Utilité du Base Excess pour la prédiction de la mortalité immédiate et précoce chez les patients traumatisés graves aux urgences

Base Excess usefulness for prediction of immediate mortality in severe trauma patients admitted to the Emergency department

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RÉSUMÉ

Introduction: La pathologie traumatique est la première cause de mortalité du sujet jeune. L'état de choc hémorragique arrive en seconde position. Toutefois, l'hypoperfusion tissulaire reste difficile à diagnostiquer cliniquement chez les sujets jeunes. Dans ce contexte, le Base Excess (BE) a été utilisé en traumatologie comme indicateur précoce d'hypoperfusion. Objectif : Evaluer la valeur pronostique du BE à l'admission chez le traumatisé sévère en termes de mortalité.

Méthodes : Nous avons mené une étude prospective pronostique avec inclusion des traumatisés sévères admis en salle d'accueil des urgences vitales selon des critères de haute vélocité (33 mois). Une gazométrie artérielle et un calcul du BE ont été effectués. Une analyse multivariée a été réalisée afin d'identifier les facteurs prédictifs de mortalité en SAUV et au 7ème jour post-traumatique. Une étude de la puissance pronostique par la courbe ROC et une étude de la survie ont été menées.

Résultats : Inclusion de 479 patients. L'âge médian=37 (18-90) et sex-ratio=4,2. Les accidents de la voie publique ont été majoritaires n (%): 35 (75%). Caractéristiques cliniques : n(%) : GCS<13 : 170(35) ; PAS<90 mmHg : 64(13) et SpO2<90% : 82(17). L'ISS moyen =22 ± 13. La mortalité immédiate en SAUV et à J7 a été respectivement de 2,2% et 27,3%. Le BE médian a été de -3,2 mmol/l (-25 ; 28). Quarante-cinq pour cent avaient un BE ≤-3,5 mmol/l. En analyse multivariée, un BE ≤ -6,5 mmol/L est ressorti comme facteur indépendant prédictif de mortalité en SAUV avec un Odds Ratio ajusté [IC95%] = 3,17 [1,4 ; 7,1] ; p=0,005. Les résultats ont été similaires lors de l'étude de la mortalité à J7 : Odds Ratio ajusté [IC95%] = 1,5 [1,14 ; 1,96] ; p=0,003. Le BE a montré un pouvoir discriminatif puissant (courbes ROC). La survie a été statistiquement meilleure pour un BE>-6,5mmol/l.

Conclusion : Le BE est ressorti comme facteur prédictif indépendant de la mortalité immédiate et précoce et a été corrélé au pronostic. Toutefois, sa valeur pronostique a été meilleure pour prédire la mortalité immédiate et peut de ce fait être proposé comme un outil de triage aux urgences

Mots-clés

Base Excess - Traumatisé sévère - mortalité - service des urgences - pronostic

SUMMARY

Background: Trauma is a leading cause of death in young people and hemorrhagic shock is a leading mechanism of this mortality. Hypoperfusion can be difficult to diagnose clinically, especially in younger patients. Arterial Base Excess (BE) has been used as an early indicator of hypoperfusion.

Aim: To evaluate the prognostic value of admission BE in severe trauma patients admitted to the emergency department (ED).

Methods: In this prospective study, severe trauma patients meeting high velocity criteria admitted to the ED during the study period were included. BE was calculated from arterial blood gas samples. Multivariate analysis was performed for Day-1 and Day-7 post trauma mortality. ROC characteristics and survival curves were used.

Results: We included 479 patients. Median age was 37 (18-90). Eighty-one per cent were male. Clinical characteristics n(%): GCS<13: 170(35); SBP<90 mmHg: 64(13) and SpO2 <90%: 82(17). Mean ISS was 22 ± 13. Mortality was at days 1 and 7: 2.2% and 27.3%, respectively. Median BE was -3.2 mmol/l (-25; 28). Forty-five per cent had a BE ≤ -3.5 mmol/l. In multivariate analysis, initial BE ≤ -6.5 mmol/l was predictive of first day mortality with an Odds Ratio; [CI95%] = 3.17; [1.4-7.1]; p=0.005. Similar results were found at Day 7: Odds Ratio; [CI95%] = 1.5; [1.14-1.96]; p=0.003. BE showed high prognostic value for both mortality rates. Survival curve was significant for BE> -6.5mmol/l.

