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원 저

응급실내 급성 중독 환자들의 예후 예측에 대한 혈액 젖산 수치의 유용성

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Prognostic Value of Blood Lactate for Mortality of Acutely Poisoned Patients in Emergency Department

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Purpose: Patients suffering from acute poisoning by different substances often visit the emergency department (ED) and receive various prognoses according to the toxic material and patients' condition. Hyperlactatemia, which is an increased blood lactate level that generally indicates tissue hypoperfusion, is commonly utilized as a prognostic marker in critically ill patients such as those with sepsis. This study was conducted to investigate the relationships between blood lactate and clinical prognosis in acute poisoned patients.

Methods: This retrospective study was conducted from January 2013 to June 2014 at a single and regional-tertiary ED. We enrolled study patients who were examined for blood test with lactate among acute intoxicated patients. The toxic materials, patient demographics, laboratory data, and mortalities were also reviewed. Additionally, we analyzed variables including blood lactate to verify the correlation with patient mortality.

Results: A total of 531 patients were enrolled, including 24 (4.5%) non-survivors. Patient age, Glasgow coma scale (GCS), serum creatinine (Cr), aspartate transaminase (AST), and serum lactate differed significantly between survivors and non-survivors in the binary logistic regression analysis. Among these variables, GCS, AST, and lactate differed significantly. The median serum lactate levels were 2.0 mmol/L among survivors and 6.9 mmol/L among non-survivors. The AUC with the ROC curve and odds ratio of the initial serum lactate were 0.881 and 3.06 (0.89-8.64), respectively.

Conclusion: Serum lactate was correlated with fatalities of acute poisoning patients in the ED; therefore, it may be used as a clinical predictor to anticipate their prognoses.

Key Words: Acute poisoning, Lactate, Mortality

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Introduction

On the widespread use of insecticides/pesticides and increasing prescriptions of medications including many psycho-tropics for chronic diseases, acute poisoned patients have visited an emergency department (ED) continuously. Though there are not overall statistical data of the prevalence with acute intoxi-

cation in Korea, previous studies reported 0.5%-1.9% of local incidence rate visited in ED annually[1]. In 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System, over two million-human exposure by poison occurred and 1,408 poison-related mortalities were reported[2]. In Korea, there were 1,281 poison-related fatalities from the data of 2014 National Statistical Office reports[3].

Meanwhile, increased level of blood lactate indicates tissue hypo-perfusion and the serum lactate was studied largely on various clinical situations including sepsis, cardiogenic shock, trauma, and certain surgeries[4-8]. And its diagnostic or prognostic utility was somewhat verified. In addition, toxicity of some substances such as carbon monoxide, metformin, paraquat, and cyanide was related with serum lactate level[9-12], but its prognostic value was not matched consistently. And there was few report with overall toxic material exposure related to serum lactate and its prognostic ability is not confirmed properly.

Hence, we intended to evaluate the prognostic capacity of serum lactate level for acute poisoned patients in ED and anticipated that there would be good correlation between mortalities of poisoned patients and serum lactate concentration. Furthermore, as the prognostic utility of lactate clearance for sepsis[13], we hypothesized that an elevation of the followed serum lactate level would be poor clinical indicator for acute poisoned patients.

Methods

This is a retrospective study and it was approved by the hospital' s institutional review boards.

1. Inclusion and Exclusion of study patients

We enrolled the patients who visited the ED from January 2013 to June 2014 and our ED is a regional-tertiary emergency medical center that annual average volume is about 42,000 visited-patients. We included acutely poisoned patients by any substances which confirmed by history taken from patients/witnesses and/or laboratory confirmation test. The routes of intoxication were both ingestion and inhalation. And all study patients were examined for one more blood test with lactate. We excluded the patients who did not have available medical data or transferred to other medical facilities. And the patients who had reported to route of skin exposure were excluded, too.

