African Journal of Emergency Medicine (2014) 4, 61–65

African Federation for Emergency Medicine

African Journal of Emergency Medicine

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ORIGINAL RESEARCH

Lactate clearance predicts outcome after major trauma

La clairance du lactate permet de prévoir l'évolution de l'état de santé après un traumatisme important

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Received 4 September 2013; revised 19 November 2013; accepted 27 November 2013; available online 10 February 2014

Introduction: To determine a correlation between lactate clearance within 48 h and survival in trauma patients at a Level I trauma centre in a developing country and compare to previous international lactate clearance studies.
Methods: We conducted a retrospective study of a prospectively collected database at a Level I trauma centre from March 2007 to November 2010. Patients of all ages were included. Metabolic parameters from initial arterial blood gas were measured in all patients, an abnormal lactate being defined as >2.5 mmol/L. A subgroup analysis of blunt versus penetrating injury was performed.
Results: Of the 657 patients in the database, 493 had complete lactate data. The survival rate of patients with lactate values <2.5 mmol/L was 88%. Of the patients with high lactate levels that cleared within 24 and 48 h the survival rates were 81% and 71%, respectively. The survival rate amongst patients not achieving a normal lactate within 48 h was 46% but was higher in those with penetrating as opposed to blunt injury (67% versus 38%). The overall survival was 81%.
Conclusion: The present results confirm previous studies showing that prolonged lactate clearance predicts increased mortality in severely injured trauma patients. Thus, the measurements of arterial serum lactate trends are simple and effective predictors of outcome.

Introduction: Déterminer la corrélation entre la clairance du lactate dans les 48 heures et la survie des patients souffrant de traumatisme dans un centre de traumatologie de niveau 1 dans un pays en développement, et comparer cette corrélation aux études internationales antérieures sur la clairance du lactate.
Méthodes: Nous avons réalisé une étude rétrospective d'une base de données constituée de manière prospective dans un centre de traumatologie de niveau 1 de mars 2007 à novembre 2010. Des patients de tous âges ont été inclus. Les paramètres métaboliques tirés des gaz du sang artériel initiaux ont été mesurés chez tous les patients, la concentration anormale de lactate étant fixée à >2,5 mmol/L. Une analyse par sous-groupe des blessures fermées par rapport aux blessures pénétrantes a été réalisée.
Résultats: Sur les 657 patients de la base de données, 493 disposaient de données complètes sur la concentration de lactate. Le taux de survie des patients présentant des concentrations de lactate <2,5 mmol/L s'élevait à 88%. Chez les patients présentant des concentrations élevées de lactate qui diminuaient au bout de 24 et 48 heures, les taux de survie s'élevaient respectivement à 81% et 71%. Le taux de survie chez les patients dont la concentration en lactate ne revenait pas à la normale sous 48 heures était de 46%, mais était plus élevé chez les patients présentant des blessures pénétrantes que chez les patients présentant des blessures fermées (67% contre 38%). Le taux général de survie s'élevait à 81%.
Conclusion: [Les résultats de l'étude confirment les études antérieures indiquant qu'une clairance prolongée du lactate est associée à une mortalité plus élevée chez les patients en traumatologie victimes de blessures graves. Par conséquent, la mesure des tendances du lactate dans le sérum artériel constitue une variable prédictive fiable et efficace de l'état de santé.]

African relevance

- Point of care blood-gas devices are common in the Emergency Centre and should be configured to detect lactate levels.
- The earlier the lactate clears during resuscitation, the better the prognosis.
- Children and adults can be assessed equally by the use of lactate clearance.

