SERUM LACTATE AND BASE DEFICIT AS PROGNOSTIC MARKERS IN ACUTE BURNS PATIENTS

VALEURS PRONOSTIQUES DU LACTATE SÉRIQUE ET DE L'EXCÈS DE BASE CHEZ LE BRÛLÉ EN PHASE AIGUË

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SUMMARY. Resuscitation of burns remains a fundamental problem in burn care. Traditional endpoints such as mean arterial pressure and urine output guide fluid therapy for optimal resuscitation, but an ideal marker remains controversial. Base deficit and serum lactate are markers of global tissue acidosis and inadequate oxygenation. The aim of this study was to determine whether serum lactate and base deficit together can be used as prognostic markers in acute burns and their association with sepsis and mortality. A prospective observational study with a sample size of 250 was conducted over 18 months, which included patients with 20-60% total body surface area (TBSA) having thermal burns or scald. Resuscitation was done according to hospital protocol and fluid administration was adapted according to clinical parameters. Serum lactate and base deficit values were analysed at the time of admission, then on day one, two, three and finally on day seven after admission. The two parameters were compared among survivors and non survivors. Patients were followed up till discharge, death or 30th post burn day. Baseline serum lactate levels are high and base deficit levels low in the patients sustaining burns and the levels normalised over seven days with adequate resuscitation in survivors. Persistently high serum lactate and low base deficit are associated with sepsis and increased mortality. This study indicates that serum lactate and base deficit are useful parameters to predict mortality and promising predictive tools for assessing resuscitation and development of sepsis. Using these tools to guide fluid resuscitation may help mortality and improve overall outcomes.

Keywords: acute burns, fluid resuscitation, serum lactate, base deficit

RÉSUMÉ. *Le remplissage initial reste un problème fondamental en brûlologie. Il est traditionnellement guidé par la pression artérielle moyenne ou la diurèse, mais la cible idéale reste discutée. La lactatémie et l'excès de base sont des marqueurs d'acidose tissulaire par oxygénation inadéquate. Le but de cette étude est de déterminer si ces deux marqueurs associés sont corrélés au sepsis et la mortalité et, de ce fait, peuvent être utilisés dans la pronostication. Il s'agit d'une étude observationnelle prospective réalisée sur un échantillon de 250 patients en 18 mois, victimes de brûlures (flamme ou ébouillantement) sur 20 à 60% SCT. Le remplissage a été conduit selon le protocole local, adapté aux paramètres cliniques. Lactatémie et excès de base ont été à l'entrée puis à J1, J2, J3 et J7. Les valeurs ont été comparées entre vivants et décédés, à la sortie, lors du décès ou à J30. À l'entrée, le lactate est augmenté et l'excès de base est diminué. Ils se normalisent pendant la première semaine, après remplissage adapté, chez ceux qui survivront. La persistance des anomalies est corrélée au sepsis et à la mortalité. Ils sont donc des marqueurs utiles et prometteurs pour surveiller la qualité du remplissage initial et prédire la survenue d'un sepsis. Leur utilisation pourrait permettre d'optimiser le remplissage et d'améliorer le devenir des brûlés.*

Mots-clés: *brûlure, remplissage, lactate, excès de base*

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Introduction

Burn shock is a multi system phenomenon in which direct heat causes increased capillary permeability and loss of fluid from intravascular to extravascular space with acute inflammatory change causing further exudation into interstitial space. This causes loss of intravascular volume, a state of hypovolemia and decreased oxygen delivery to tissues leading to hypoxia. This can also lead to systemic inflammatory response syndrome, which may progress to organ dysfunction and sepsis.[1,2] Hence fluid resuscitation should be started as early as possible to maintain the intravascular volume and restore homeostasis.

