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Editorial Adress:
d/a Laboratorium Patologi Klinik RSUD Dr. Soetomo, Gedung Diagnostik Center Lt. IV
Jl. Mayjend. Prof. Dr Moestopo 6–8 Surabaya, Indonesia
Telp/Fax. (031) 5042113, 085-733220600 E-mail: majalah.ijcp@yahoo.com, jurnal.ijcp@gmail.com
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RESEARCH

AGREEMENT OF SIMPLIFIED FENCL-STEWART WITH FIGGE-STEWART METHOD IN DIAGNOSING METABOLIC ACIDOSIS IN CRITICALLY ILL PATIENTS

(Kesesuaian Metode Fencl-Stewart yang Disederhanakan dengan Figge-Stewart dalam Mendiagnosis Asidosis Metabolik di Pasien Critically Ill)

Reni Lenggogeni[1], Rismawati Yaswir[1], Efrida[1], Desywar[2]

ABSTRAK

Asidosis metabolik adalah kasus yang paling sering ditemukan pada pasien critically ill. Pendekatan Henderson-Hasselbalch gagal menjelaskan gangguan metabolik yang rumit karena hanya tertuju pada kenasaban pH dengan tekanan parsial karbondioksida dan ion bikarbonat. Pendekatan keseimbangan asam-basa metode Stewart lebih akurat dan dapat menggambarkan gangguan metabolik yang rumit. Modifikasi metode Stewart yang digunakan saat ini adalah metode Figge-Stewart dan Fencl-Stewart yang disederhanakan, dapat digunakan di tempat dengan sumber daya terbatas. Tujuan penelitian ini adalah mengetahui kesesuaian metode Fencl-Stewart yang disederhanakan dengan Figge-Stewart dalam mendiagnosis asidosis metabolik di pasien critically ill. Penelitian analitik potong lintang terhadap 40 pasien critically ill yang dirawat di ICU, CVCU dan HCU RSUP Dr. M. Djamil Padang masa waktu Oktober–November 2015. Analisis gas darah diukur dengan potensiometri, elektrolit dengan ion selective electrode dan kadar albumin dengan immunoturbidimetri. Hasil dianalisis dengan program komputer. Kesesuaian metode Fencl-Stewart yang disederhanakan dengan Figge-Stewart dianalisis dengan uji Kappa, bermakna jika nilai p<0,05. Sebanyak 40 orang pasien (18 laki-laki, 22 perempuan) diikutkan dalam penelitian ini. Rerata umur pasien adalah 48,35(18,4) tahun dan diagnosis terbanyak adalah gagal jantung (30%). Hiponatremia, hipernatremia, hipokalemia, hiperkalemia, hipokloremia dan hipoalbuminemia ditemukan masing-masing sebanyak 37,5%, 12,5%, 2,5%, 12,5%, 17,5%, 20% dan 87,5% pasien. Terdapat kesesuaian yang baik antara metode Fencl-Stewart yang disederhanakan dengan Figge-Stewart dengan nilai kappa=0,529 dan bermakna secara statistik (p<0,001). Kesesuaian metode Fencl-Stewart yang disederhanakan dengan Figge-Stewart dalam mendiagnosis asidosis metabolik di pasien critically ill adalah baik.

Kata kunci: *Asidosis metabolik, Fencl-Stewart yang disederhanakan, Figge-Stewart, pasien critically ill*

ABSTRACT

Metabolic acidosis is the most often case found in critically ill patients. The Henderson-Hasselbalch method fails to explain the complicated metabolic disorder because it is only focused on the correlation of pH with the partial pressure of carbon dioxide and bicarbonate ion. The Stewart method is more accurate and can describe complex metabolic disorder. Modifications of the Stewart method are the Figge-Stewart and simplified Fencl-Stewart methods, which can be used in a place with limited resources. The aim of the study was to determine the agreement of simplified Fencl-Stewart with Figge-Stewart method in diagnosing metabolic acidosis in critically ill patients. This was a cross-sectional analytical study on 40 critically ill patients admitted to the ICU, CVCU and HCU of the Dr. M. Djamil Hospital Padang in October-November 2015. Blood gas analysis was measured with potentiometric, electrolytes with ion selective electrode and albumin with immunoturbidimetry. The results were analyzed with a computer program. Agreement between simplified Fencl-Stewart with Figge-Stewart method was analyzed by kappa test, significant if p value was <0.05. Fourty patients (18 males, 22 females) was participated in this study. The mean age of the patients was 48.35 (18.4) years and the most diagnosis was heart failure (30%). Hyponatremia, hypernatremia, hypokalemia, hyperkalemia, hipocloremia and hypoalbuminemia were found in 37.5%, 12.5%, 52.5%, 12.5%, 17.5%, 20% and 87.5% patients, respectively. There was a good agreement between