2. Demographic characteristics and Serum lactates measurement

We reviewed enrolled patients' demographics, classifications and estimated dosage of ingested/inhaled toxic material, basic laboratory test, and mortality. Serum lactate levels were measured using a medical device (GEM Premier 3000® blood gas analyzer, IL Headquarters Bedford, Massachusetts, U.S.A) and the initial serum lactate was draw in at least 30 minutes later after ED arrival. It was collected from arterial blood mostly or from venous blood partly in pediatric poisoned patients. Its reference range is 0.3-15.0 mmol/L as the manual. We defined the followed serum lactate as the second serum lactate level if there was additional serum lactate value after the initial one. One occasion that there were three more serum lactate values, we chose the followed lactate as the one which was closed to three-hour value from the initial blood lactate discretionally. As the serum lactates in this study were measurements of point of care testing (POCT) for blood gas analysis, blood pH and bicarbonate level which considered as confounding variables were recorded simultaneously with each serum lactate.

We chose the in-hospital mortality as primary result of study and the mortality was single factor for a prognostic indicator in this study. Therefore, we divided the study patients to two groups as the survivors and non-survivors. And we did subgroup analyses for patients who were tested with the followed serum lactate.

For additional analysis, we defined two indices of the lactate clearance as the follows: Hourly lactate clearance (hLC) and Contrastive lactate clearance (cLC).

Hourly lactate clearance is defined as the value that difference between the followed lactate level and the initial one was divided by the time interval between examined moments of the two serum lactates:

$$hLC = \frac{\text{followed lactate-initial lactate (mmol/L)}}{\text{time gap from initial lactate to followed lactate (hour)}}$$

Contrastive lactate clearance is defined as the value that difference the followed lactate level and the initial one was divided by initial lactate level:

$$cLC = \frac{\text{initial lactate-followed lactate (mmol/L)}}{\text{initial lactate (mmol/L)}}$$

Using these values, we tried to verify the relationship between the change of serum lactate level and the in-hospital mortality.

3. Statistical analyses

Pearson's Chi-square test or Fisher's exact test were used to compare two groups divided by survival. Student t-test or Mann Whitney U-test was used according to the result of test for normality to compare age and each laboratory values. The Receiver-Operating Characteristic (ROC) curves were drawn and Area under the curves (AUCs) were collected if there were the significant different variables after comparing data. To evaluate the contributable factors for the mortality, binary logistic regressions were used. All continuous and ordinal variables are presented as the mean value (standard deviation) or the median value (interquartile range) according to the normality analysis. The p-value <0.05 was considered to be statistically significant. All statistical analyses except for analysis of ROC curves were performed using the SPSS 21.0 program (SPSS, Chicago, IL, USA). To calculate the sensitivity and specificity for ROC curves, we used the MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium).

Results

1. Demographics of patients and Comparison of laboratory measurements

During the study period, a total of 531 patients were included and the numbers of fatalities were 24 patients (4.5%) among them. 258 patients (50.9%) in survivor group and 15 patients (62.5%) in non-survivor group were male. The median ages of two groups were 50 years in survivors, and 70 years in non-survivors. And this discrepancy of age was statistically significant ($p<0.001$). Another demographic feature of patients was summarized in Table 1.

Patients' vital signs of two groups were differently as the following: systolic blood pressure (SBP, $p<0.001$), heart rate (HR, $p=0.005$), peripheral oxy-

Table 1. Demographic characteristics of patients

Variables	Survivor group (N=507)	Non-survivor group (N=24)
Age, year, median (IQR*)	50 (35-62)	70 (62-77)
Males	258 (50.9%)	15 (62.5%)
Comorbidities		
Hypertension	98 (19.3%)	10 (41.7%)
Diabetes mellitus	43 (8.5%)	7 (29.2%)
Hepatitis	8 (1.6%)	0
Pulmonary tuberculosis	5 (1%)	0
Heart failure	7 (1.4%)	0
Obstructive lung disease	3 (0.6%)	0
Renal failure	2 (0.4%)	0
Malignancy	6 (1.2%)	0
Liver cirrhosis	3 (0.6%)	0