Fluid resuscitation is done by weight and surface area based formula, but in small full thickness burns with inhalational injury systemic insult is much greater, even though the surface area is less. The fluid resuscitation is titrated to achieve normal urine output and mean arterial pressure. The end point of resuscitation is to restore the volume, correct cellular oxygenation and achieve end-organ aerobic metabolis.[3] However despite adequate resuscitation as suggested by the clinical parameters and lab values, the presence of systemic inflammatory response syndrome (SIRS) and organ dysfunction in burn patients suggests that tissue hypoxia is present and cellular oxygenation is impaired.[4] The traditional markers of adequate resuscitation such as urine output and mean arterial pressure do not help in determining the presence of tissue hypoxia.[5,6]

The use of traditional parameters alone might result in inadequate resuscitation in burn patients. This suboptimal resuscitation leads to persistent hypoxia, continued anaerobic metabolism in the end organs and acidosis, which contributes to mortality and the development of sepsis. The parameters such as base deficit and serum lactate have been found to be good markers of tissue perfusion and are measurable physiological parameters that relate to tissue perfusion.[7] These have been used to predict outcomes in trauma patients but their role in burn patients has not been evaluated. There is a paucity of literature studying the association of these markers with the outcome in burn patients. This study aims to determine the relationship between plasma lactate and base deficit with sepsis and mortality in acute burns and their potential usage as markers of resuscitation.

Materials and method

A prospective observational study was carried out in the department of burns, plastic and maxillofacial surgery, VMMC and Safdarjung Hospital. The patients who presented within 24 hours of sustaining burns with 20-60% of TBSA burn injuries between the age group of 18-60 years, having either thermal and scalds were included. Patients with uncontrolled diabetes mellitus, hypertension, hypo or hyperthyroidism etc, pregnancy, chemical burns, electrical burns and inhalational burns were excluded from the study.

All the patients were resuscitated according to modified Brooke's formula and treated according to standard protocols after obtaining proper consent. Routine investigations were sent along with 1 ml of arterial blood in a heparinised syringe for arterial blood gas analysis. Serum lactate and base deficit values were noted at admission followed by day 1, day 2, day 3 and day 7 after admission. The arterial blood gas (ABG) analysis was done using a Radiometer ABL flex ABG analyser. The data were analysed using SPSS software version 21.

Sepsis was defined by 3 or more of the following criteria:

Tachypnoea (respiratory rate >20 breaths/min)

Tachycardia (heart rate >90beats/min)

Fever or hypothermia (temperature >38 or <36 °C),

Leukocytosis or leukopenia (white blood cells >1,2000/mm3 or <4,000/mm3 respectively) along with documented infection or clinical suspicion of infection.

The patients were followed up to the end point of either death/discharge or post burn day 30th. The data was then used to assess the correlation of serum lactate and base deficit with fluid resuscitation, sepsis and mortality.

Results

A total of 250 patients were included in the study. Out of the 250 patients, 69.8% were in the 18-40

years category, 16% were 41-50 years, and 23.2% were between 51-60 years. The mean age was found to be 38.02 +/- 12.879 years. 39.2% of subjects were female and 60.8% were male. Male to female ratio was 1.55. The mean weight was found to be 67 +/- 7.82 kgs. Mean TBSA was 41.40 +/- 13.82%. Out of the 250 subjects, 14 had scalds and the rest had thermal burns. Adequate fluid resuscitation was seen among 88.8% of the study subjects and sepsis was seen in 18.8%. Out of the 250 subjects, 77 died and 173 got discharged over a 30-day follow up period.

To determine the relationship with the outcome, the subjects were divided into survivors and non survivors and the mean lactate value was calculated on admission, day 1, day 2, day 3 and day 7 (*Table I*). The mean lactate values between the two groups were compared using an independent t test with p <0.05 and the difference between them was found to be statistically significant (*Fig. 1*). The mean lactate value was significantly higher among subjects who died, with a mean value of 9.81 mmol/L on admission, reaching up to 17.30 mmol/L on day seven.

The base deficit values among the subjects who died and those who got discharged were also compared using independent t test with p <0.05 at baseline, day 1, day 2, day 3 and day 7 and it was found to be significantly less among the subjects who died (*Table II, Fig. 2*). The mean value in non survivors on admission was -8.97mEq/L and on day 7 decreased to -17.27mEq/L.