Introduction

Lactate levels in the blood are a function of the balance between lactate production and clearance, with a normal value of less than 2.5 mmol/L. Clearance of lactate is a surrogate marker of improvement and survival in critically ill patients. This clearing process occurs mostly in the liver (60%) and

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Peer review under responsibility of African Federation for Emergency Medicine.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.afjem.2013.11.006

the kidney (30%).[1] Under aerobic conditions, lactate is produced in skeletal muscle, skin, brain, intestine, and red blood cells.[2] Woods and Cohen created a classification model for lactic acidosis that is still used today.[3] High lactate values correlated with mortality in early smaller study populations.[4] Bakker and co-workers demonstrated that in septic patients, measuring lactate levels and lactate clearance was superior to other parameters for outcome prediction.[5,6]

In 2006, Pal et al. undertook a large-scale study with 5995 trauma patients, comparing the admission lactate value to mortality. This large study did not demonstrate a correlation between a single elevated lactate value and survival. Since overall mortality was only 3%, the researchers suggested that the initial lactate value might be worth measuring in more severe trauma cases, but should not be obtained routinely.[4] A BEST-BET-analysis from 2008 by Hung compares six studies all looking at the initial lactate value. It suggests that the initial lactate value does not identify patients at high risk of death, but it may have a role in identifying patients at low risk of death following blunt trauma.[7]

Abrahamson's team initiated research on serial lactate values in trauma patients in 1993. In their study, all patients who normalized their serum lactate levels within 24 h survived, and 75% of those that normalized by 48 h had an increased survival. Of those patients not clearing lactate within 48 h, only 14% survived.[8] McNelis and partners conducted a study of 95 trauma patients in 2006 that showed similar outcomes.[9] In a study by Blow and co-workers, the researchers not only detected hypoperfusion in admitted trauma patients, but also corrected it within 24 h. They showed that early aggressive correction of occult hypoperfusion (as demonstrated by increased lactate levels) led to fewer cases of multi-organ failure, respiratory complications, and death in severely ill trauma patients.[10]

The trauma unit in Durban, KwaZulu-Natal (KZN), South Africa, is a modern facility equipped to Level 1 standards and currently is the only public facility of this type in the city.[11] It is situated within a subspecialist hospital and acts as a referral hospital for around 25 district and regional hospitals in more rural areas of KZN, parts of Eastern Cape, and some parts of Mozambique.[12] Cases are received either from referring hospitals or directly from the scene, provided admission criteria are met- namely, haemodynamic instability or severe mechanism of injury. Around 25% of the patients included in the study were admitted directly from the scene.

Upon admission, patients are managed by a trauma team consisting of a consultant attending certified in critical care and trauma surgery and a resident each from orthopaedics, anaesthetics, and general surgery, in addition to nurse and critical care technicians. Initial assessment and resuscitation are as per the Advanced Trauma Life Support approach with the use of permissive hypotension where applicable. Early placement of invasive monitoring is performed when necessary. Focussed assessment with ultrasound is used in the initial assessment and further imaging is undertaken with the in-house 128 slice CT-scanner (Siemens, Germany). Immediate access is available to two operating theatres within 20 metres from the resuscitation base. Point of care blood gas analysis and thrombelastography are available within the unit.

Ongoing care is provided by the same team of physicians in a trauma intensive care unit (ICU) with eight ICU beds and eight high-dependency beds. Once patients are stable, they are referred back to their base hospitals for further management. All non-survivors undergo medico-legal post-mortem examination, as required by the legal provisions for all unnatural deaths.

This study aims to determine whether there is a correlation between lactate clearance and the outcome of severely injured trauma patients admitted to a recently opened Level 1 Trauma Centre in South Africa, a developing country, with the hypothesis being that decreased lactate clearance in these patients will be associated with increased mortality.

Methods

Following class-approval from the University of KZN ethics committee (BREC Class Approval BE207/09), patient data were collected from the approved databank using retrospective analysis of a prospectively collected dataset. Data were collected prospectively for all patients admitted to the Trauma ICU during the period from March 2007 to November 2010. Patients of all ages were included if they had daily lactate levels recorded at admission and thereafter, were admitted via direct or inter-hospital transfer routes. They were excluded if death occurred before blood sampling, injury mechanism was unclear, or the injuries were minor (no blood taken). Patients with incomplete data were also excluded. Gunshot wounds (GSW) and stab wounds (SW) were classified as penetrating trauma, whereas blunt intentional or unintentional injury, motor vehicle accidents, and fall from height counted as blunt trauma.