Conclusion: in this study, a high BE above 6.5mmol/L showed a significant prognostic value in immediate and early mortality and is proposed as a marker of injury severity in trauma patients admitted to the ED. Prediction was better for the immediate mortality and thus could be proposed as a triage tool in the ED

Key-words

Base Excess- polytrauma- mortality- emergency department- prognosis

INTRODUCTION

Trauma is a global leading cause of mortality among young people. Hemorrhagic shock represents a leading cause of traumatic death, second only to traumatic brain injury [1,2]. Hypoperfusion leading to hemorrhagic shock can be difficult to diagnose. Particularly in young people with effective compensatory mechanisms, early stages of hypoperfusion may be subtle and the evolution of hemorrhagic shock may be silent. Hence, many tools have been proposed to improve the recognition of hypoperfusion and hemorrhagic shock. The clinical Advanced Trauma Life Support (ATLS) classification had been described, but has shown limitations in detecting patients in early stages of hemorrhagic shock [1,2]. It is incumbent on the emergency care provider, both in prehospital and in-hospital settings, to recognize and treat hypoperfusion within those important first minutes and golden hour of serious polytrauma [3]. Moreover, given that 80% of all trauma deaths occur within the first 48 hours, an accurate way to recognize early stages of hemorrhagic shock can positively impact mortality of this at risk population [4]. As a result, many biomarkers have been proposed over the last decades to guide the management of, and the early decision making in severe trauma[5-7].

Base excess has been described as a prognostic indicator by predicting shock, resuscitation needs and mortality in polytrauma [8-10]. Moreover, this biomarker can be rapidly obtained, and has been shown to be a superior prognostic indicator to the more commonly used lactate [7].

The aim of this study was to evaluate the prognostic value of arterial Base Excess (BE) drawn immediately at admission to predict mortality in severe trauma patients admitted to the Emergency Department.

METHODS

Study design

This observational and prognostic single center study was conducted in a teaching hospital Emergency Department (ED) with 125,000 visits per year. Patients were enrolled prospectively over 33 months (April 2013 to December 2015). Data were collected using a pre-determined check-list.

We included all successive trauma patients aged 18 years and older who presented to the ED within six hours of the traumatic event and who met the criteria for severe trauma. A patient met the criteria for severe trauma if, after first assessment, they met of at least one of the high velocity criteria of Vittel [11] or the Trauma Team Activation (TTA) criteria [12] used at our care center. Patients who were transferred from another hospital after first resuscitation care were not included. Patients in whom initial injury assessment or other data was incomplete were excluded. After the first ED assessment and before initial resuscitation, blood samples for laboratory investigation were drawn, including a venous sample and arterial blood gas (ABG). The heparinized ABGs were immediately analyzed in the ED using a GEM Premier 3000® blood gas analyzer from Instrumentation Laboratory-Worldwide Headquarters Massachusetts, USA. Base (BE) excess was calculated from arterial pH and partial pressure of CO_2 ($PaCO_2$) using the following formula: BE = 0.02786 * $PaCO_2$ * 10 (pH - 6.1) + 13.77 * pH - 124.58, calculated by the Cornell University Calculator from http://www-users.med.cornell.edu/~spon/picu/calc/basecalc.htm

Severity injury was recorded using The Injury Severity Score (ISS). As it was calculated using the site http://www.Trauma.org All patients were followed from day one to 90 days after enrollment and clinical course was obtained by phoning patients, family and/or contacting the receiving structure (Intensive Care Units, surgical wards, etc). The primary outcome measures were immediate mortality, defined as mortality on day one of presentation, and early mortality defined as mortality on day seven of their hospital stay.