* IQR: interquartile range

Table 2. Vital signs and laboratory test values of patients

Test values	Survivor group	Non-survivor group	*p* value
	Mean (±SD*) or Median (IQR†)		
Vital signs			
SBP‡ (mmHg)	130 (110-140)	105 (50-140)	<0.001
HR§ (/min)	87 (78-101)	80 (60-90)	0.005
RR‖ (/min)	18±3	19±4	0.547
SpO_2¶ (%)	99 (97-99)	96 (89-98)	0.031
BT** (˚C)	36.3 (36.0-36.6)	36.0 (36.0-36.1)	0.121
GCS††	15 (12-15)	10 (3-12)	<0.001
Laboratory studies			
WBC‡‡ (/μL)	8600 (6600-11300)	13850 (9175-22775)	<0.001
Hemoglobin (g/dL)	13.9±1.9	13.6±2.7	0.587
Platelet ($\times 10^3$/μL)	246±65	220±89	0.162
BUN§§ (mg/dL)	12.3 (9.0-16.0)	17.1 (12.4-26.3)	<0.001
Creatinine (mg/dL)	0.8 (0.6-0.9)	1.3 (1.1-2.0)	<0.001
Sodium(mmol/L)	138±4	139±6	0.405
Potassium(mg/dL)	3.7 (3.4-4.0)	3.4 (2.7-5.4)	0.341
AST‖‖ (IU/L)	28 (22-37)	59 (37-102)	<0.001
ALT¶¶ (IU/L)	19 (15-28)	24 (17-52)	0.018
Albumin (g/dL)	4.0 (3.7-4.3)	3.7 (3.1-4.3)	0.022
INR***	0.97±0.15	1.01±0.12	0.197
Glucose (mg/dL)	121 (104-146)	213 (152-289)	<0.001
CRP††† (mg/L)	7.22±13.69	7.43±9.67	0.946
CK‡‡‡ (IU/L)	98 (67-170)	119 (71-161)	0.6
CK-MB§§§ (ng/mL)	1.70 (1.00-3.15)	2.70 (1.70-5.70)	0.006
cTnI‖‖‖ (ng/mL)	0.00 (0.00-0.01)	0.01 (0.00-0.03)	0.342
Initial pH	7.40 (7.37-7.44)	7.20 (7.01-7.35)	<0.001
Initial pCO_2 (mmHg)	36 (32-41)	35 (27-41)	0.499
Initial pO_2 (mmHg)	88 (76-105)	78 (43-103)	0.1
Initial HCO_3 (mmol/L)	22.8 (19.8-24.9)	12.5 (9.3-18.9)	<0.001
Initial lactate (mmol/L)	2.0 (1.1-3.3)	6.9 (4.4-10.7)	<0.001
hLC¶¶¶ (mmol/L · hr)	-0.06 (-0.33-0.48)	0.76 (0.31~2.26)	<0.001
cLC****	0.12 (-0.11-0.46)	-0.35 (-0.73~-0.17)	<0.001

* SD: standard deviation
† IQR: interquartile range
‡ SBP: systolic blood pressure
§ HR: heart rate
‖ RR: respiratory rate
¶ SpO_2: peripheral oxygen saturation
** BT: body temperature
†† GCS: glasgow coma scale
‡‡ WBC: white blood cell
§§ BUN: blood urea nitrogen
‖‖ AST: aspartate transaminase
¶¶ ALT: alanine transminase
*** INR: international normalized ratio
††† CRP: C-reactive protein
‡‡‡ CK: creatine kinase
§§§ CK-MB: creatine kinase-myocardial band
‖‖‖ cTnI: cardiac troponin I
¶¶¶ hLC: Hourly lactate clearance {(followed serum lactate - initial serum lactate) / time gap from initial lactate to followed lactate}
**** cLC: Contrastive lactate clearance {(initial serum lactate - followed serum lactate) / initial serum lactate}

gen saturation (SpO2, p=0.031), and Glasgow coma scale (GCS, p<0.001). Other measurements were presented similarly between two groups.

