Ann Med Res 2021;28(5):996-1002

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.05.504

Original Article

Association between the initial blood lactate level and prognosis in patients with stroke treated with intravenous thrombolysis

Fettah Eren[1], Aysegul Demir[1], Gullu Eren[2]

[1]Department of Neurology, University of Health Sciences, Konya Education and Research Hospital, Konya, Turkey
[2]Department of Public Health, Meram Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey

Abstract

Aim: Decreased oxygen in cerebral tissues induces anaerobic glycolysis and lactate production increases. It has been demonstrated that blood lactate level is an independent risk factor for poor outcome in patients with acute ischemic stroke (AIS). In this study, the association between initial blood lactate level and short-term prognosis in patients with AIS treated with intravenous thrombolysis was evaluated.

Materials and Methods: Three hundred and sixty one patients treated with intravenous thrombolytic treatment (IVT) were included in the study. Initial symptoms, comorbid diseases and localization of ischemia were recorded. Blood samples were obtained after stroke symptoms within 4.5 hours. Lactate levels were tested before IVT. Disability was calculated with National Institutes of Health Stroke Scale (NIHSS). At 24th and 72th hours, cerebral hemorrhagic transformation was evaluated with brain computed tomography. In-hospital mortality rate was determined. Patients were divided into 2 groups according to difference of NIHSS score (clinical improvement=NIHSS score decreased 4 points or more and no clinical improvement=other patients). Patients were divided into 2 groups according to lactate levels (low=lactate ≤2 mmol/L and high=lactate> 2 mmol/L).

Results: A total of 361 patients, 188 (52.1%) female and 173 (47.9%) male were included in the study. Lactate level and base excess (BE) were higher in patients with severe disability (p <0.001). Serum pH and bicarbonate (HCO3) levels were lower in this group (p <0.001, p=0.006). Lactate cut off value was calculated as 1.72 (59% sensitivity, 58% specificity). Serum lactate level was higher in patients with cerebral hemorrhagic transformation (p=0.028). Lactate cut off value was calculated as 1.79 (56.0% sensitivity, 61.0% specificity).

Conclusion: Lactate is a valuable parameter in ischemia. Blood lactate level is associated with disability and cerebral hemorrhagic transformation in patients with AIS treated with IVT.

Keywords: Intravenous thrombolysis; ischemic stroke; lactate; prognosis

INTRODUCTION

Acute ischemic stroke (AIS) is one of the most common causes of mortality and disability. It also contains many economic and social problems (1). Intravenous thrombolytic treatment (IVT) and endovascular treatments (intraarterial thrombolysis, mechanical thrombectomy, etc.) are options for treatment of AIS (3). Providing recanalization with these treatments may cause some complications (cerebral hemorrhagic transformation, brain edema, reocclusion, etc.). Clinical disability and mortality increase with these complications (4,5). Although many prognostic scoring models are defined to determine the prognosis in these patients, it is also very important to define laboratory markers (6,7).

Glucose, the main energy of brain, is oxidized to carbon dioxide and water after being metabolized. Cerebral oxygen decreases with disruption of cerebral perfusion as a result of ischemia. Thus, lactate occurs with anaerobic glycolysis (8). In magnetic resonance imaging (MRI) spectroscopy studies, it has been detected that lactate levels increase in ischemic brain tissues in patients with AIS and animal models (8-11). Hyperlactatemia is associated with metabolic stress and increased mortality in patients treated in critical intensive care (12-14). Increased cerebrospinal fluid (CSF) lactate level is associated with severity of stroke and its long-term prognosis (15). Blood lactate level is independent risk factor for poor outcome in patients with AIS (16).

Received: 18.05.2020 **Accepted:** 06.07.2020 **Available online:** 24.05.2021
Corresponding Author: Fettah Eren, Department of Neurology, University of Health Sciences, Konya Education and Research Hospital, Konya, Turkey **E-mail:** dreren42@hotmail.com

In this study, venous blood gas samples were obtained before treatment with IVT in patients with ischemic stroke. The relationship between blood lactate level and short-term prognosis was evaluated. In literature review, there was no study evaluating the relationship between lactate level and prognosis in patients with ischemic stroke treated with IVT.

MATERIALS and METHODS

Ethical Approval and Patient Population

The study was approved by University of Health Sciences Turkey, Konya Training and Research Hospital, Ethics Committee (08/05/2020; 38-14). AIS patients treated with IVT in the neurology clinic were included in the study. The purpose and possible complications of IVT were explained to all patients and/or their relatives. No patients were treated without informed consent, and their data were not included in the study. Some diseases that could change the results were excluded (Figure 1). Sociodemographic characteristics (age, gender, etc.), chronic diseases (hypertension, diabetes mellitus, hyperlipidemia, etc.) were questioned. Initial symptoms were grouped as consciousness, sensory, motor, cerebellar and other symptoms.

