Paediatrica Indonesiana

VOLUME 47 January • 2007 NUMBER 1

Original Article

Hyperlactacemia in critically ill children: comparison of traditional and Fencl-Stewart methods

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Abstract

Background Base excess is a single variable used to quantify metabolic component of acid base status. Several researches have combined the traditional base excess method with the Stewart method for acid base physiology called as Fencl-Stewart method.
Objective The purpose of the study was to compare two different methods in identifying hyperlactacemia in pediatric patients with critical illness.
Methods The study was performed on 43 patients admitted to the pediatric intensive care unit of Cipto Mangunkusumo Hospital, Jakarta. Sodium, potassium, chloride, albumin, lactate and arterial blood gases were measured. All samples were taken from artery of all patients. Lactate level of >2 mEq/L was defined as abnormal. Standard base excess (SBE) was calculated from the standard bicarbonate derived from Henderson-Hasselbalch equation and reported on the blood gas analyzer. Base excess unmeasured anions (BE_{UA}) was calculated using the Fencl-Stewart method simplified by Story (2003). Correlation between lactate levels in traditional and Fencl-Stewart methods were measured by Pearson's correlation coefficient .
Results Elevated lactate levels were found in 24 (55.8%) patients. Lactate levels was more strongly correlated with BE_{UA} ($r = -0.742$, $P<0.01$) than with SBE ($r = -0.516$, $P<0.01$).
Conclusion Fencl-Stewart method is better than traditional method in identifying patients with elevated lactate levels, so the Fencl-Stewart method is suggested to use in clinical practice. **[Paediatr Indones 2007;47:35-41]**.

Keywords*: Hyperlactacemia, Fencyl-Stewart method, acid base status*

In many forms of critical illness, lactate is the most important cause of metabolic acidosis.[1] Hyperlactacemia may be caused by an increased lactate production (due to hypoxia or inhibition of tissue oxidative metabolism), or a decreased rate of lactate utilisation by liver and kidney. Normal arterial blood lactate levels are usually less than 2 mEq/L.[2,3] Standard base excess (SBE) is defined as the quantity of strong acid or base required to restore pH to 7.40 in blood equilibrated at standard conditions [pCO2 of 40 mmHg, 37°C (originally at 38°C), and hemoglobin of 5 g% which 100% oxygenated].[4,5] The traditional method which is used for measuring base excess (SBE) as the cause of metabolic acid base disturbance is often inadequate to quantify the degree of acid-base disturbance.[6]

A new method to measure acid-base balance has been proposed by Stewart.[7] According to him, there are three important independent variables controlling the acid-base status ($[H^+]$, $pH = -\log [H^+]$). These variables are strong ion difference (SID) (difference

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between fully dissociated anions and cations), total concentration of non volatile weak acid (A_{tot}) (consisting mainly of albumin) and partial pressure of carbon dioxide (pCO_2). Based on Stewart's studies, Gilfix and colleagues[8] used the work of Figge and colleagues[9,10] to derive equation in order to estimate base excess effects of strong ion difference and total weak acid concentration. Balasubramanyan and colleagues[11] called this method as base excess of Fencl-Stewart method. Story and colleagues[12] have simplified this equation. This study aimed to compare two different methods in identifying hyperlactacemia in pediatric patients with critical illness.

Methods

We performed a comparative cross-sectional study at pediatric intensive care unit (PICU) of Cipto Mangunkusumo Hospital Jakarta from February 2005 until March 2005. We asked inform consent to the parents although the intervention in this study was not different from the traditional one. Approval for the study was obtained from local medical ethical committee.

The subjects consisted of medical, surgical and trauma patients requiring critical care. The only criteria for inclusion was agreement from the parents to follow the study by signing informed consent. Damaged blood sample and incomplete laboratory data were excluded from this study.