Among the laboratory tests, there were statistically different values as the following: white blood cell counts (WBC), blood urea nitrogen (BUN), creatinine (Cr), aspartate transaminase (AST), alanine transaminase (ALT), glucose, creatine kinase-myocardial band (CK-MB), initial serum lactate, pH, bicarbonate (HCO3), Hourly lactate clearance (hLC) and Contrastive lactate clearance (cLC). Each absolute values and p values of laboratory data between two groups were summarized in Table 2.

2. Exposed substances

Patients with a single exposure of poisoned material were 446 (88%) in survivor group and 22 (91.7%) in non-survivor group. Most common toxic substances identified in ED were carbon monoxide (15.5%) in survivors and paraquat (41.6%) in non-survivors. Other toxic materials exposed to patients were summarized in Table 3.

3. Receiver-Operating Characteristic curves and logistic regression analyses

Among statistically significant measurements between two groups above mentioned, we draw ROC curves to select the variables for carrying out the logistic regression analyses. The AUCs of ROC curves were showed in Table 4 and there were the following as descending order: Cr (0.891), lactate (0.881), pH (0.869), HCO3 (0.858), age (0.823), glucose (0.815), AST (0.808), GCS (0.779), SpO2 (0.75), WBC (0.742), BUN (0.712), CK-MB (0.684), SBP (0.668), HR (0.663), ALT (0.642), and albumin (0.637). Thereafter, for analyzing with logistic regression, we input the following variable that AUC was higher than 0.7 due to generally considering fair ability of discrimination above 0.7 of AUC: age, SpO2, GCS, WBC, BUN, Cr, AST, glucose, lactate, pH and HCO3. Moreover, we selected bicarbonate value as the input variable for preventing the collinearity because there was interrelationship between pH and HCO3 on blood gas analysis. On binary logistic regression analyses, age, Cr, lactate, AST, and GCS were significant variables. And on the last model of logistic regression, significant predictors for the mortality were GCS, AST, and initial serum lactate especially. The characteristics of this regression model were 0.091 of Hosmer-Lemeshow statistics, 0.581 of Nagelkerke R square, and 74.4 of Akaike information criterion. The odds ratios (OR) with 95% confidence intervals (CI) of initial serum lactate was summarized in Table 5.

Table 3. Exposed toxic materials of patients

Substances	Survivor group (N=507)	Non-survivor group (N=24)
Single exposure	446 (88%)	22 (91.7%)
Paraquat	12 (2.7%)	10 (41.6%)
Glyphosate	41 (9.2%)	7 (29.1%)
Carbon monoxide	69 (15.5%)	1 (4.2%)
Glufosinate	4 (0.9%)	1 (4.2%)
Hydrochloric acid	2 (0.4%)	1 (4.2%)
Organophosphate	8 (1.8%)	1 (4.2%)
Sulfosate	-	1 (4.2%)
Benzodiazepine	13 (2.9%)	-
Doxylamine	12 (2.7%)	-
Acetaminophen	10 (2.2%)	-
Unknown	82 (18.4%)	-
*Etc.	193 (31.3%)	-
Multiple exposure	61 (12%)	2 (8.3%)

* Each single toxic material of formed etc. was below 2%.

Table 4. AUCs of ROC curves with statistically significant variables for the in-hospital mortalities

Variables	AUC	Variables	AUC
Creatinine	0.891	SpO_2[‡]	0.75
Initial lactate	0.881	WBC[§]	0.742
Initial pH	0.869	BUN[‖]	0.712
Initial HCO_3	0.858	CK-MB[¶]	0.684
Age	0.823	SBP**	0.668
Glucose	0.815	HR[††]	0.663
AST*	0.808	ALT[‡‡]	0.642
GCS[†]	0.779	Albumin	0.637

* AST: aspartate transaminase
† GCS: glasgow coma scale
‡ SpO_2: peripheral oxygen saturation
§ WBC: white blood cell
‖ BUN: blood urea nitrogen
¶ CK-MB: creatine kinase-myocardial band
** SBP: systolic blood pressure
†† HR: heart rate
‡‡ ALT: alanine transminase

Table 5. Logistic regression of serum lactates for in-hospital mortalities of acute poisoned patients