[1] Department of Clinical Pathology, Faculty of Medicine, Andalas University-M. Djamil Hospital, Padang, Indonesia.
E-mail: oggnel@gmail.com
[2] Central Laboratory Unit of M. Djamil Hospital, Padang, Indonesia

simplified Fencl-Stewart with Figge-Stewart method with a kappa value=0,529 and statistically significant (p<0.001). Agreement of simplified Fencl-Stewart with Figge-Stewart method in diagnosing metabolic acidosis in critically ill patients was good.

Key words: Metabolic acidosis, simplified Fencl-Stewart, Stewart-Figge, critically ill patients

INTRODUCTION

Metabolic acidosis is the most common case in critically ill patients. Metabolic acidosis is also considered as a predictor of severity as well as a prognosis of a disease. Henderson-Hasselbalch's approach is commonly used to assess acid-base disorders. However, the Henderson-Hasselbalch's approach is less accurate to detect acid-base disorders in complex metabolic disorders, such as critically ill patients with hypoalbuminemia since it focuses more on pH correlation, partial carbon dioxide (pCO_2) pressure and bicarbonate ion concentration (HCO_3–).[1,2]

On the other hand, Stewart's physicochemical method is more accurate to detect acid-base balance in complex metabolic disorders. Unfortunately, Stewart's method requires more laboratory parameter examinations, thus causing obstructions in its laboratory applications with limited resources.[3-5] Experts then have modified Stewart's calculations to simplify the examinations. There are two modifications of the Stewart method used today, namely Figge-Stewart method and Fencl-Stewart method. The Fencl-Stewart approach uses Strong Ion Difference (SID) based on strong cation and anion concentrations (sodium, potassium, magnesium, calcium, chloride and lactate) and total acid concentration/ATOT (albumin and phosphate) as important components to estimate base deficit excess (BDE) in acid-base balance disorders. This measurement is accurate (not practical), expensive and not fast.[6,7] Consequently, Story *et al.*[7] made a simpler calculation using four equations (BDENaCl, BDEAlbumin, BDEcalc and BDEgap), called as simplified Fencl-Stewart method to assess the metabolic acid-base disorder. The simplified Fencl-Stewart approach is more practical, easy and quick to observing the metabolic acidosis disorder that occurs.[7,8]

In contrary, Figge-Stewart method performs a calculation by assessing the effects of SID apparent/SIDa and SID effective/SIDe differences to measure the strong ion gap/SIG in plasma. Strong ion gap provides a more precise picture of the mechanism underlying metabolic acidosis progression because it takes into account all electrolytes and corrects the albumin concentration.[1,8] Therefore, this research aimed to assess the suitability of the simplified Fencl-Stewart method with the Figge-Stewart method in diagnosing metabolic acidosis in critically ill patients.

METHODS

This research was an analytical research with a cross-sectional design performed on patients of the Internal Medicine unit in the ICU, ICCU and HCU of the M. Djamil Hospital in Padang from October to November 2015. The research materials used were heparin rinse and serum of the patients' blood. Laboratory tests performed were blood gas analysis (including sodium, potassium and calcium ions), chloride test and serum albumin test.

Moreover, inclusion criteria determined were patient aged more than 14 years, a blood pH of less or equal to 7. 35, electrolyte imbalance and willingness to participate in this research. Next, this research was approved by the Research Ethic Committee of the Medical Faculty Andalas University. Data were then analyzed by Cohen's coefficient of agreement Kappa test using a computer program.

RESULTS AND DISCUSSION

During the research period, seventy-six samples were collected from the research subjects. Nevertheless, there were only forty samples that met the inclusion criteria. The basic characteristics of the research subjects can be seen in Table 1.