Table I - Relationship between serum lactate and mortality

Serum lactate	Outcome	N	Mean	Standard deviation	Std mean	P value
Admission	Death	77	9.8118	2.81497	.32080	<0.00001
	Discharge	173	6.8360	2.38506	.18133	
Day 1	Death	76	12.12	3.292	.378	<0.00001
	Discharge	173	2.52	.624	.048	
Day 2	Death	73	14.4958	3.85368	.45104	<0.00001
	Discharge	173	1.6780	.40019	.03043	
Day 3	Death	67	16.0815	4.37750	.53480	<0.00001
	Discharge	173	1.2039	.39821	.03028	
Day 7	Death	48	17.3017	3.83605	.55369	<0.00001
	Discharge	173	.8920	.33929	.02580	

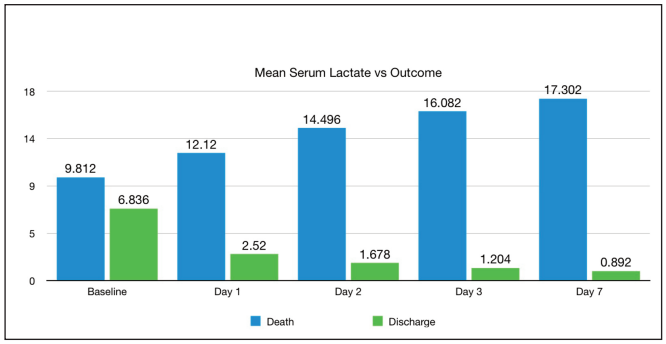

Fig. 1 - Relation of serum lactate levels with mortality. The serum lactate levels show progressive increase in the group of patients who did not survive

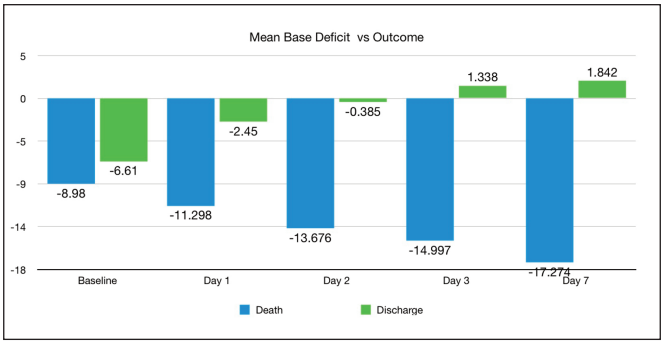

Fig. 2 - Base deficit in relation to mortality. The graph shows the base deficit over 7 days with non survivors showing progressive decrease in the base deficit value

Table II - Relationship between base deficit and mortality

Base Deficit	Outcome	N	Mean	Standard deviation	Std mean	P value
Admission	Death	77	-8.9795	3.49244	.32080	<0.00001
	Discharge	173	-6.6098	2.07638	.18133	
Day 1	Death	76	-11.2978	3.93573	.45146	<0.00001
	Discharge	173	-2.4499	.83419	.06342	
Day 2	Death	73	-13.6764	4.35347	.50953	<0.00001
	Discharge	173	-0.3852	1.34428	.10220	
Day 3	Death	67	-14.9972	5.69387	.69562	<0.00001
	Discharge	173	1.3379	.48277	.03670	
Day 7	Death	48	-17.2740	4.52384	.65296	<0.00001
	Discharge	173	1.8421	.26316	.02001	

The study population was also divided into groups with sepsis and a group without sepsis in order to study the relationship of sepsis with the plasma lactate and base deficit (*Table III*). Significant differences were seen in the base deficit among the subjects with and without sepsis when compared using independent t test p <0.05 at baseline, day 1, day 2, day 3, and day 7 (*Fig. 3*) and it was found to be less among subjects with sepsis.

The mean serum lactate levels among the subjects with and without sepsis were compared on admission and then on days 1, 2, 3 and day 7 (*Table IV*). The difference was statistically significant between the two groups. The baseline mean lactate value in those who developed sepsis was 10.70 mmol/L and after 7 days increased to 17.65 mmol/L (*Fig. 4*).

