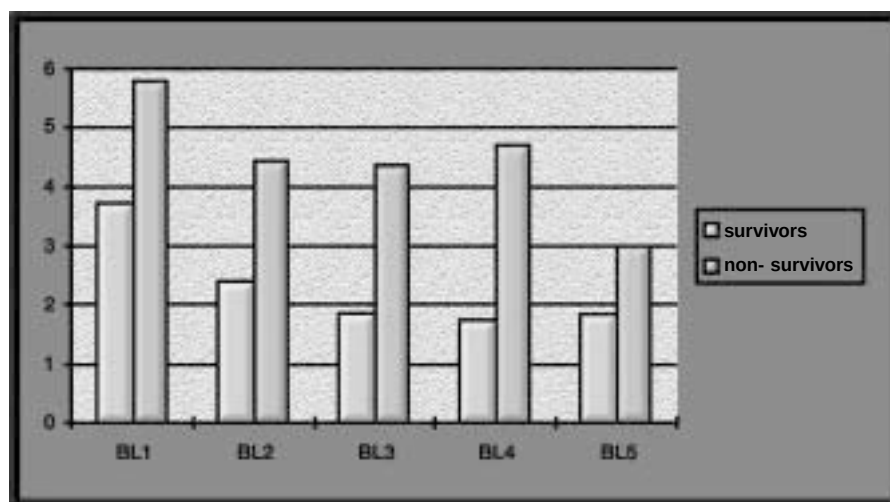
also recorded. Sepsis was diagnosed according to ACCP/SCCM criteria, that is, when two or more of the following were present: temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, heart rate >90 beats/min; respiratory rate >20 breaths/min; white blood cell count >12000 cells/ mm^3 , <4000 cells/ mm^3 or $>10\%$ immature cells and/or identified focus of infection or positive culture. MOF was diagnosed according to Marshall and Meakins criteria [26] (table 1). Blood lactate was measured in all patients by gasometric method, using Radiometer-Copenhagen BL3 machine. Statistical methods used: Spearman's correlation coefficient to compare variables (APACHE II x MOF, APACHE II x lactate and lactate x MOF) and Mann-Whitney test to compare APACHE II, blood lactate and MOF between surviving and the non-surviving groups; p value $< 0,05$ was considered significant.

RESULTS

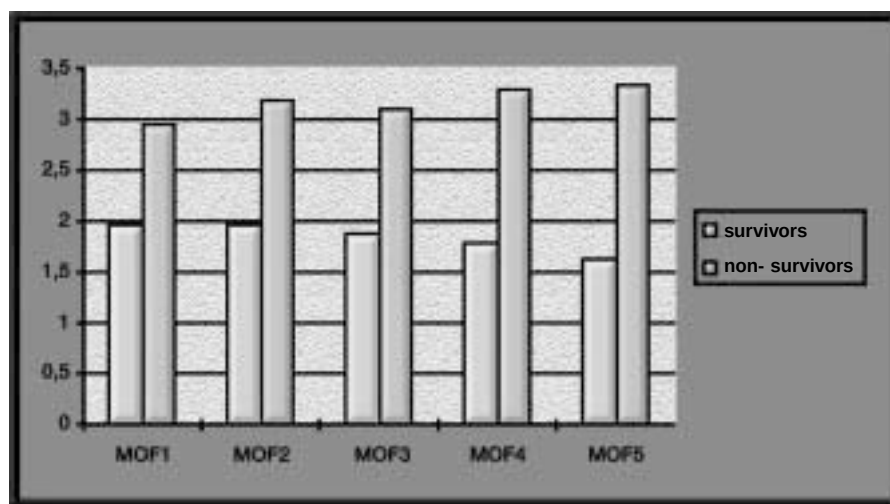
The incidence of sepsis in our ICU during the four months period was 21,68%. All septic patients presented high levels of blood lactate on the first day, but these levels decreased to normal values in the surviving group on the third day, while they remained high in the non-surviving group of patients (graph 1). There was good statistical correlation between lactate