Table 1. Characteristics of research subjects

	N (%)	Mean (SD)
Age (year)		48.35±18.4
Sex		
Males	18 (45)	
Females	22 (55)	
Mechanical ventilation	25 (62.5)	
Intensive care diagnosis:	12 (30)	
Heart failure	11 (27.5)	
Post surgery	7 (17.5)	
Renal failure	6 (15)	
Systemic - Sepsis	5 (10.5)	
- Metabolic		

The research subjects consisted of 18 males and 22 females. The mean age of the research subjects was 48 years (48.35±18.4) with the youngest age of 15 years

and the oldest age of 83 years. These results did not differ greatly from results of a research performed by Story *et al.*[6] on the use of the simplified Fencl-Stewart method in ICU patients in Australia illustrating that the age range of those patients was 12–94 years.[6]

In contrary, a research conducted by Rocktaeschel *et al.*[8] on the status of acid-base balance in critically ill patients with acute renal failure based on the Figge-Stewart method obtained an older age range of 61.2±18.8 years.[8] Similarly, a research performed by Lee[5] on the clinical meaning of a strong ion gap in ICU patients with hemodialysis and metabolic acidosis in Korea also found an older age range of 62.4±17.2 years.[5] Difference in these results is probably due to the differences in the diagnosis of most patients treated in intensive care units. The older age range is mostly found in patients with chronic obstructive pulmonary disease and drug overdose, while the younger age range is mostly found in patients with sepsis and post surgery.[5,6,8]

Furthermore, the results of this research were similar to the results of a research conducted by Tuhay *et al.*[9] on patients treated in the ICU in Argentina revealing that based on the quantitative analysis of lactate and base-excess enhancement using conventional and Stewart methods, the number of females was higher, about 51%, than males (49%).[9] Like the previous research, a research performed by Gezer *et al.* on ICU patients with metabolic disorders in Turkey using the Stewart method also found more females (52.7%) than males (47.3%).[10]

In contrast to those previous researches, results of a research conducted by Moviat *et al.*[11] on ICU patients with metabolic acidosis in the Netherlands using conventional and psychochemical approaches revealed that the number of males was smaller, about 52% than females (48%).[11] The research performed by Rocktaeschel *et al.* on the acid-base status of critically ill patients with acute renal failure in Australia using the Figge-Stewart method also showed that the number of males was higher (58%) than females (42%).[8] Thus, demographically, there is no significant difference in number between males and females treated in the ICU with metabolic acidosis disorder.

In addition, the results of this research also indicated that most of the patients treated in the ICU used mechanical ventilators (62.5%). Similarly, the research performed by Moviat *et al.*[11] also found that 92% of ICU patients used mechanical ventilators, while a research conducted by Jung *et al.*[12] in France showed that 88% of intensive care patients used mechanical ventilators.[11,12] Unlike the previous researches, the research conducted by Tuhay *et al.*[9] revealed that there were only 40% of intensive care patients using mechanical ventilators. These differences were due to the magnitude of respiratory disturbance and the diagnosis of those patients in the ICU.[9,13,14]

The most common cause of intensive care is heart failure (30%) followed with post surgery (27.5%) and renal failure (17.5%). These results are slightly different from the research conducted by Moviat *et al.*[11] on criticaly ill patients with metabolic acidosis showing that the highest diagnosis was sepsis (37%) followed by cardiogenic (22%) and postoperative shocks (15%).[11] Similarly, the research conducted by Jung *et al.*[12] revealed that most patients treated in the ICU suffered from sepsis (35%), other diseases (14%) and respiratory failure (12%).[12] Decrease in cardiac output will also cause decreased circulation to the visceral regions, such as hepatic, kidney, muscle and intestine as compensation of the body for sufficient circulation to the brain and heart. As a result, visceral organs will experience hypoxia. Hypoxia will increase the production of acid anions (organic acids), such as lactic acid (most), sulphate and phosphate as anaerobic metabolism results. These organic acids are excreted in the kidneys. The hypoxic kidneys then will retain fluid and electrolytes to maintain the circulating volume. Renal hypoxia will also decrease HCO_{3-} formation and organic acid excretion.[15]

Moreover, results of blood gas analysis showed a mean pH of 7.26 with a range of 6.85–7.35. The partial pressure of CO_2 gas was 30.55 mmHg with a range of 7–44 mmHg. There were two patients with very low pCO_2 (<10 mmHg). The lowest respiratory compensation limit in the metabolic acidosis is generally 10 mmHg. A decrease in pCO_2 (<10 mmHg) may be due to hyperventilation in patients using ventilators and/or sepsis patients. Hyperventilation then can lead to excessive CO_2 elimination which will decrease pCO_2, about <10 mmHg.[15,16] BE levels of all research subjects were negative, with the lowest level of -26 mEq/L.