Variables	Adjusted OR*	95% CI[†]	*p* value
Initial serum lactate	3.06	0.89-8.64	<0.001
Hourly lactate clearance[‡]	3.74	1.83-7.64	<0.001
Contrastive lactate clearance[§]	0.14	0.05-0.39	<0.001

* OR: odds ratio
† CI: confidence interval
‡ Hourly lactate clearance = (followed serum lactate - initial serum lactate) / time gap from initial lactate to followed lactate
§ Contrastive lactate clearance = (initial serum lactate - followed serum lactate) / initial serum lactate

4. Subgroup analysis for patients who was examined the followed serum lactate

A total of 268 patients were tested with followed serum lactate and we performed a subgroup analysis to these patients groups. While the initial serum lactates were 2.0 mmol/L (1.1-3.0) in survivors and 6.9 mmol/L (4.4-1.7) in non-survivors, hourly lactate clearance (hLC) were -0.06 mmol/L · hr (-0.33-0.48) in survivors and 0.75 mmol/L · hr (0.31-2.26) in non-survivors. On contrastive lactate clearance (cLC), the value of survivor and non-survivor groups were 0.12 (-0.11-0.46) and -0.35 (-0.73--0.17) respectively. Both the initial and two lactate clearances were statistically different between two groups (p<0.001). As a result of statistical analysis of the identical process as mentioned above, 0.903 of AUC with hLC and 0.904 of AUC with cLC were higher than 0.881 of AUC with the initial serum lactate. It was showed in Fig. 1. And the cut-off points of initial serum lactate level and two lactate clearances which maximized both sensitivity and specificity were above 3.5 mmol/L of initial lactate (sensitivity 87.5%, specificity 78.1%), above 0.18 mmol/L · hr of hLC (sensitivity 82.4%, specificity 84.1%), and below -0.16 of cLC (sensitivity 83.3%, specificity 78.2%).

Also, as shown in Table 5, two lactate clearances were also good predictors for in-hospital mortalities like as the initial serum lactate and ORs with 95% CIs of two values were 3.74 (1.83-7.64) of hLC and 0.14 (0.05-0.39) of cLC.

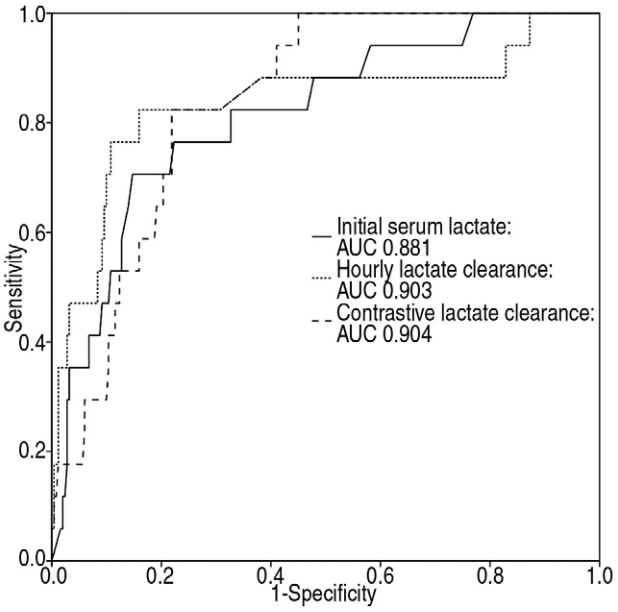

Fig. 1. ROC curves and AUCs of initial and two lactate clearances for mortalities between two groups.
The AUC with the followed serum lactate is larger than the AUC with the initial serum lactate.
AUC: Area under curve, ROC: Receiver-Operating Characteristic

Discussion

In this study, the serum lactate level had good correlation with the mortality of acute poisoned patients in ED. Additionally the followed serum lactate level had more predictive value for fatality than the initial serum lactate level on subgroup analysis.