Table 1. Marshall and Meakins criteria for organ dysfunction

SYSTEM/ORGAN	DYSFUNCTION
1. Respiratory	lung injury score ≥ 1
2. Kidney	serum creatinine $>1,8\text{mg/dl}$ ($160\mu\text{mol/L}$)
3. Hepatic	total bilirubin $>2,5\text{mg/dl}$ ($40\mu\text{mol/L}$) and elevation of transaminase or alkaline phosphatase more than twice normal
4. Cardiovascular	PCWP $>16\text{mmHg}$ and requirement for dopamine, dobutamine, epinephrine and/or norepinephrine to maintain pressure $>80\text{mmHg}$
5. CNS	Glasgow coma scale <10 in the absence of sedation
6. Coagulation	platelet count <60000 and elevation of the prothrombin or partial thromboplastin time greater than 1,5 times the control value in the absence of the anticoagulation
7. Metabolic	insulin requirements $>5\text{U/h}$
8. Gut	nasogastric drainage $>300\text{ml/d}$ and an ileus (not due to gut surgery) upper gut bleeding



Graph 1. Blood lactate levels (mmol/l) in septic patients during the first five days of the stay at the ICU (p-values can be seen in table 1 - difference between the two groups was statistically important all days).



Graph 2. Multiple Organ Failure (MOF) in septic patients during the first five days of the stay at the ICU (p-values can be seen in table 2 - difference between the two groups was statistically important all days)

values for each day compared between surviving and non-surviving groups (table 2).

Multiple organ failure affected more systems in non-surviving patients (graph 2) and the difference between survivors and non-survivors reached statistical importance for each day (table 3).

Blood lactate levels were predictive for MOF from the second day of the stay at the ICU for the whole group of septic patients. However, separately for the surviving and the non-surviving groups the levels of blood lactate didn't have correlation

to number of organs affected by sepsis (table 4).

The mean value $\pm$ SD of APACHE II for the surviving group was $21,11 \pm 18,49$ and for the non-surviving group it was $41,70 \pm 25,81$ (p-value 0,001).

Mortality for septic patients in our ICU was 55,55%.

DISCUSSION

Different mechanisms could be responsible for raise in concentration of blood lactate in septic patients, such as: tissue hypoxia, increased glycolysis, transamination from alanine,

down-regulation of pyruvate dehydrogenase, reduced lactate clearance etc [2,3,4,5,6]. However, there is no evidence that any of these mechanisms should be the main cause for hyperlactatemia and further investigations are necessary.

In our study, blood lactate levels were initially high for all patients but they were more likely to decrease in those patients who survived. The difference between the levels of lactate for the two groups, survivors and non-survivors, was statistically important from the first day.

In a study by Marik [26], the arterial lactate concentrations were higher in those patients who developed MOF and in those patients who died, but the differences, however, didn't reach statistical importance. It has been suggested that septic patients demonstrate less hyperlactatemia since hepatic perfusion in patients with sepsis is usually better than in patients with hypovolemic or cardiogenic shock. Vitek and Cowley [13] examined lactate levels in patients with various forms of shock and found that in survivors group the average level was 4,5 mEq/l while it was 8,1 mEq/l in the non-survivors group.

In a study by Bakker et al. [12] the duration of lactic acidosis was the best predictor of survival in patients with septic shock. This was confirmed for patients with circulatory shock by Vincent et al. [20]. They suggested that repeated lactate measurements are more reliable than an initial value taken alone. We observed that blood lactate levels decreased in surviving group of patients reaching the normal values on the third day and these findings also confirm that persistence of acidemia predicts a poor outcome.

Weil and Afifi [16] demonstrated that the likelihood of survival for patients with circulatory shock decreases from 90% to 10% as blood lactate increases from 2,1 to 8 mmol/l.