Routine arterial blood gas, sodium, potassium, chloride, albumin and lactate measurements were made in patients admitted to PICU. All measurements were taken from a single arterial blood vessel by nursing staff and handled according to standardized hospital-approved procedures. Arterial blood samples were collected using a vacuum lithium heparin tubes. Blood gas analysis and lactate measurements were performed using the i-STAT portable clinical analyzer 200 series (i-STAT Corporation, East Windsor, USA) in the bed side which underwent daily calibration and quality control checks. Samples for sodium, potassium, chloride and albumin measurements were sent to the hospital core laboratory in the Department of Clinical Pathology. Serum electrolytes measurement were performed using the Ciba Corning 644 (Ciba Corning Diagnostics, Beverly, MA, USA) and serum albumin measurement was performed using the Miraplus (ABX Diagnostics, Montpellier, France).

Normal acid-base status was defined as a standard base excess (SBE) of between $\geq$2 mmol/L and $\leq$2 mmol/L.[5] A lactate level of >2 mEq/L was defined as being abnormally elevated for this study.[2,3] SBE was calculated from standard bicarbonate derived from the Henderson-Hasselbalch equation and reported on the blood gas analyzer. Base excess unmeasured anions (BE_{UA}) was calculated using the Fencl-Stewart method simplified by Story (2003)[12] with the formula BEua = SBE – {[Na^+]–[Cl^-]–38} – {0.25x(42–[albumin] g/L)}, the value between $\geq$-2 mmol/L and $\leq$2 mmol/L was defined as normal. Strong ion difference (SID) was calculated using the formula SID = [Na^+] + [K^+] – [Cl^-]. Because plasma concentration of calcium and magnesium were low so quantitatively unimportant in determining plasma pH, it was not included in the calculation.[7]

Data were stored on a computer spread-sheet (Excel, Microsoft, Seattle, WA, USA). Correlation between lactate levels of two different methods were measured using Pearson's correlation coefficient. All analysis were performed using SPSS version 11.0.

Results

Fourty three patiens were enrolled in the study. Patient characteristics are presented in **Table 1**. The mean

Table 1. Subjects' characteristics

Patient Characteristics	Number of patients (%)
Age :	
- Birth – <30 days	14 (32%)
- 1 – 11 months	11 (26%)
- 1 – 4 years	9 (21%)
- 5 – 9 years	7 (16%)
- 10 – 14 years	2 (5%)
Sex :	
- Male	23 (53%)
- Female	20 (47%)
Mechanical ventilation	21 (49%)
Organ dysfunction:	
- Nervous system	10 (23%)
- Cardiovascular system	8 (19%)
- Respiratory system	11 (26%)
- Gastrointestinal system	15 (35%)
- Genitourinary system	3 (7%)
- Systemic (sepsis)	13 (30%)
- Surgical	21 (49%)
- Others	4 (9%)

Table 2. Minimum, maximum and mean (SD) values for all variables

Variable	Minimum	Maximum	Mean ± SD
Measured quantities			
PH	6.717	7.630	7.36 (0.167)
pCO_2 (mmHg)	18.1	110.2	45.05 (20.94)
HCO_3 (mmol/L)	8.4	55.1	24.86 (8.86)
SBE (mmol/L)	-28.0	30.0	-0.71 (9.74)
Na (mEq/L)	122.0	144.0	134.35 (5.24)
K (mEq/L)	2.39	7.19	3.90 (0.81)
Cl (mEq/L)	87.0	112.0	102.14 (6.02)
Albumin (g/L)	17.2	49.2	32.04 (7.21)
Lactate (mEq/L)	0.73	18.98	3.43 (3.61)
Derived quantities			
BE_{UA} (mmol/L)	-24.3	21.8	2.59 (7.61)
SID (mEq/L)	28.25	50.31	36.11 (4.91)
Effect Na-Cl (mmol/L) (= $[Na^+]$–$[Cl^-]$–38)	-14	8	-5.79 (4.84)
Effect Alb (mmol/L) (= 0.25x(42–[alb] g/L))	-1.8	6.2	2.49 (1.80)

Tabel 3. Comparison of unmeasured ions level in traditional method (SBE) and the Fencl-Stewart method (BE_{UA})

