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Serum lactate is a useful predictor of death in severe sepsis in patients with pemphigus vulgaris

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Abstract

Background: Serum lactate is a useful prognostic marker in severe sepsis; high levels of serum lactate in critically ill patients are related to high mortality risk; assessing serum lactate levels in patients with pemphigus vulgaris is justified. The objective was to determine the role of serum lactate as a predictor of shock and its outcome in patients with pemphigus vulgaris and severe sepsis without acute organ dysfunction.
Methods: Thirty-seven patients with pemphigus vulgaris, 22 with severe sepsis and 15 without sepsis. Blood lactate levels were analyzed. The outcome was recorded as survival or non-survival.
Results: High serum lactate levels, compared with intermediate and low levels, were significantly associated with increased 28-day mortality in patients with severe sepsis. The 28-day mortality for the cohort was 27.3%.
Conclusions: Initial serum lactate was associated with mortality in pemphigus vulgaris with severe sepsis. Patients with severe sepsis and with high serum lactate levels (≥ 4 mmol/L) constitute a potential risk group that may benefit from more aggressive treatment.

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Introduction

Severe sepsis and septic shock result in 215,000 deaths annually in the United States (1). Given the morbidity and mortality associated with these conditions, the ability of clinicians to risk-stratify these patients may lead to effective treatments and improve their outcomes. Elevated serum lactate (SL) is strongly associated with high morbidity and mortality in patients with acute organ dysfunction (2-4). SL is potentially a useful biomarker to risk-stratify patients with severe sepsis without shock and organ failure; however, there is a lack of information about the behavior of SL in chronic organ dysfunction and its association with mortality (4). Given this prior evidence, we tried to ascertain the role of SL as a predictor of shock and its outcome in patients with pemphigus vulgaris (PV), a chronic, autoimmune, bullous disease, in which infection remains the major cause of death.

Methods

This was a prospective cohort of 37 patients with PV with and without severe sepsis admitted to our dermatology department from January 2007 to May 2011. Exclusion criteria included septic shock, chronic organ dysfunction comorbidities (congestive heart, renal, or liver failure), diabetes mellitus, malignancy, and organ transplantation. Sepsis was defined as a suspected infection in the presence of two or more criteria of systemic inflammatory response syndrome. Severe sepsis was defined as sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion was defined as a SL ≥ 2 mmol/L and > 3 mmol/L in a sensitivity analysis based on the 2001 International Sepsis Definitions Conference Criteria (5). Hypotension and organ dysfunction were defined according to the 2001 criteria. Septic shock was defined as hypotension (systolic blood pressure < 90 mm Hg) despite adequate fluid resuscitation (> 1500 mL) or the use of vasoactive agents.

The following data were collected: demographic data, initial vital signs, laboratory measurements, and infection source. Serum lactate was measured with a serum-based assay catalyzed by lactate oxidase (Spinreact, S.A., Sant Esteve de Bas (GI), Spain). The primary outcome was 28-day mortality. Initial SL was measured at admission, and a priori stratified as low (< 2 mmol/L), intermediate (2.0-3.9 mmol/L), or high (≥ 4 mmol/L). Age, sex, and severity of illness (body surface area affected) were considered as potential confounders. We compared the results with patients with PV without sepsis. The groups were paired by age, gender, and disease severity.

The nonparametric Mann-Whitney test was used to compare continuous variables and the chi-squared statistic or Fisher's exact test was used to compare categorical variables. Binomial logistic regression, stratified on the presence or absence of death, was used to adjust for potential confounding variables, including SL levels. Statistical analyses were performed using SPSS 10 software and two-sided p values ≤ 0.05 were considered significant.

Results

Twenty-two PV patients (Group 1) had severe sepsis; they were compared with 15 patients with PV without sepsis (Group 2). Patient characteristics are shown in Table 1.

The most common sources of infection in Group 1 were respiratory (10/22, 46%), skin and soft tissue (6/22, 27%), urologic (4/22, 18%), and bacteremic infections including catheter-related infections (2/22, 9%). All infections were demonstrated by culture and isolation of the causative agents.

The initial mean SL level (at admission) was 3.42 ± 2.47 mmol/L (range 1.3-5.9); in Group 1, 3.52 ± 1.93 mmol/L; in Group 2, 1.33 ± 0.504 mmol/L (p = 0.001). The 28-day mortality for the cohort was 27.3%, or 10 patients, eight of them related to sepsis/septic shock (Group 1) and two related to pulmonary embolism (Group 2). During the follow-up, 19 patients (51%) of the cohort fulfilled two or

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more of the three severe sepsis criteria; only three patients (8%) fulfilled one criterion of severe sepsis; 15 patients (41%) did not develop sepsis or shock.