Furthermore, measurements of electrolyte variables in all research subjects indicated that they suffered from electrolyte imbalance with the lowest Na^+ level of 117 mEq/L and the highest of 160 mEq/L. Hyponatremia was found in 37.5% of patients, while hypernatremia in 12.5% of patients. Similar results were also found in a research conducted by Fencl *et al.*[17] on critivcaly ill patients with BE or HCO_3 within normal limits illustrating that hyponatremia was found in 55% of the patients, while hypernatremia in 10% of them.[17] Hyponatremia may be due to an increase in the body's total water, higher than an increase in sodium. Hyponatremia can be found in cardiac abnormalities,

renal failure and hepatic disease. Hypernatremia, on the other hand, may be due to an increase in sodium, more excessive than an increase in the body's total water during the administration of NaCl and $NaHCO_3$ caused by a hypertonic state and or water deficiency beyond sodium deficiency in hyperventilation, burns, osmotic diabetic melitus diuresis, diarrhea, or vomiting.[18,19]

In addition, the results of this reserach revealed that the lowest K^+ level was 1.9 mEq/L, while the highest one was 6.8 mEq/L. The results also indicated that 52.5% of the research subjects suffered from hypokalemia, while 12.5% of them suffering from hyperkalemia. Hypokalemia may be due to Kalium displacement from extracellular to intracellular during the administration of diuretics (as heart failure treatment), lack of intake, nausea and vomiting in treated patients. Meanwhile, hyperkalemia may be due to Kalium displacement from intracellular to extracellular in acidosis state, hypoxia state, digitalis overdose, renal excretion and decreased gastrointestinal tract.[20]

Moreover, the results of this research illustrated that the lowest chloride level was 82 mEq/L, while the highest one was 130 mEq/L. It is also known that 17.5% of the research subjects suffered from hypochloremia, while 20% of them suffered from hyperchloremia. On the other hand, the lowest HCO_3 level was 3 mmol/L. The HCO_3 level in 82.5% of the research subjects was below normal. Similarly, results of a research conducted by Malat *et al.*[15], showed that 70% of metabolic acidosis patients with sepsis shock had hyperchloremia. Like the previous research, the research performed by Fencl *et al.*[17] revealed that 10% of critically ill patients with normal BE or HCO_3 levels suffered from hyperchloremia, while 40% of them suffered from hypochloremia. Hyperchloremia may be due to increased reabsorption of chloride in the renal tubules as the body's compensation in maintaining plasma electronecity caused by a decreased bicarbonate level. Chloride and bicarbonate are the main anions of extracellular fluid.[15,17,21]

The average of albumin level in this research, furthermore, was known to be 2.8 g/dL with the lowest level of 1.4 g/dL and the highest level of 4.4 g/dL. It is also known that hypoalbuminemia was found in 87.5% of the reserach subjects. Similarly, results of a research performed by Hatherill *et al.*[22] showed that 76% of criticaly ill patients suffered from hypoalbuminemia shock.[22] Story *et al.*[1] even found that all criticaly ill patients studied suffered from hypoalbuminemia. Hypoalbuminemia is a frequent disorder in criticaly ill patients that may influence the interpretation of metabolic acidosis abnormalities with traditional approach into normal one.[1,17] Hypoalbuminemia can be caused by the impairment of albumin synthesis in the hepatic of patients with heart failure and hepatic disease. Hypoalbuminemia may also be due to albumin loss in renal disease as well as a lack of protein intake in bed rest patients.[23] Results of blood gas analysis, chloride test, and serum albumin test can be seen in Table 2.

Results of the calculation using the Figge-Stewart method showed that 25% of the research subjects had a SIG value of ≥5 mEq/L, while 75% of them had a SIG value of <5 mEq/L. Results of the calculation using the Fencl-Stewart method, on the other hand, found that 35% of the research subjects had a BDEgap

Table 2. Results of blood gas analysis, chloride test and albumin serum test

Examinations	Range (n=40)		Mean (SD)
	Minimal	Maximal	
Measurred variables			
pH	6.85	7.35	7.26 (0.11)
pCO_2 (mmHg)	7	45	30.55 (11.52)
BE (mEq/L)	-26	-1	-11.43 (6.84)
Na^+ (mEq/L)	117	160	138.05 (8.17)
K^+ (mEq/L)	1.9	6.8	3.61 (1.19)
Cl^- (mEq/L)	82	130	104.75 (9.68)
Albumin (g/L)	14	44	28 (7.3)
Calculated variables			
HCO_3 (mmol/L)	3	24.8	14.55 (6.56)
BDE_{Na-Cl} (mEq/L)	-21	19	-4.7 (8.51)
BDE_{Alb} (mEq/L)	-0.5	7	3.32 (1.83)
BDEgap/ua (mEq/L)	-34.90	14.9	-3.42 (10.36)
SIDa (mEq/L)	20.64	59.34	37.43 (7.90)
SIDe (mEq/L)	18.10	54.84	38.00 (9.27)
SIG (mEq/L)	-17.22	32.46	-0.57 (10.95)

Table 3. Suitability of the simplified Fencl-Stewart method with the Figge-Stewart method

Method		Figge-Stewart (SIG)		Total	kappa	p
		≥5 mEq/L	<5 mEq/L			
Simplified Fencl-Stewart (BDEgap)	≤-5 mEq/L	8	6	14	0.529	0.001
	>-5 mEq/L	2	24	26		
Total		10	30	40		

of ≤-5 mEq/L, while 65% of them had a BDEgap of >-5 mEq/L. Suitability of the simplified Fencl-Stewart method with the Figge-Stewart method can be seen in Table 3.