Data were collected for all patients regarding gender, age, injury severity score (ISS), new injury severity score (NISS),[13] type of trauma (blunt vs. penetrating), length of stay at ICU, referral hospital, and lactate levels measured at admission, after 0–24 h, after 24–48 h, and after 48–72 h from admittance to ICU. Since the trauma service provides the only tertiary trauma care facility for injured children in KZN, these patients are included in this study. Children admitted to trauma ICU are mostly over two years old. Those younger than two years are generally referred to a paediatric ICU due to greater technical skill and better access to age appropriate equipment, but are co-managed by the Trauma Service.

The serum lactate was measured in arterial blood. The first sample was taken upon arrival at the trauma unit, within the first hour of care; thereafter, the lactate was measured daily or more frequently, when needed. The range of normal values for the method for measurement is from 0.5 to 2.20 mmol/L. 2.5 mmol/L and less was accepted as the limit for clearance.

The collected data were analysed using GraphPad InStat (Graphpad Software, La Jolla, CA). Continuous variables (age, stay, ISS, NISS, lactate levels) were analysed with Student's *t*-test for each group, calculating the mean, standard deviation, and the *p*-value. Contingency tables were created for the outcomes for the categorical variables (clearance vs outcome, trauma mechanism vs outcome). *p*-Values for these were calculated with the Chi-Squared test for trend and independence and Fisher's exact test.

Results

657 patients (495 men and 162 women) were included in the study. 113 children ranging from 1 to 17 years old are included in the data set. 164 patients were excluded from this study. 45 of the excluded patients died in the resuscitation area before

blood samples were taken, while two of the patients were excluded because of abnormal trauma mechanism (snake bite and drowning). In the rest of the cases, the collected data were incomplete due to either minor injury with no need for repetitive blood collection or problems with documentation. Documentation by doctors and nurses was captured in electronic patient record databases. There were occasions where the electronic patient record systems were not working due to computer down-time, and the blood samples from those days were not documented. Patients with stays shorter than 24 h were included, provided the initial blood samples were taken.

Demographics are displayed in Table 1. Age, including childhood, did not appear to influence outcome.

The patients were divided into two subgroups based upon whether the mechanism of injury was blunt or penetrating. The blunt trauma group included 470 patients (72% of total) and penetrating trauma included 187 (28%). The overall survival was 77%, including those subsequently excluded from evaluation, with slightly better survival in the penetrating group (79% versus 76%), which did not achieve statistical significance. Fig. 1 shows the distribution of trauma mechanisms. Amongst all patients, motor vehicle accidents were the most common reason for admission (58%).

Of the 657 patients in the dataset, 610 had complete data to review lactate clearance over time. These data are shown in Fig. 2. Most of the excluded patients had only one single value measured, either because they did not survive for 24 h ($n = 25$), or because they were discharged before 24 h ($n = 5$); 17 patients had inadequate documentation of the lactate values. Lactate clearance was documented in 287 patients with elevated lactate values at admission. The overall survival rate for the study population was 81%. 330 patients had elevated lactate levels upon admission, whereas the admission lactate levels of 327 patients were within normal limits. The survival amongst the patients with elevated lactate levels at admission was 66%, whereas it was 88% amongst those patients with normal lactate levels on admission. Of the patients who cleared to normal (<2.5 mmol/L) within 24 h, 81% survived. The survival rate for patients clearing lactate within 48 h was 71%. The patients who did not clear their lactate within 48 h had a survival rate of only 46%. Across all groups, the ability to clear lactate was found to statistically predict survival ($p < 0.001$). This was true at both 24 and 48 h, as shown in Table 2.