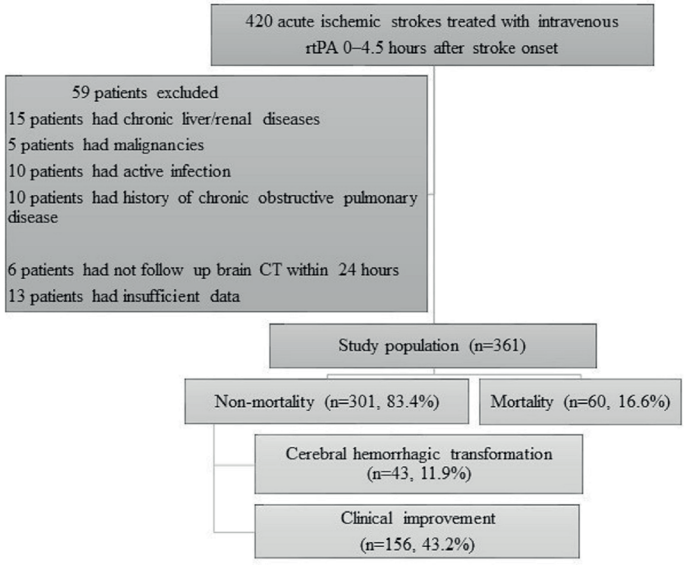

Figure 1. Study flow diagram. rtPA, recombinant tissue plasminogen acti¬vator; CT, computed tomography

This study was designed as a retrospective cohort study. Data were collected in patients with AIS treated with IVT (between January 2014 and March 2020). Data of 420 patients with stroke were included in the study. However, 59 patients were excluded because of missing data and some diseases. The results of 361 AIS patients were analyzed (Figure 1).

Definition and Treatment Period

Pre-treatment, treatment and post-treatment period was managed according to American Heart Association/ American Stroke Association recommendations (3,17). Brain computed tomography (CT) and CT angiography were used to diagnose ischemic stroke and to confirm stroke localization. Vascular localizations were divided into two groups as anterior and posterior. Alteplase was given intravenously (0.9 mg/kg, maximum 90 mg) for treatment. Treatment protocol: 10% of total dose was given in 1 minute and the remaining dose in 1 hour (intravenously). If neurological examination deteriorated, emergency brain CT scan was obtained. Brain CT was routinely scanned 24th hours after treatment. Patients were divided into 2 groups according to neuroimaging (positive cerebral hemorrhagic transformation and negative cerebral hemorrhagic transformation). Disability was evaluated with National Institutes of Health Stroke Scale (NIHSS) (before treatment and before discharge) (18). If NIHSS score decreased 4 points or more, it was accepted as clinical improvement. Mortality rate was calculated.

Blood Tests

Blood samples were obtained from the antebrachial vein before IVT. Blood gas test was analyzed with ABL 800 FLEX blood gas analyzer (Radiometer). Patients were divided into 2 groups according to lactate levels (lactate ≤2 mmol/L and lactate> 2 mmol/L) (19, 20). Partial carbon dioxide pressure (pCO2), partial oxygen pressure (pO2), pH, actual bicarbonate ((HCO3 (act)), standard bicarbonate ((HCO3 (std)), blood base excess ((BE (b)) and extracellular fluid base excess ((BE (ecf)) were evaluated.

Statistical Analysis

Data were analyzed with SPSS® version 17.0 statistical package software program (SPSS Inc., Chicago, IL, United States). Mean±standard deviation (SD) and median (min-max) were used to summarize the numerical data. Categorical data were summarized with number (n) and percentage (%). Also, categorical data were compared with Chi-Square or Fisher's exact test. Normality analysis was evaluated with Kolmogorov-Smirnov test or Shapiro-Wilk test. Numerical data between two groups were analyzed with Student T test (normally distribution) and Mann Whitney U test (not normally distribution). The cut-off point of lactate was calculated according to receiver operating characteristic (ROC) curve analysis. Area under the curve (AUC) was calculated. Confidence interval (CI) was specified. The results were evaluated at 95% CI and p-value below 0.05 was considered statistically significant.

RESULTS

General Results

The study consisted of 188 (52.1%) female and 173 (47.9%) male patients. The mean age was 71.67±12.060 (35-97). The most common symptom was hemi/ monoparesis. (n=303, 83.9%). Anterior vascular ischemia was more common (n=286, 79.2%). Hypertension was the most common comorbid chronic disease (n=243, 67.3%). Demographic characteristics and laboratory parameters of patients were summarized (Table 1).