In those patients with inadequate resuscitation due to late presentation to our centre, serum lactate showed an increasing trend with a mean value of 12.78mmol/L after day 3. The mean serum lactate in a group without adequate resuscitation and with adequate resuscitation also showed a significant difference with p value of <0.0001 after day 1, day 2 and day 3. Similar results were observed when comparing the base deficit between the two groups. The mean base deficit in the patients without adequate resuscitation was -9.90 mEq/L after day 1 and after day 3 it was 12.5067mEq/L. For the group with adequate resuscitation, the mean value increased from -4.57 mEq/L to -2.46mEq/L after the third day, with a significant difference in the value between the two groups.

Table III - Relationship of base deficit to sepsis

Base Deficit	Sepsis	N	Mean	Standard deviation	Std mean	P value
Admission	No	203	-6.7977	2.45477	.17229	<0.00001
	Yes	47	-9.6804	3.06936	.44771	
Day 1	No	202	-3.4897	3.06428	.21560	<0.00001
	Yes	47	-12.2883	3.53865	.51617	
Day 2	No	199	-1.8172	4.24787	.30112	<0.00001
	Yes	47	-14.9657	3.60751	.52621	
Day 3	No	193	-.0646	4.40976	.31742	<0.00001
	Yes	47	-16.1891	5.72219	.83467	
Day 7	No	174	1.8407	.26304	.01994	<0.00001
	Yes	47	-17.6755	3.60571	.52595	

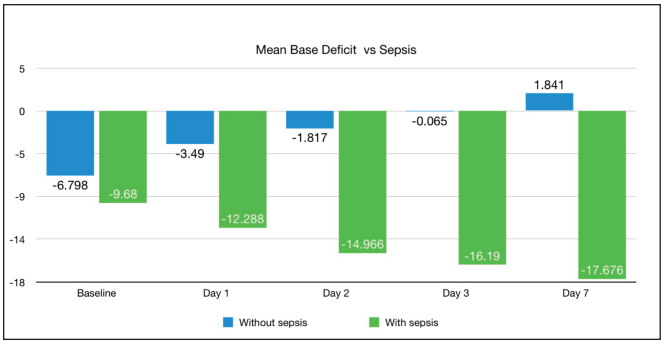

Fig. 3 - Base deficit in relation to development of sepsis. The base deficit decreases in the group which developed sepsis whereas it increases in the one which did not

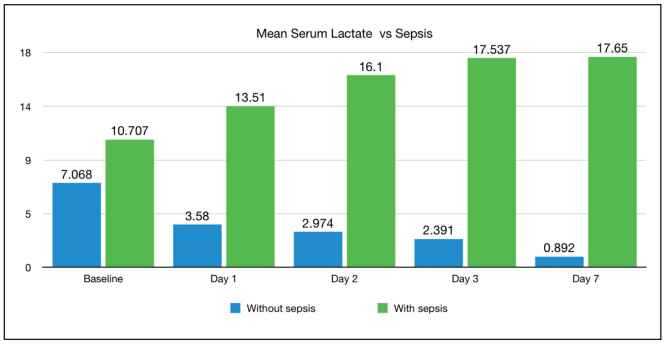

Fig. 4 - Mean serum lacate levels in relation to sepsis. The graph shows progressive increase of the mean lactate levels in the group which developed sepsis

Table IV - Relationship of mean serum lactate to sepsis

Serum lactate	Sepsis	N	Mean	Standard deviation	Std mean	P value
Admission	No	203	7.0684	2.49246	.17494	<0.00001
	Yes	47	10.7072	2.52080	.36770	
Day 1	No	201	3.58	2.862	.202	<0.00001
	Yes	47	13.51	2.747	.401	
Day 2	No	199	2.9739	3.58153	.25389	<0.00001
	Yes	47	16.0996	3.09696	.45174	
Day 3	No	193	2.3912	3.86699	.27835	<0.00001
	Yes	47	17.5368	3.09588	.45158	
Day 7	No	174	.8923	.33833	.02565	<0.00001
	Yes	47	17.6498	3.01525	.43982	