Methods		Fencl –Stewart (BE_{UA}) Normal (-2 to +2)	Abnormal (<-2 and >+2)	Total
Traditional methods (SBE)	Normal (-2 to +2)	3	4	7
	Abnormal (<-2 and >+2)	14	22	36
	Total	17	26	43

age of the patients was 28 months (range 1 day to 14 years). The range of values and means for the variables included in the study are given in **Table 2.**

The traditional method (SBE) showed different result from that of Fencl-Stewart (BE_{UA}) methods in 17 of 43 (39.5%) patients (**Table 3**). The range of Na-Cl and albumin effect to SBE were -14 to 8 and -1.8 to 6.2 mmol/L (**Table 2**) and equal to zero in 2 (4.7%) and 0 (0%) of samples, respectively. The range of serum albumin concentration was very wide (17.2 to 49.2 g/L). In 26 (60.5%) patients, albumin concentration was <34 g/L and in 2 (4.7%) patients it was <20 g/L (**Table 2**). Plasma lactate concentration measured in all patients increased (>2 mEq/L) in 24 (55.8%) patients. Plasma lactate concentration was more strongly correlated to BE_{UA} (r = - 0.742, P<0.01) than to SBE (r = - 0.516, P<0.01) (**Figure 1**).

Figure 2 shows the influence of 3 independent variables [the strong ion different (SID), the concentration of non volatile weak acid (mainly albumin) and the partial pressure of pCO_2] on acid-base status (pH). There was a moderate and significant correlation between pCO_2 and pH (r =-0.646, P<0.01), a very weak and not significant correlation of pH with SID (r = 0.045, P>0.05) as well as with albumin (r = -0.042, P>0.05). The influence of sodium, potassium and chloride on SID is shown in **Figure 3**. There was weak but significant correlation between SID and chloride

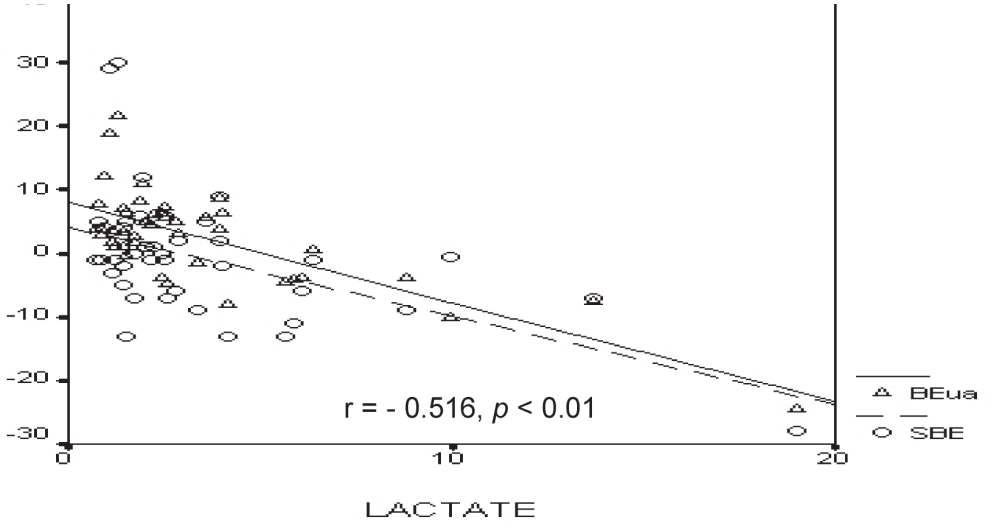


Figure 1. Correlation of plasma lactate concentration between the traditional methods (SBE) and the Fencl-Stewart method (BE_{UA})