Statistical analysis

We used the Statistical Package for Social Sciences (SPSS 20.0, IBM) for analysis. All continuous variables were tested for normality using Kolmogorov-Smirnoff test. Continuous, normally distributed variables were expressed by mean with standard deviation (SD) whereas non-continuous and continuous non-normally distributed ones were expressed in median with Interquartile Ranges (IQR). Categorical variables were expressed in percentages. Comparison between two Independent series averages were made using the Student's Independent T-test and in the case of non-normal distribution, by the non-parametric Mann-Whitney test. Comparison of percentages on Independent series were made by the Pearson chi-square test, and when not appropriate, by Fisher's exact test. To determine the cut-off value, we used Receiver Operating Characteristics (ROC) curves and the threshold value was selected by choosing the best couple sensitivity-

specificity. in a first step, we made a univariate analysis to identify the risk factors related to mortality. From the retained factors in first univariate method, multivariate analysis was conducted to identify factors directly related to the event, using binary logistic multiple regression. Relevant regression diagnostics were tested (Hosmer and Lemeshow goodness of fit test). Survival data were studied by establishing survival curves according to the Kaplan Meier method. The search for prognostic factors of survival was carried out by comparing the survival curves by the Log rank test. In all statistical tests, a p-value less than 0.05 was considered as statistically significant.

RESULTS

Characteristics of the population

During the study period, 698 successive severe trauma patients were admitted over the 33 months period. As shown in the flow chart of patient's selection (figure 1), 479 (79%) patients were enrolled in the final analysis. Median age was 37 years with IQR 25-57 years. Sex-ratio was 4.2 with male predominance (81%). Road traffic accidents were the most common mechanism, and in 31% it was involving pedestrians. 189 trauma patients (39%) had no past medical history. 320 severe trauma patients (67%) had an ISS score ≥ 16 (median ISS=22±13). Eleven patients were unstable and died at day 1 in the ED (2.2%). Furthermore, death rate on day 7 was 17.5% and 21% on day 30. The intra-hospital mortality rate was 19.4%.

The clinical features at admission were: Glasgow Coma Scale (GCS) <13 in 110 patients (23%); Systolic Blood Pressure (SBP) <90mmHg in 46 patients (9%) and pulse oximetry (SpO2) <90% in 68 cases (14%).

163 patients (34%) were acidotic with a pH<7.35. The median BE was -3.2 mmol/L (-25-28). BE was ≤-3.5 mmol/L in 45% of cases and a BE ≤-6.5 mmol/L was found in 22% of cases.

189 patients (39%) underwent mechanical ventilation. 114 patients (24%) required the use of vasoactive drugs, and tranexamic acid (Exacyl®) was used in 74 cases (15%). 13 patients required blood transfusion (3%). 245 patients (51%) underwent at least one surgical intervention during their hospital stay.

130 patients were transferred to a surgery ward (27%). 121 (25,3%) of enrolled patients were hospitalized in the emergency intensive care unit, 76 (7%) were secondarily transferred to polyvalent resuscitation service after stabilization (16%) and 32 patients (7%) were kept in the short-term hospitalization unit.

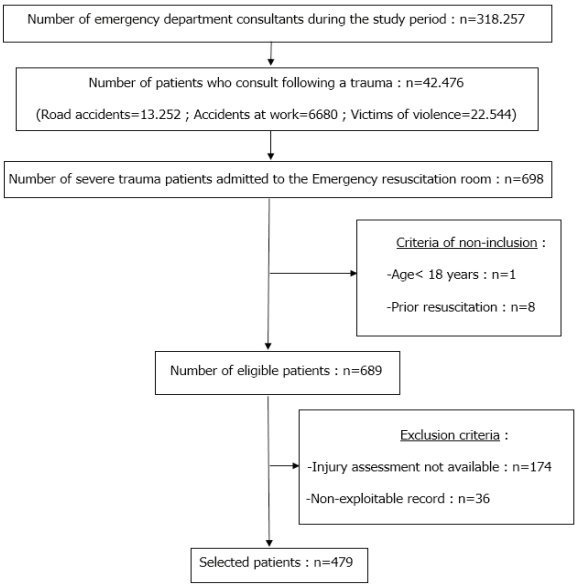

Figure 1 : Patients flow chart

Predictive value of Base Excess on mortality:

The predictive value of Base Excess in terms of mortality on day 1 in emergency department and on day 7 was studied using ROC curves (Figure 2). The BE showed both strong predictive value in the two terms of mortality but was superior to predict mortality on day 1.

Table 1 shows different characteristics of the ROC curves after fixing the cut-off value of BE towards immediate and early mortalities.

Table 1: Diagnostic power of Base Excess in terms of mortality

	Immediate mortality at Day 1							
Parameter	**AUC**	**CI [95%]**	**P**	**Cut-off**	**Se**	**Sp**	**PPV**	**NPV**
BE (mmol/L)	0,852	[0,753; 0,952]	<0,001	≤-6,5	82%	79%	8%	99%
	Early mortality at Day 7							
BE (mmol/L)	0,619	[0,558; 0,679]	<0,001	≤-6,5	37%	83%	44%	78%

BE: Base Excess; AUC: Area under the curve; CI: Confidence Interval; p: p-value; Se: sensitivity; Sp: Specificity; PPV: positive predictive value; NPV: negative predictive value

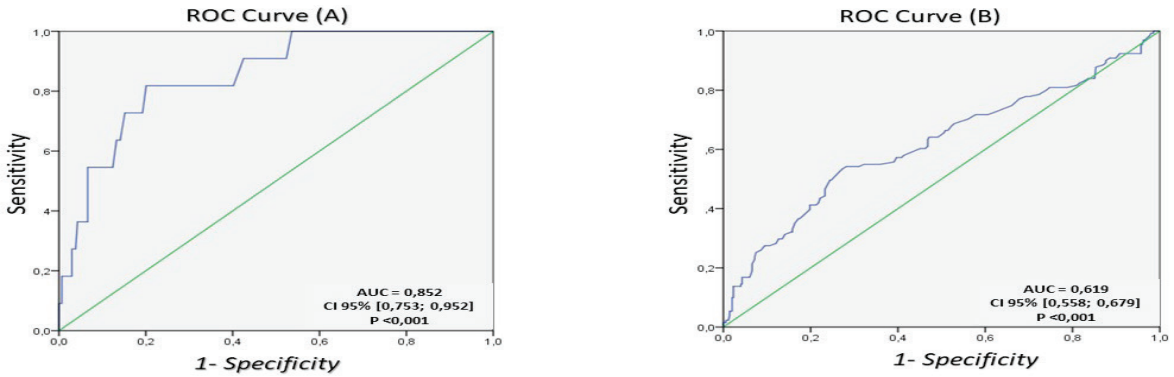

Figure 2 : Base Excess ROC Curves for immediate (A) and early (B) mortality

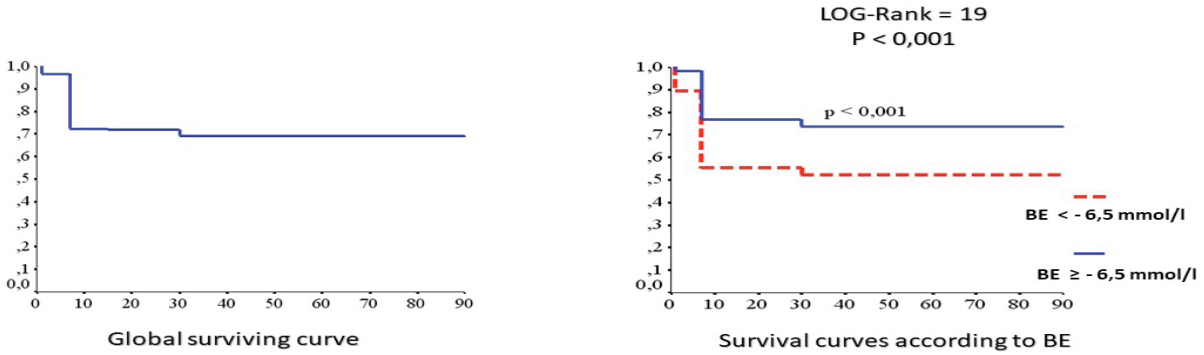

Figure 3 : Overall survival curve and according to BE

Mortality analysis

BE was statistically different between the deceased and survivors both for immediate mortality on day 1 and early mortality on day 7. Significant factors were identified by univariate analysis (table 2) and were associated to higher mortality. On univariate analysis a BE≤ -6.5 mmol/l had an odds ratio of 17 for immediate mortality with CI [95%] = [3.5-79] and p<0.001 and 2.7 at day 7 mortality with CI [95%] = [1.7-4.3] and p<0.001.