Serum lactate is a final product from pyruvate during anaerobic metabolism in the cells. Normally, with sufficient oxygen supply, pyruvate transforms to oxaloacetate and acetyl-CoA to enter TCA cycles for generating energy (i.e. adenosine triphosphate). So, traditionally, increased serum lactate level implies lactate accumulation of tissue and suggests that there was tissue hypo-perfusion with metabolic distress such as oxygen-debt. But, hyperlactatemia may be due to multifactorial causes than single cause of tissue hypo-perfusion in sepsis[14]. And those situations with hyperlactatemia by multiple factors could occur at various clinical diseases.

Generally, serum lactate is known as useful clinical marker for sepsis patients[14] and its prognostic ability applies for septic patients in ED, too[4]. That is, elevated serum lactate level anticipates the mortality of septic patients. And serum lactate was utilized as guide to select therapeutic bundle of modalities for sepsis such as early goal-directed therapy. Recently, serum lactate includes the diagnostic definition of new sepsis[15]. And, in previously clinical study, serum lactate level was increased at other disease entities such as trauma[6], some major surgery[7,8], medical diseases like pulmonary embolism[16] or gastrointestinal bleeding[17], and critically ill patients[18,19]. Those studies reported that several organ failure and/or fatality related to increased level of serum lactate.

Furthermore, increased serum lactate level was reported that it used as clinical predictor for certain confirmed toxic substances such as metformin, paraquat, carbon monoxide, acetaminophen, and cyanide. In other words, hyperlactatemia was associated with the severity of those toxic materials and resulted from some different mechanism according to each substance. For example, increased lactate level by metformin intoxication was resulted from metabolic derangement with impaired gluconeogenesis to convert to pyruvate[10,20]. In paraquat intoxication, hyperlactatemia might be resulted from mechanism of mitochondrial dysfunction involving cyclic reduction -oxidation and depletion of reduced nicotinamide adenine dinucleotide phosphate (NADPH) with producing reactive oxygen species[21,24]. In carbon monoxide inhalation, hyperlactatemia might be resulted from tissue hypoxia directly by decreased oxygen saturation[22]. Increased serum lactate by acetaminophen intoxication was resulted from lowering hepatic lactate clearance and impaired extrahepatic tissue oxygen utilization[23]. In cyanide poisoning, hyperlactatemia was resulted from mitochondrial dysfunction, catecholamine release, and decreased systolic blood pressure[12].

Our study showed that increased serum lactate was correlated with the fatality of acute poisoned patients in ED. Among the non-survivors, paraquat poisoning as toxic substance was most common and glyphosate poisoning was the second toxic material. Among survivors, but, the most common toxic substance was

unknown material. On confirmed materials, carbon monoxide intoxication was the second one and glyphosate poisoning was the third one. With generally known, the paraquat poisoning is very life-threatening and their high mortality has been reported in spite of small dosage ingestion. This study included twenty two paraquat poisoned patients and nearly half of them were fatal. It also was reported that increased serum lactate level was correlated with paraquat toxicity in previous study[11]. The second lethal substance was glyphosate. Glyphosate toxicity was composed of combined surfactant as well as original glyphosate (N-phosphonomethyl glycine) and its toxicity is various from mild to fatal[25,26]. Eunet al.[27] study reported that non-survivors with glyphosate ingestion had low systolic blood pressure. This hypotension could induce to tissue hypo-perfusion to increasing serum lactate and finding of this study for glyphosate poisoning with hyperlactatemia could be supported. In case of CO poisoning, the fatality (1.4%) was fairly small in this study while the mortality by CO intoxication was 7.3% in other study[28]. We assumed that it might be resulted from transferring other facilities when CO poisoned patients had high carboxy hemoglobin level or clinically critical status because our hospital do not have hyperbaric oxygen therapy device.

On subgroup analyses, AUC of two lactate clearances were slightly bigger than AUC of the initial serum lactate and it may suppose that the prognostic abilities of lactate clearances were also good. Perhaps, it may be natural that the followed serum lactate will be higher than the initial value due to increasing frequency of hypotension ad metabolic disability if patients' disease is getting worse. If the followed lactate was increased, hLC would be increase and cLC would be decrease according to definitions in this study. Add to this, because there was not the specific therapy protocol dealt with acute poisoned patients in our study, the physicians might order to check the serial lactate to clinically severe intoxicated cases. That is, in company with progressing tissue hypo-perfusion and impairing metabolic derangement, this selection bias by physicians may contribute to good prognostic results of two lactate clearances.