In our study, the number of organs

Table 2. Values of blood lactate for septic patients during the first five days of the stay at the ICU

Days	Group	Mean value	SD	p-value
BL1	survivors	3,72	3,35	0,031*
	non-survivors	5,81	4,75	
BL2	survivors	2,39	1,55	0,009*
	non-survivors	4,45	3,83	
BL3	survivors	1,86	1,03	0,001*
	non-survivors	4,37	3,46	
BL4	survivors	1,76	0,82	0,002*
	non-survivors	4,73	4,76	
BL5	survivors	1,86	0,82	0,014*
	non-survivors	3,03	2,2	

* there was statistical importance

affected was also related to outcome, being a more serious MOF related to worse prognosis. Blood lactate had statistical correlation with MOF from the second day when considering the whole group of septic patients. On the first day, its levels were equally high in all patients, but they failed to decrease to normal values only in patients more likely to develop MOF. However, when the groups of survivors and non-survivors were considered separately, there was no correlation between blood lactate levels and

MOF, showing that blood lactate doesn't have good prognostic value for morbidity in septic patients.

It has also been suggested that gastrointestinal system should be among the first affected by sepsis and ischemia and consequently bacterial translocation might be the motor for MOF [26]. Therefore, gastric intramucosal pH (pHi) should be an early indicator of inadequate tissue perfusion [26,27,28,29].

Joynt G. M. et al. [29] reported that, for septic patients, blood lactate

was a better predictor at 48h than pHi. Besides that, it is less invasive, much cheaper and easier measurement than pHi. Marik [26] found that low pHi is a better predictor of MOF and death than hemodynamic and oxygen-derived variables obtained by invasive hemodynamic monitoring [25] in patients with sepsis.

In the same study, APACHE II was a poorer predictor of MOF than indices of tissue oxygenation.

APACHE II in the surviving group of patients (21/11) was the half of its value in the non-surviving group (41/70), so in our study APACHE II showed to be a good predictor of MOF and mortality.

Whichever the reasons that lead to hyperlactemia in septic patients,

Table 4. Statistical correlation between blood lactate (BL) and MOF for septic patients during the first five days of the stay at the ICU.

Variables – total	p-value
BL1 and MOF1	0,156
BL2 and MOF2	0,10*
BL3 and MOF3	0,002*
BL4 and MOF4	0,00*
BL5 and MOF5	0,039*

Variables	p-value
BL1 and MOF1	0,548
BL2 and MOF2	0,224
BL3 and MOF3	0,402
BL4 and MOF4	0,016*
BL5 and MOF5	0,283

Variables	p-value
non-survivors	
BL1 and MOF1	0,558
BL2 and MOF2	0,284
BL3 and MOF3	0,058*
BL4 and MOF4	0,254
BL5 and MOF5	0,938

*there was correlation

Table 3. Multiple organ failure in septic patients during the first five days of the stay at the ICU

Days	Group	Mean value	SD	p-value
MOF1	survivors	1,96	1,1	0,008*
	non-survivors	2,96	1,48	
MOF2	survivors	1,96	1,34	0,003*
	non-survivors	3,18	1,44	
MOF3	survivors	1,88	1,33	0,001 *
	non-survivors	3,12	1,15	
MOF4	survivors	1,79	1,35	0,001
	non-survivors	3,32	1,46	
MOF5	survivors	1,65	1,23	0,003*
	non-survivors	3,35	1,5	

* there was statistical importance

blood lactate is the indicator of disease and persistence of high concentrations predict a poor outcome. Serial measurements should help the physician to evaluate patients' state and when lactate levels fail to decrease, changes in treatment should be considered.

In conclusion, APACHE II and blood lactate have prognostic value in patients with sepsis. There is difference between values of APACHE II and blood lactate in survivors and non-survivors, and in survivors blood lactate levels reach normal values until the third day of the stay at the ICU.

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