Furthermore, a multivariate analysis for both terms of mortality was made by logistic regression to detect the independent predictive factors of mortalityFive parameters were retained from the univariate analysis to make a multivariate regression of mortality at Day 1: Systolic blood pressure < 90 mmHg; BE ≤ -6,5 mmol/l ; Prothrombin time < 70% ; mechanical ventilation ; injury severity score ≥ 16. Whereas, multivariate analysis for the mortality at Day 7 was done based on the 6 factors selected on respective univariate analysis wich were: systolic blood pressure < 90 mmHg; Glasgow coma scale < 13; Injury severity score ≥ 16: mechanical ventilation; vasopressors use : BE ≤ -6,5 mmol/l.Results are summarized on table 3

Table 2: Univariate analysis of mortality

Univariate analysis of mortality at Day 1			
Parameter	**Crude Odds ratio**	**CI [95%]**	***p-value***
SBP < 90 mmHg	8,3	[2,5-28,3]	***<0,001****
SpO2 < 90%	6,2	1,5-25,4	***0,016****
GCS <13	19,3	2,4-152	***<0,001****
PH < 7,35	9	2- 43	***0,001****
Prothrombin time <70%	4,6	1,3-16	***0,001****
BE ≤ -6,5 mmol/l	17	3,5 -79	***< 0,001****
ISS ≥ 16	4,7	0,6 – 37,7	*0,069*
Mechanical ventilation	16	2 - 127	***< 0,001****
Vasopressors use	35	4,4-277	***< 0,001****
Univariate analysis of mortality at Day 7			
SBP < 90 mmHg	2	1,1- 3,5	***0,001****
SpO2 < 90%	3,9	2,2-6,6	***< 0,001****
GCS <13	6,4	4,1- 10	***< 0,001****
BE ≤ -6,5 mmol/l	2,7	1,7 -4,3	***<0,001****
ISS ≥ 16	6,1	3,2 – 11,4	***< 0,001****
Mechanical ventilation	8,8	5,5-14	***< 0,001****
Intracerebral hemorrhage	3,9	2,4-6,4	***< 0,001****
Hepatic injury	3,7	1,7-8	***< 0,001****

SBP: Systolic blood pressure; SPO2 : Pulse oximetry ; GCS : Glasgow Coma scale; p-value < 0,05

Table 3: Multivariate analysis of mortality

Immediate mortality on Day 1			
Items	**Adjusted OR**	**CI [95%]**	**p**
SBP<90 mmHg	2,31	[1,1; 4,6]	0,01
BE≤-6,5 mmol/L	3,17	[1,4; 7,1]	0,005
Early Mortality on Day 7			
Items	**Adjusted OR**	**CI [95%]**	**p**
ISS≥16	1,65	[1,17; 2,34]	0,004
Mechanical ventilation	2,68	[2,08; 3,47]	<0,001
BE ≤-6,5 mmol/L	1,5	[1,14; 1,96]	0,003