This study had some limitations. First, our study was retrospective and we could not control some specific therapeutic modalities for each toxic material. Second, while the initial serum lactate nearly was drawn in thirty minutes after ED arrival, the examined time of the followed serum lactate were not consistent though we tried to correct time gap using concepts of two lactate clearances. Third, two groups of this study were heterogeneous with basic demographic feature such as age and causative toxic material though we tried to correct by logistic regression model. Fourth, as above mentioned, there was pretty possibility that the patients who tested the followed serum lactate might have worse severity than the patients who tested only initial serum lactate. Fifth, because the upper limit of measurement for blood lactate analysis in our facility was up to 15 mmol/L, it might not be analyzed quantitatively for the patients who had above 15 mmol/L serum lactate level. Sixth, though the frequency of major toxic materials with two groups was different, we did not analyze using case-control matching. Seventh, serum lactate values were from both arterial and venous. So, the results from their statistical analyses using both lactate values might be discrepant. But, the serum lactate could be used interchangeably if it is collecting within thirty-minutes[29]. Lastly, the numbers of non-survivors defined as our primary outcome were so small that the statistical result might not be powerful.

The serum lactate level was correlated with the fatality of acute poisoned patients in ED. Therefore, it might help to anticipate prognosis of acute poisoned patients and it is necessary for prospective study to confirm this finding.

REFERENCES

1. Kang JH LH, Jin YH, Lee JB. A Clinical Analysis of Acute Drug Intoxication in Emergency Department Setting. J Korean Soc Emerg Med 1999;10:431-40.
2. Mowry JB, Spyker DA, Brooks DE, McMillan N, Schauben JL. 2014 Annual Report of the American Association of Poison Control Centers' National Poison