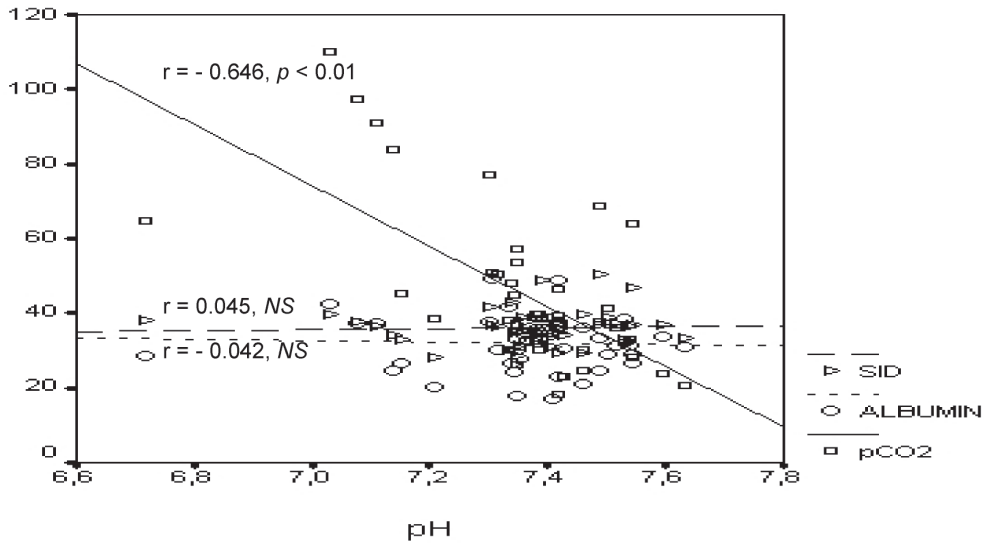


Figure 2. Correlation of acid base status (pH) with the strong ion difference SID (SID = $[Na^+]$ + $[K^+]$ – $[Cl^-]$), the concentration of non volatile weak acid ([albumin]), and pCO_2.

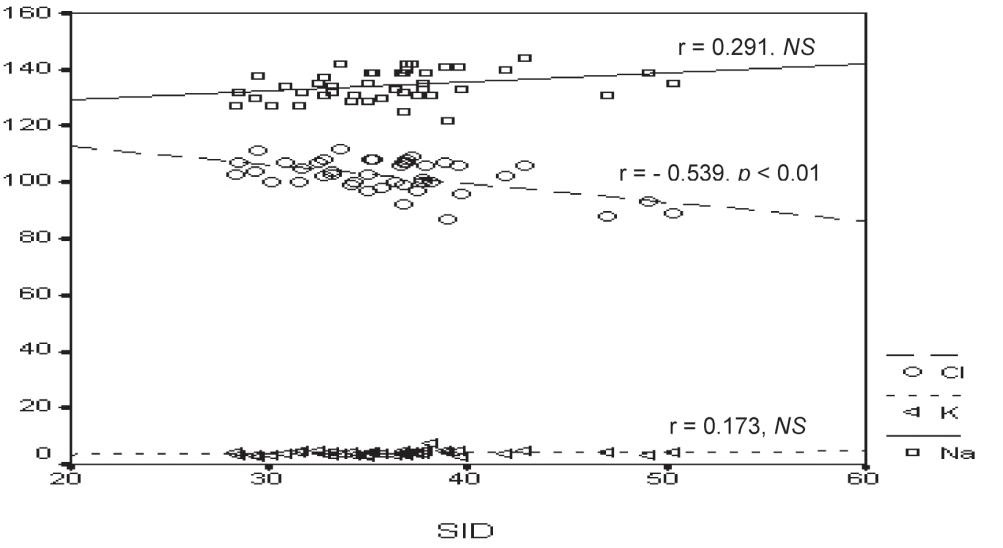


Figure 3. Correlation of SID with sodium, potassium and chloride.

(r = -0.539, P<0.01). There were a very weak and not significant correlation of SID with sodium (r = 0.291, P>0.05) as well as with potassium (r = 0.173, P>0.05).