Results of the suitability test on the simplified Fencl-Stewart method towards Figge-Stewart method showed a kappa value of 0.529 (p<0.001) with good interpretation and a statistically significant meaning. The results of this research indicated a good suitability betweeen the simplified Fencl-Stewart method to Figge-Stewart method with a sensitivity of 80% and a specificity of 80%. In contrary, a research performed by Sinaga *et al.*[24] showed an excellent suitability between the simplified Fencl-Stewart method and the Figge-Stewart method in diagnosing critical metabolic acidosis with a positive result agreement of 95.65% and a negative result agreement of 98.51%.[24] Meanwhile, a research conducted by Kurnia *et al.*[25] comparing traditional method with the simplified Fencl-Stewart method in assessing the unmeasured anion as a cause of metabolic acidosis found a sensitivity of 94.3% and a specificity of 84%. On the other hand, in comparing traditional method with the Figge-Stewart method in assessing the unmeasured anion, the reserach showed a sensitivity of 100% and a specificity of 76%.[25]

Story *et al.*[1], stated that the simplified use of the Fencl-Stewart method is easier and faster in assessing the abnormalities of metabolic acidosis in criticaly ill patients.[1] In contrary, Rocktaesch el *et al.*[8] showed that an analysis based on the Figge-Stewart method in critically ill patients with acute renal failure is more preferably in diagnosing metabolic acidosis.[8] Plasma proteins (albumin) actually have a major impact on acid-base balance disorders. Albumin provides anionic effects in plasma which means hyperalbuminemia can cause metabolic acidosis due to an increase in total weak acid concentration. Hypoalbuminemia, on the other hand, will cause metabolic alkalosis.

Most of criticaly patients who have hypoalbuminemia then will neutralize the blood pH not detected by the traditional approach. Plasma albumin levels, as a result, should be considered in assessing acid-base disorders, especially in criticaly ill patients. The Figge-Stewart method approach, thus, can correct albumin levels to give more accurate results.[16] Meanwhile, SID changes in criticaly ill patients can be considered as a result of electrolyte and albumin changes, as well as an incresae in unmeasured anions (lactate, phosphate, sulphate and ketone).[17,20] Anion enhancement, however, is not measured primarily by lactate level triggered by severe tissue hypoxia due to shock, heart failure, severe anemia, hepatic failure and pulmonary insufficiency.[23] Gunnerson *et al.*[26] also explained that metabolic acidosis due to increased lactate is mainly found in heart problems, hepatic diseases, infections and drugs, such as salicylates, paraaminophenols, barbiturates and sulfonamides.[26]

Some researchers actually have criticized Stewart's method because of the many variables that must be considered as well as the complexity of its calculation. Nevertheless. Stewart's method is still widely applied in hospitals in Europe, especially in the ER, ICU, Trauma Center and anesthesia department since it can identify most of the complex acid-base disorders encountered in patients with severe injury and criticaly ill patients.[11,27] The simplified Fencl-Stewart method, on the other hand, can simplify the complex calculation. Therefore, it can be used in places with limited facilities.

Unfortunately, this research still has some limitations. Firstly, this research did not measure lactate level as the most cause of unmeasured anion enhancement. Secondly, this research also did not measure phosphate and magnesium levels as the main factors causing SID changes. Finally, this research did not measure urea and creatinine levels as markers of kidney damage affecting electrolyte regulation.

CONCLUSION AND SUGGESTION

There was a good suitability of simplified Fencl-Stewart method with Figge-Stewart method in diagnosing metabolic acidosis in critically ill patients. The simplified Fencl-Stewart method could be used in

diagnosing metabolic acidosis in critically ill patients with limited laboratory facilities. However, further researches had better to focus more on the use of Stewart's method in hospitals to assess metabolic acidosis. Further researches are also suggested to measure lactate, magnesium, and phosphate levels to assess the magnitude of increased anion unmeasured as well as to measure urea and creatinine levels as indicators of renal impairment.

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