Data System (NPDS): 32nd Annual Report. Clin Toxicol (Phila) 2015;53:962-1147.
3. kosis.kr. Statistics Korea. The cause of death (236 items)/Sex/Age (5 years) The number of deaths (1983~), Mortality (2000~). 2014. Available from: http://kosis.kr/. [cited 6 April 2016].
4. Shapiro NI, Howell MD, Talmor D, Nathanson LA, Lisbon A, Wolfe RE, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med 2005;45:524-8.
5. Lazzeri C, Valente S, Chiostri M, Gensini GF. Clinical significance of lactate in acute cardiac patients. World J Cardiol 2015;7:483-9.
6. Caputo ND, Kanter M, Fraser R, Simon R. Comparing biomarkers of traumatic shock: the utility of anion gap, base excess, and serum lactate in the ED. Am J Emerg Med 2015;33:1134-9.
7. Badreldin AM, Doerr F, Elsobky S, Brehm BR, Abuldahab M, Lehmann T, et al. Mortality prediction after cardiac surgery: blood lactate is indispensible. Thorac Cardiovasc Surg 2013;61:708-17.
8. Singhal R, Coghill JE, Guy A, Bradbury AW, Adam DJ, Scriven JM. Serum lactate and base deficit as predictors of mortality after ruptured abdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 2005;30:263-6.
9. Dogan NO, Savrun A, Levent S, Gunaydin GP, Celik GK, Akkucuk H, et al. Can initial lactate levels predict the severity of unintentional carbon monoxide poisoning? Hum Exp Toxicol 2015;34:324-9.
10. Dell'Aglio DM, Perino LJ, Kazzi Z, Abramson J, Schwartz MD, Morgan BW. Acute metformin overdose: examining serum pH, lactate level, and metformin concentrations in survivors versus nonsurvivors: a systematic review of the literature. Ann Emerg Med 2009;54:818-23.
11. Lee Y, Lee JH, Seong AJ, Hong CK, Lee HJ, Shin DH, et al. Arterial lactate as a predictor of mortality in emergency department patients with paraquat intoxication. Clin Toxicol (Phila) 2012;50:52-6.
12. Baud FJ, Borron SW, Megarbane B, Trout H, Lapostolle F, Vicaut E, et al. Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning. Crit Care Med 2002;30:2044-50.
13. Bolvardi E, Malmir J, Reihani H, Hashemian AM, Bahramian M, Khademhosseini P, et al. THE ROLE OF LACTATE CLEARANCE AS A PREDICTOR OF ORGAN DYSFUNCTION AND MORTALITY IN PATIENTS WITH SEVERE SEPSIS. Mater Sociomed 2016;28:57-60.
14. Chertoff J, Chisum M, Garcia B, Lascano J. Lactate kinetics in sepsis and septic shock: a review of the literature and rationale for further research. J Intensive Care 2015;3:39.
15. Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:775-87.
16. Vanni S, Socci F, Pepe G, Nazerian P, Viviani G, Baioni M, et al. High plasma lactate levels are associated with increased risk of in-hospital mortality in patients with pulmonary embolism. Acad Emerg Med 2011;18:830-5.
17. Shah A, Chisolm-Straker M, Alexander A, Rattu M, Dikdan S, Manini AF. Prognostic use of lactate to predict inpatient mortality in acute gastrointestinal hemorrhage. Am J Emerg Med 2014;32:752-5.
18. Fuller BM, Dellinger RP. Lactate as a hemodynamic marker in the critically ill. Curr Opin Crit Care 2012;18:267-72.
19. Smith I, Kumar P, Molloy S, Rhodes A, Newman PJ, Grounds RM, et al. Base excess and lactate as prognostic indicators for patients admitted to intensive care. Intensive Care Med 2001;27(1):74-83.
20. Piel S, Ehinger JK, Elmer E, Hansson MJ. Metformin induces lactate production in peripheral blood mononuclear cells and platelets through specific mitochondrial complex I inhibition. Acta Physiol (Oxf) 2015;213:171-80.
21. Liu XW, Ma T, Qu B, Ji Y, Liu Z. Prognostic value of initial arterial lactate level and lactate metabolic clearance rate in patients with acute paraquat poisoning. Am J Emerg Med 2013;31:1230-5.
22. Damlapinar R, Arikan FI, Sahin S, Dallar Y. Lactate Level Is More Significant Than Carboxihemoglobin Level in Determining Prognosis of Carbon Monoxide Intoxication of Childhood. Pediatr Emerg Care 2015. [Epub a head of print]
23. Bernal W, Donaldson N, Wyncoll D, Wendon J. Blood lactate as an early predictor of outcome in paracetamol-induced acute liver failure: a cohort study. Lancet 2002;359:558-63.
24. Dinis-Oliveira RJ, Duarte JA, Sanchez-Navarro A, Remiao F, Bastos ML, Carvalho F. Paraquat poisonings: mechanisms of lung toxicity, clinical features, and treatment. Crit Rev Toxicol 2008;38:13-71.
25. Gil HW, Park JS, Park SH, Hong SY. Effect of intravenous lipid emulsion in patients with acute glyphosate intoxication. Clin Toxicol (Phila) 2013;51:767-71.
26. Seok SJ, Park JS, Hong JR, Gil HW, Yang JO, Lee EY, et al. Surfactant volume is an essential element in human

toxicity in acute glyphosate herbicide intoxication. Clin Toxicol (Phila) 2011;49:892-9.
27. Eun HM PJ, Suh JH, Jung JH, Eo EK, Roh HK. The Clinical Feature and Prognostic Factor of Glyphosate Intoxication Patients. J Korean Soc Clin Toxicol. 2013;11: 89-95.
28. Ku CH, Hung HM, Leong WC, Chen HH, Lin JL, Huang WH, et al. Outcome of patients with carbon monoxide poisoning at a far-east poison center. PLoS One 2015;10: e0118995.
29. Reminiac F, Saint-Etienne C, Runge I, Aye DY, Benzekri-Lefevre D, Mathonnet A, et al. Are central venous lactate and arterial lactate interchangeable? A human retrospective study. Anesth Analg 2012;115:605-10.