Because more than 50% patients had lactate concentration >2 mEq/L in this study, we also try to include lactate in the calculation of SID with the formula: SID = $[Na^+]$ + $[K^+]$ - $[Cl^-]$ - $[Lactate^-]$. Hence, it demonstrated that SID was significantly correlated to $[Lactate^-]$, $[Cl^-]$, and $[Na^+]$, but not to $[K^+]$. The correlation between SID and lactate was stronger (**Figure 4**).

Discussion

The subjects in this study demonstrated a variety of pathology from relative stable condition after surgery to serious illness because of septic shock. Twenty-four

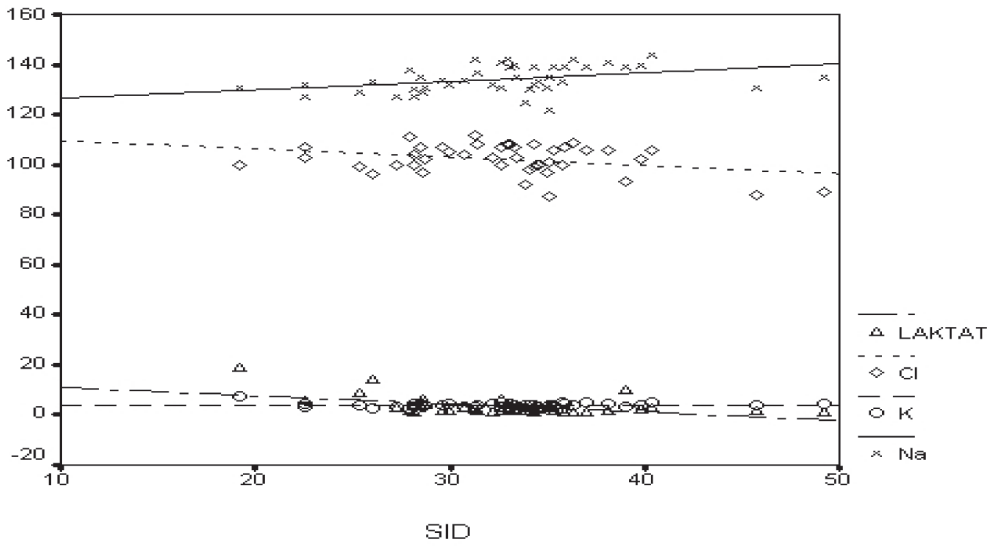


Figure 4. Correlation of SID with sodium, potassium, chloride and lactate (SID = $[Na^+] + [K^+] - [Cl^-] - [Lactate^-]$)

patients had elevated lactate levels between 2.01 and 18.98 mEq/L. SBE is commonly used to assess acid-base disturbances[13]. However, the traditional methods (SBE) frequently fail to identify unmeasured ion that can be found using the BE_{UA} method.[11,14] SBE is influenced by abnormalities of plasma sodium, chloride, and albumin[8,15] as often seen in critically ill patients. The greater the deviations in plasma sodium, chloride, and albumin from normal, the greater the differences between the SBE and BE_{UA} methods. Base excess unmeasured anions (BE_{UA}) represents corrected base excess for changes in sodium, chloride, and albumin. Therefore, theoretically BE_{UA} method is better than SBE method in identifying patients with unmeasured ion. We found that the BE_{UA} method is superior to the SBE method in identifying patients with increased plasma lactate concentrations. Results of this study supported the findings of others[11,16] that BE_{UA} identifies a greater number of patients with an acid-base derangements than SBE.

Abnormalities in fluid status, electrolytes, and albumin caused significant changes in base excess or defisit in these patients. SBE would be equal to BE_{UA} if there were no abnormalities in sodium, chloride, and albumin. However, SBE and BE_{UA} were never the same. SBE caused by effects of NaCl and albumin were equal to zero in 2 (4.7%) and 0 (0%) of samples, respectively, showing these important contribution to SBE.