Discussion

Burn injury results in the release of many inflammatory mediators at the site of the burn wound and elsewhere, which are responsible for systemic inflammatory response syndrome.[8] The processes of time-related capillary leak and compartment syndrome are responsible for further increases in SIRS. It may result in multiple organ failure, which is the most common cause of death in the ICU.[9] Burn shock is initially hypovolemic and is characterised by profound hemodynamic changes such as decreased plasma volume, cardiac output, urinary output, and increased systemic vascular resistance.[10] Timely and adequate resuscitation is one of the most important aspects of the management of major burns and may be responsible for a good or bad prognosis. Currently, there is no ideal marker for adequate resuscitation and the traditional markers used may not help in the determination of tissue perfusion and oxygenation which are impaired in burn patients due to widespread inflammation and capillary leak. Mean arterial pressure and urine output are preserved due to the effects of catecholamines and so they do not sufficiently reflect regional microcirculation or the reversal of shock. Hence, it is imperative to find a reliable indicator of perfusion as most deaths are secondary to multiple-organ failure, an end stage of systemic inflammatory response syndrome, which in itself is most often a result of repeated or unresolved hypoperfusion.[9]

In states of global or severe local hypoperfusion or shock, anaerobic metabolism predominates due to which lactate accumulates and changes in base deficit results.[11] The inflammatory process and shock also result in decreased liver perfusion due to capillary leak, which may result in an even more pronounced serum lactate increase due to decreased lactate metabolism. In the setting of septic and hemorrhagic shock, the relation of lactate with outcome has been established and it is used as an indicator of sepsis. This study explores the relation of serum lactate and base deficit with the outcome and development of sepsis in acute burn patients.

In our study, 250 patients were enrolled with burns involving 20-60% of total body surface area, which is associated with significant systemic inflammatory response and fluid shift mandating admission for intravenous resuscitation. The majority of the cases sustained thermal burns and only a few had scalds. No significant differences were found in the distribution of types of burns between the survivors and non survivors. 30-days mortality of 30.8% was present in our study and 18.8% of patients developed sepsis.

In a study by Jeng et al.[12] on 49 patients with 15-90% TBSA, a central venous sample was checked for lactate levels every 2 hours. The trend of lactate in the first 48 hours showed that only age and lactate have a relation to survival and no correlation was found for gender, TBSA and full thickness burns. Lactate levels were high in 90% of the patients despite achieving target urine output and mean arterial pressure, showing that lactate levels are reflective of the severity of the injury as well as the host response. These findings are in accordance with our study, which shows a significant association of higher lactate levels with the severity of burns that is total body surface area and mortality.

The study conducted by us also shows concordance with another study by Husain et al.[9] who studied 137 surgical patients in the ICU and found that both initial and 24 hour arterial lactate were predictive of mortality. This study also demonstrated an association between raised initial lactate levels and mortality. If lactate normalised by 24 hours, mortality was only 10%, whereas if it took 24-48 hours to normalise, mortality rate was 20%. Those failing to normalise lactate had increased mortality of up to 67%.

In another study by Mokline A et al.[13] serum lactate serial measurement was done in 80 patients with mean TBSA of 33+/- 21%. Lactate measurements were obtained within 4 hours of admission and then checked every 6 hours till normalisation. The study concluded that serum lactate with a cut off value of >4.46mmol/L was an independent predictor of mortality and that of >4 mmol/L an independent predictor of sepsis. Similarly our study concluded that serum lactate can be used to predict mortality, with non survivors showing an increasing trend of serum lactate while in survivors it decreased over time.

In our study, serum lactate was raised in all the patients at admission with a mean value of 6.83mmol/L in survivors and 9.81mmol/L in non survivors. Patients who survived showed a falling

trend from the time of admission to day 7, whereas non survivors showed increasing values over the period of 7 days with a mean value of 17.30 mmol/L on day 7, thus indicating that serum lactate tends to normalise by day 7 in survivors whereas it continues to increase in the non survivors. Also, serum lactate in survivors at the time of admission was less elevated compared to non survivors. The results are similar to a study conducted by Cochran et al.[14] on 128 patients with burn TBSA of 20-96%. The patients who did not survive had significantly higher lactate values at admission, 12 hours, 18 hours and 24 hours after sustaining burns. The lactate levels in survivors showed a downward trend, whereas in non survivors it continued to rise through 12 hours after admission.