The initial median SL level was significantly higher in patients with severe sepsis that developed shock (8/22, 36%) compared with patients with severe sepsis that did not develop shock (14/22, 64%), (4.63 ± 1.27 vs. 2.75 ± 1.47 mmol/L, p = 0.001); we observed the same tendency in non-survivors (8/22, 36%) compared with survivors (14/22, 64%), (4.167 ± 0.53 vs. 2.55 ± 0.38 mmol/L, p = 0.001) (Table 2). In Group 2, the initial median SL level was similar in patients that died by pulmonary embolism (2/15, 13%) compared with those that did not (13/15, 87%), (2.15 ± 0.48 vs. 2.05 ± 0.53 mmol/L, p = 0.563).

High SL levels, compared with intermediate and low ones, were significantly associated with increased 28-day mortality in patients with severe sepsis (OR 13.28, CI95% 4.32-18.35, p = 0.001). After adjusting for potential confounding variables, high SL levels remained significantly associated with 28-day mortality (OR 11.47, CI 95% 2.25-15.36, p = 0.001).

Discussion

Blood lactate level is used as a marker for tissue hypoperfusion in shock patients, adequate post-shock resuscitation, prognostic index after resuscitation, and prognostic factor in the case of severe disease (6). We found that initial SL was associated with mortality in patients with PV and severe sepsis without shock. These observations suggest that an initial SL measurement could potentially guide medical decisions and thus improve patient outcomes (4). The association between SL level and mortality was independent of clinical evidence of organ dysfunction in the proximal phase of sepsis and also independent of hemodynamic stability.

PV patients with severe sepsis and high SL levels (≥ 4 mmol/L) constitute a potential risk group that may benefit from more aggressive treatment.

We observed no differences between patients with PV with sepsis compared with those without sepsis. However, we observed a significant elevation of SL levels in patients with PV that developed septic shock. This could reflect their response to systemic inflammatory response syndrome, along with alterations in glucose metabolism, coagulopathy, and hepatic dysfunction, such as occur in other critical illnesses (4).

Although statistically significant, these observations should be interpreted with caution and confirmatory studies are required. Our study reveals that the initial SL is associated with mortality in patients with PV admitted with severe sepsis. Further studies are necessary to better understand the etiology of elevated SL levels in these patients.

Table 1 | **Patient characteristics of the cohort. PV - pemphigus vulgaris, NS - not significant**

Variable	Group 1 (PV with severe sepsis), n = 22	Group 2 (PV without sepsis), n = 15	P-value
Age (years)	31.27 ± 8.21	33.12 ± 7.25	NS
Sex (female), n (%)	16 (73)	10 (67)	NS
Temperature (°C)	38.2 ± 0.87	36.8 ± 0.55	0.001
Heart rate	103.13 ± 12.35	95 ± 13.45	0.065
Respiratory rate	17.3 ± 0.8	14.4 ± 0.47	0.001
Mean arterial pressure	79.4 ± 11.35	75.22 ± 8.45	0.209
White blood cell count	11.33 ± 1.35	8.95 ± 2.12	0.002
Hematocrit	32.4 ± 2.12	30.4 ± 2.22	0.005
Platelets	332.27 ± 75.35	312.2 ± 44.25	0.315
Serum creatinine (mg/dL)	0.935 ± 0.35	0.634 ± 0.55	0.001
Total bilirubin (mg/dL)	1.45 ± 1.13	0.77 ± 0.25	0.011
Prothrombin time (sec)	12.42 ± 0.65	11.22 ± 0.68	0.005
Partial thromboplastin time (sec)	32.8 ± 1.86	33.1 ± 2.31	NS
Serum lactate (mmol/L)	3.52 ± 1.93	1.33 ± 0.504	0.001
Body surface affected (%)	33.12 ± 15.36	31.47 ± 13.4	NS

Table 2 | **Initial characteristics in the 22 PV patients with severe sepsis. PV - pemphigus vulgaris, NS - not significant**

Variable	Survivor, n = 16	Non-survivor, n = 6	P-value
Age (years)	31.19 ± 7.65	31.5 ± 10.36	NS
Sex (female), n (%)	13 (81)	3 (50)	NS
Temperature (°C)	38.46 ± 0.78	38.15 ± 0.96	NS
Heart rate	102.75 ± 10.69	105 ± 15.81	NS
Respiratory rate	17.63 ± 0.8	17.17 ± 0.98	NS
Mean arterial pressure	77.5 ± 8.42	77.5 ± 11.97	NS
White blood cell count	11.57 ± 1.68	11.2 ± 1.1	NS
Hematocrit	32.88 ± 1.45	33 ± 2.53	NS
Platelets	306.38 ± 66.38	305.5 ± 33.53	NS
Serum creatinine (mg/dL)	0.812 ± 0.27	1.067 ± 0.42	NS
Total bilirubin (mg/dL)	1.26 ± 1.11	1.66 ± 1.13	NS
Prothrombin time (sec)	12.73 ± 0.83	12.56 ± 0.77	NS
Partial thromboplastin time (sec)	31.1 ± 2.05	33 ± 1.1	0.001
Serum lactate (mmol/L)	2.55 ± 0.38	4.167 ± 0.53	0.001
Body surface affected (%)	35.4 ± 12.45	32.7 ± 15.32	NS

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