The mean ISS was 19.9 ± 10.1 (SD) for the group with penetrating trauma and 25.4 ± 14.0 for the blunt trauma patients ($p < 0.001$). The mean NISS was 27.6 ± 13.0 and 30.6 ± 15.6, respectively ($p < 0.001$). Lactate clearance was measured in both penetrating and blunt trauma patients. Since both the mean ISS and NISS were higher in the blunt trauma cohort, one would expect higher mortality in that group of patients. The results, depicted in Fig. 3, show that there is no significant overall difference in survival between the two groups of patients when it comes to clearance within 48 h. However, patients who had not cleared their lactate within 48 h had an apparent better chance of survival if they had experienced penetrating trauma, although this did not achieve statistical significance (67% versus 38%, $p = 0.09$).

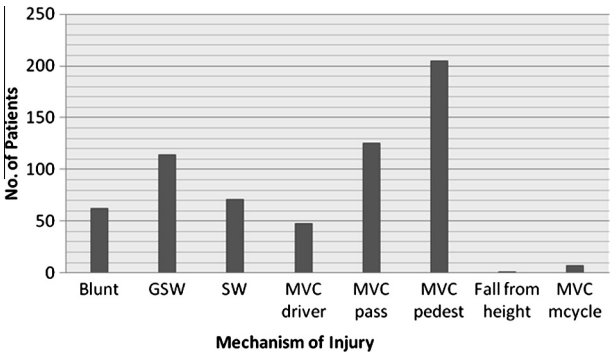

Figure 1 Mechanism of injury.

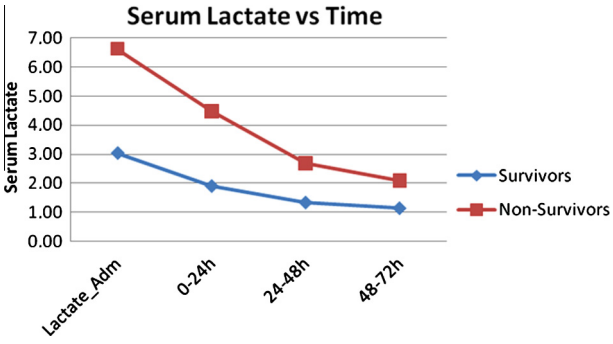

Figure 2 Mean serum lactate values for Survivors and Non-survivors.

Discussion

This retrospective study was performed to assess for a correlation between lactate clearance and mortality in patients admitted to a Level 1 Trauma Unit and ICU at a large teaching hospital in Durban, South Africa, a developing country with a major trauma burden.

Mortality was significantly increased when the lactate clearance is prolonged, and concurs with the earlier studies in the field of trauma.[8–10] Compared to Abramson's and McNelis' studies, the present data showed a lower survival rate even if

Table 1 Demographics ($N = 505$ survivors, 152 Non-survivors).

Parameter	Survivors			Non-survivors			*p*-Value
	Mean ± SD	Range	Median	Mean ± SD	Range	Median	
Age (years)	28.28 ± 14.30	1–78	26	34.01 ± 16.84	5–83	30	0.99
ISS	21.19 ± 10.43	1–57	20	32.67 ± 17.24	1–75	29	<0.001
NISS	26.84 ± 12.72	1–66	26	39.58 ± 17.54	1–75	41	<0.001
ICU stay (days)	14.66 ± 25.29	0–115	10	7.77 ± 11.96	0–106	5	0.0012
EC lactate (mmol/L)	3.05 ± 2.79	0.49–22.6	2.22	6.62 ± 5.99	0.66–50.0	4.92	<0.001

Table 2 Lactate normalization versus time.

Lactate clearance	Survivors (*n*)	Non-survivors (*n*)	Survival (%)	Odds ratio*	95% CI	*p*-Value
Normal at admission	288	39	88	–	–	–
Cleared < 24 h	132	30	81	1.68	0.99–2.82	0.05
Cleared > 24 < 48 h	61	25	71	3.03	1.71–5.37	<0.001
Cleared after 48 h	16	19	46	8.77	4.16–18.46	<0.001
Total	**497**	**113**	**81**	–	–	–

CI = Confidence interval.
* Odds ratio compared those with normal lactate at admission.