SBP: Systolic Blood Pressure; BE: Base Excess; OR: Odds Ratio; CI: Confidence Interval; P: p-value significant if < 0,05

Survival curves:

Survival curves were statistically different between survivors and non-survivors depending on BE as shown in figure 3 with p<0.001

DISCUSSION

In the present study, initial point of care BE at the early assessment in the ED is shown to be an independent predictor of prognosis for both immediate and early mortality among victims of trauma. This predictive value was stronger for the immediate mortality with an AUC = 0,852 and a CI [95%] =[0,753- 0,952] and a couple of sensitivity and a predictive negative value of the test both equal to 82% and 99%. BE failed to predict survival at Day 7 post –trauma as shown by the low sensitivity of 37 % and the AUC of 0,619 with CI [95%] = [0,558-0,679]. These results were similar with the logistic regression studied for mortality with a higher adjusted odds ratio for Day 1 compared to odds ratio at Day 7 mortality. Our findings support the usefulness of inclusion of BE in the early evaluation of severe trauma patients in the ED. Moreover, this finding may be useful in the prehospital settings or in non-trauma care centers in order to improve the triage of severe trauma patients especially regarding to the early mortality when other biomarkers are not available.

The determination of the ROC curve fixed a cut-off value of -6.5 mmol/L. In our study, a BE ≤ -6.5 mmol/L increased the risk of mortality on day 1 and day 7 post-trauma respectively by 3.17 and 1.5 in multivariate analysis.

The present study agrees with existing data showing that BE and lactate have been widely described as tools of prognostic values helping to detect high-risk patients [13,14]. BE was first used in sepsis and further in pediatric trauma [15-16]. A systematic review of BE showed that this biomarker is correlated to occurrence of severe post-traumatic complications: renal failure, coagulopathies, Adult Respiratory Distress Syndrome, and multiple organ failure. In addition, it was also correlated with an increase in the length of stay in intensive care units and a higher mortality rate [18].

A BE ≤ -6.5 mmol/L on admission was selected as an Independent predictor of immediate mortality and post-traumatic day 7. This cut-off value was comparable with previous published data. In a retrospective study of 2954 patients, Davis et al reported that 72% of traumatized patients requiring a transfusion had a BE <-6 mmol/L [19]. Furthermore, BE has also been proposed as a component of trauma severity score systems combining anatomic, physiological and laboratory data. These scores have been found to correlate with mortality [20].As for the cut-off value, in our study, we were interested in arterial BE taken upon presentation. We initially considered a BE of ≤ -3.5 mmol/L to be significant as found in many further studies. Various cut-off values have been cited in the literature and depend on the aetiology of illness. However, a widely used cut-off value of -3 mmol/L has largely been associated with severity illness whereas in more recent reviews the cut-off of -6mmol/L has been associated with mortality especially in severe trauma [18].

Limitations

This study is limited by its single-center recruitment. Furthermore, normotensive and hypotensive subgroup analysis was not carried out. Hence, the prognosis value of BE in the hypotensive subgroup could be different from patients in whom shock is less clinically evident. In this study, the outcome measure focused only on mortality only. Other clinically important outcomes that have been described in the literature such as predicting the need for massive transfusion were not evaluated. This is explained by the study center's limited capacity of in administering massive blood product transfusions.

CONCLUSIONS

This study showed the utility of Base Excess as a powerful prognostic predictor of mortality at Day 1 in the initial stage of the trauma evaluation in an emergency setting.

We recommend the adoption of the BE marker in the early severe trauma evaluation in order to increase sensitivity of detecting at-risk patients for hypovolemic shock and thus activating advanced trauma care pathways.

The use and interpretation of the Base Excess, which is readily available from the moment of initial evaluation of a patient the ED or even a pre-hospital setting, can be a major element in triggering higher level management of severe trauma. This could ultimately improve the prognosis of traumatized patients, especially in the more difficult to detect hemodynamically stable subset of patients who present with clinically occult hypoperfusion.

Conflict of interests : There are no conflicts of interest

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