Sodium chloride is the main component of plasma strong ion difference and albumin is the main component of plasma total weak acid concentration. Using simplified sodium chloride equation we can estimate the base excess effects of electrolyte changes from i.v. fluid therapies. For example, Kellum and colleagues[17,18] studied acid base changes during resuscitation. Patients received 0.9% saline, Hextend, or Lactated Ringer's solution. The saline group had greater metabolic acidosis shown by more negative base excess. One of the causes was a decreased strong ion difference. In addition to the acidifying effects of saline, Hatherill *et al*[19] and Durward *et* al[20] found that hypoalbuminaemia is associated with low observed anion gap that may fail to detect significant amounts of lactate and other occult tissue anions. Decreased plasma albumin leads to decreased total weak acid concentration that produces metabolic alkalosis. Our work supportted this finding because the physiology is the same i.e. changes in plasma sodium, chloride, and albumin will alter the SBE.

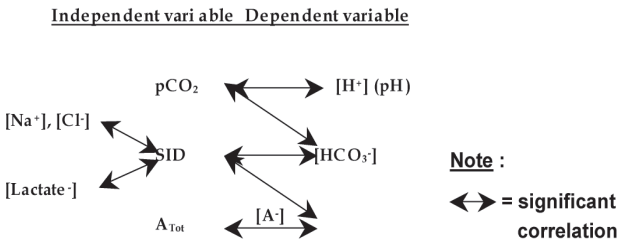
Unmeasured anion shown by increased base deficit may be organic (e.g lactate, keto acids, albumin), inorganic (e.g. sulfate, phosphate), exogenous (e.g. salicylate, formate, nitrate, penicillin, carbenicillin), and others (e.g. paraldehyde, acetate, ethylene glycol, methanol, salicylates, urea, glucose). Proteolysis associated with sepsis may release organic

and inorganic acids, some of which are poorly defined. High concentrations of some of these acids are not present during healthy condition, and thus, the presence of unmeasured anion may serve as a marker for organ dysfunction.[11]

As discussed by Stewart,[7] acute acid-base disturbances is caused by a change in pCO_2 or SID. The compensatory response will make adjustment to minimize the change in pH. Although $[A_{tot}]$ (mainly albumin) does not change acutely, it has a direct influence on the final concentration of $[H^+]$ for a given pCO_2 and SID. SID influences the concentration of weak electrolytes, as a net positive charge, it must be balanced by the sum of all weak anions to maintain electrical neutrality. The magnitude of the dissociation is constant for bicarbonate and weak for acids compared with other dissociation in which SID is closely approximated by the sum of $[HCO_3^-]$ and $[A^-]$.[4,6,7]

SID is the charge difference between the sum of strong cations and strong anions ($[Na^+]+[K^+]+[Ca^{2+}]+[Mg^{2+}]$-$[Cl^-]$-[unmeasured strong anions]). In critical illness, the most important of unmeasured anion is lactate. We didn't include calcium, magnesium and lactate in the calculation of SID because in normal condition those concentration in plasma is low so that quantitatively unimportant in determining plasma pH. Our data supported the findings of Wilkes[21] that pH ($[H^+]$) was significantly correlated to pCO_2, but lack of correlation to SID and albumin ($[A_{tot}]$). SID was inverse significantly correlated to $[Cl^-]$, but not to $[Na^+]$ and $[K^+]$. Wilkes[21] also demonstrated that $[HCO_3^-]$ and [A] were significantly correlated to SID. pCO_2 was significantly correlated to $[HCO_3^-]$, but not to [A]. $[A_{tot}]$ was not correlated to $[HCO_3^-]$, but [A] was directly related to $[A_{tot}]$. $[Cl^-]$ was inverse significantly correlated to $[A_{tot}]$, but had a stronger correlation to SID.

This study demonstrated that SID was significantly correlated to $[Lactate^-]$, $[Cl^-]$, and $[Na^+]$, but not to $[K^+]$. The relation between lactate and pH ($[H^+]$) can be described as follows:



In summary, the Fencl-Stewart method is better than traditional method in identifying patients with unmeasured ion. Elevated lactate levels identified by the Fencl-Stewart method were not reliably identified by traditional method (SBE). We suggest to use Fencl-Stewart method in clinical practice.

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