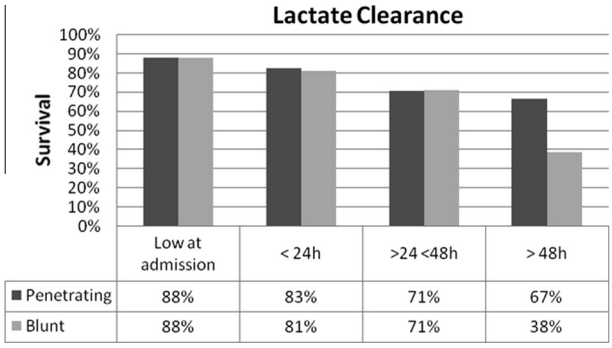

Figure 3 Survival in the different groups of blunt and penetrating trauma depending on lactate clearance.

the lactate levels cleared to normal within 24 h.[8,9] The survival in patients clearing between 24 and 48 h was still lower than the previously reported series, which documented 75% and 96.7%, respectively. In patients who did not clear their lactate within 48 h, only 46% survived, whereas the value was between 14% and 33% for the previously reported studies[8,9]; this is possibly explained by the selected patient population of more severely injured patients in the present cohort and changes in intensive care support over the past 20 years.

There was no significant survival difference by mechanism of injury (penetrating versus blunt) between those who cleared their lactate within 24 and 48 h, respectively, although there was a difference in those patients who did not clear their lactate within 48 h. The survival was better after 48 h in the group with penetrating trauma (67%), whereas it was only 38% in the group with blunt trauma. This is an observation in keeping with the work of Blow et al.[8] who reported a correlation between elevated lactate levels and poor outcome in patients who had experienced blunt trauma; they also could not demonstrate any correlation between lactate levels and outcome in patients who sustained penetrating trauma. The difference in this study can most certainly be explained by the difference in the extent of trauma. Patients in the blunt trauma group had experienced high-energy transfer and had generally higher ISS and NISS, with the expectation therefore that the outcomes in this group would be lower despite optimal care.

Attention must be given to the different inclusion and exclusion criteria used for the various studies in this field. The present study decided not to exclude any patients purely because of low injury severity scores or due to short stay, which was the case in both the comparator studies. Thus, the present sample is more representative for the overall patient population treated at a major trauma unit with an integrated ICU. In a similar study published in Journal of Trauma and Acute Care, Odom and co-workers sought to evaluate the outcome with six hour lactate clearance in a cohort of over 4000 trauma patients, of whom 547 patients were found with elevated lactate.[14] They also noted that less severely injured patients often had no measured lactate, but found that those not clearing lactate within 6 h had a higher mortality and need for comfort measures at end-of-life.

When interpreting these results, the geographical position of South Africa and the economical and infrastructural limitations of a middle-income country must be considered. Although Linton was optimistic in 1994 about the infrastructure and the future of critical care medicine,[15] there remain many inadequacies. Trauma care in South Africa is organized as a stepwise system with district hospitals in rural areas referring to regional centres with general specialist cover. From there, patients may be referred to a larger sub-specialist hospital, such as the hospital discussed. The time from injury to admission at the trauma ICU can therefore vary significantly, and there are often delays in transfer due to inefficiencies in the prehospital and inter-hospital transfer system. This has been explored in a previously published study from this institution.[16] These markedly disparate groups of patients are included in the current study, which must be considered when interpreting the results.

Conclusion

The results of this study are in line with earlier publications in traumatology showing that prolonged lactate clearance does predict increased mortality in severely injured patients. It can therefore be concluded that the measurement of serial arterial serum lactate trends to assess lactate clearance is a simple and effective predictor of poor outcome and may aid in triaging care when access to ICU facilities is limited, particularly in developing countries where point-of-care devices may be the only laboratory facilities available to make this decision.

Conflict of interest

The authors declare no conflict of interest.

Author contribution

E.H. collected and analysed the data, T.C.H. supervised the research, H.B. was the Swedish supervisor and statistical expert and D.J.J.M. is the Data-PI and edited the final version.

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