Serum lactate is also a useful guide for adequate resuscitation. In our study, the serum lactate continued to increase in the group with inadequate resuscitation and the levels declined over 7 days in those with adequate resuscitation. Inadequate resuscitation was measured using the clinical parameters of urine output and mean arterial pressure. Our study also showed a similar result with the base deficit values with significant differences in the 2 groups on day one, day two and day three. This was also seen in a study done by Salehi et al.[15] in 2011 on 78 patients, where the patients were divided into 2 groups based on the value of base deficit at the time of admission. The study concluded that base deficit is related to the resuscitation of burn patients and subsequent development of SIRS, multiple organ system failure, and eventual mortality.

In our present study, the base deficit was measured in all patients at the time of admission. The patients who survived showed an increase in the value of base deficit from day 0 to day 7 with a mean value of 1.842mEq/L on day 7. The non survivors showed a decreasing trend from day 0 to day 7 with a mean value of -17.27mEq/L on day 7. This shows that the base deficit normalises by day 7 in survivors, while it continues to decrease in non survivors. Also, base deficit in non survivors at the time of admission was less compared to survivors. Patients with sepsis had a mean base deficit of -9.68mEq/L on admission, which continued to decrease through day 7 with a mean of -17.67mEq/L. Those who did not develop sepsis showed an increase in the base deficit from -6.79mEq/L at the time of admission to 1.84mEq/L on day 7. The base deficit at the time of admission in patients who did not develop sepsis was greater compared to those who did. This shows concordance with a Cartotto et al.[16] study in which 38 patients with a mean TBSA of 36 +/- 15% were studied and base deficit was measured in the first 24 hours. The patients were divided into 2 groups having base deficit < -6 mEq/L and base deficit > -6 mEq/L. The group with base deficit value of < -6 mEq/L had a significant association with development of systemic inflammatory response syndrome, acute respiratory distress syndrome and multiple organ dysfunction syndrome when compared to the group with base deficit of > -6 mEq/L. The group with base deficit < -6 mEq/L also had a higher incidence of sepsis.

In another study by Megahed et al.,[17] serial base deficit measurement along with serum albumin and haemoglobin was done on the day of admission, third day and 1 week after admission on 42 patients with burns. The study concluded that excess base deficit had a significant association with mortality and can be used as a prognostic factor for mortality in major burns. Our study shows a similar conclusion in which patients with lower base deficit had significant association with development of sepsis and mortality with decreasing trend of base deficit value in non survivors.

In our study, we found that serum lactate and base deficit had a significant association with prognosis in acute burns. The main finding in our study was the strong predictive value of serum lactate and base deficit in determining adequacy of fluid resuscitation, development of sepsis and mortality. Fluid resuscitation guided by base deficit and serum lactate values will help in decreasing the morbidity and improving the outcome after burn injury.

Conclusion

Burn injury is an important source of morbidity and mortality, but there are limited studies regarding the association of serum lactate and base deficit with the adequacy of fluid resuscitation, morbidity and mortality. The currently used markers of adequate resuscitation may not reflect ongoing tissue ischemia, and hence serum lactate and base deficit can

be used as markers to determine the state of perfusion. Resuscitation parameters and goals may need to be adapted for burn patients with persistent lactic acidosis or a base deficit due to the ongoing state of hypo perfusion indicated by these values. Additional clinical means of monitoring perfusion during burn shock resuscitation should be sought along with these to prevent over-resuscitation, which may contribute to secondary complications such as compartment syndrome and pulmonary failure.

Arterial serum lactate and base deficit are promising predictive tools for assessing adequate fluid resuscitation, the development of sepsis, and mortality. Based on our study, lactate and base deficit can be measured in all major burns and may be used as a guide for the management of these patients. Fluid therapy guided by serum lactate and the base deficit value, to normalise them, can be a promising method to decrease burn mortality and improve outcome.

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