Table 1. Gender and disease characteristics of all patients (n=361)

	Number (n)	Percentage (%)
Gender		
Female	188	52.1
Male	173	47.9
Symptom-treatment time		
0-1 hour	4	1.1
1-2 hour	63	17.5
2-3 hour	131	36.3
3-4.5 hour	163	45.2
Initial symptom		
Consciousness	139	38.5
Hemi/mono-paresis	303	83.9
Sensory symptoms	103	44.3
Cerebellar disorder	23	6.4
Others	228	63.2
Ischemia localization		
Anterior	286	79.2
Posterior	113	31.3
Chronic diseases		
Diabetes mellitus	108	29.9
Hypertension	243	67.3
Hyperlipidemia	54	15
Others	52	14.4

Table 2. Disability, mortality, hemorrhagic transformation and clinical improvement status of patients according to lactate level. The data are expressed as numbers (percentage)

	Lactate level ≤2 mmol/L (n=232, 69.3%)	Lactate level >2 mmol/L (n=103, 30.7%)	p
Gender			
Female	124 (53.4%)	50 (48.5%)	0.410
Male	108 (46.6%)	53 (51.5%)	
Disability			
Mild disability	170 (73.3%)	58 (56.3%)	0.003*
Severe disability	62 (26.7%)	45 (43.7%)	
Clinical improvement			
Improvement (-)	131 (56.5%)	59 (57.3%)	0.532
Improvement (+)	101 (43.5%)	44 (42.7%)	
Mortality			
Mortality (-)	194 (83.3%)	83 (80.6%)	0.905
Mortality (+)	38 (16.4%)	20 (19.4%)	
Cerebral hemorrhagic transformation			
Hemorrhage (-)	204 (87.9%)	88 (85.4%)	0.037*
Hemorrhage (+)	23 (12.1%)	20 (14.6%)	

* Statistically Significant

Patients with high initial NIHSS score had higher disability in discharge (p <0.001). Mortality and cerebral hemorrhagic transformation were higher in these patients (p <0.001, p=0.007). Clinical improvement was higher in patients treated with IVT before 3 hours (p=0.036). There was no difference between cerebral hemorrhagic transformation and mortality in treatment time groups (p> 0.05). Clinical improvement decreased with development of cerebral hemorrhagic transformation (p <0.001). Lactate (mmol/L) level of all patients was 1.79±0.74 (0.50-5.53). Also, lactate level was low in 232 (69.3%) patients (≤2 mmol/L) and high in 103 (30.7%) patients (> 2 mmol/L). Disability, mortality, cerebral hemorrhagic transformation and clinical improvement frequency of patients according to lactate level were summarized (Table 2).

The Association Lactate Levels with Initial Disability

Patients were compared in 2 groups according to NIHSS (mild disability: NIHSS 15>, severe disability: NIHSS ≥15). NIHSS was made before IVT. There was mild disability in 245 (67.8%) patients and severe disability in 116 (32.2%) patients. Lactate levels were higher in patients with severe disability (p <0.001) (Figure 2). Serum pH and HCO3 (std) levels were lower in group with severe disability (p <0.001, p=0.006). In addition, BE (b) and BE (ecf) were higher in group with severe disability (p=0.003, 0.013). Blood gas values were summarized according to disability (Table 3).

In ROC analysis, lactate cut off value was calculated as 1.72 with 59% sensitivity and 58% specificity (p=0.002, AUC=0.607, CI=0.54-0.67) (Figure 3). pH cut off value was calculated as 7,39 with 62% sensitivity and 58% specificity (p=0.000, AUC=0.653, CI=0.59-0.71). HCO3 (std) cut off value was calculated as 22.95 with 55% sensitivity and 56% specificity (p=0.006, AUC=0.59, CI=0.53-0.65). BE (b) cut off value was calculated as -1.05 with 58% sensitivity and 56% specificity (p=0.003, AUC=0.60, CI=0.54-0.66). BE (ecf) cut off value was calculated as -1.25 with 55% sensitivity and 52% specificity (p=0.013, AUC=0.58, CI=0.52-0.64).

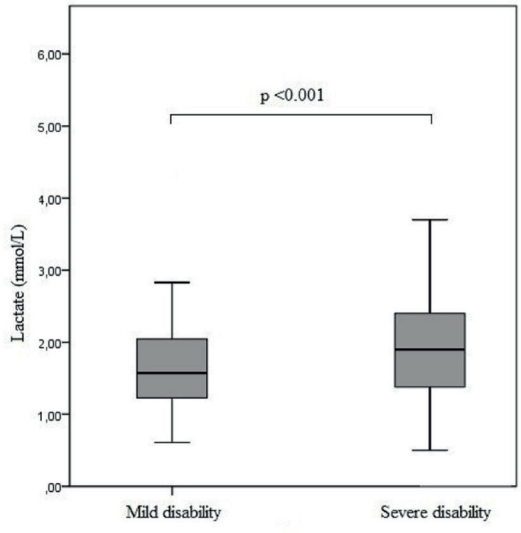

Figure 2. Box plot graph: lactate levels according to initial disability

Table 3. Blood gas parameters according to initial disability. Data are shown as mean±standard deviation and min-max

Blood gas parameters	Mild disability (n=245, 67.8%)		Severe disability (n=116, 32.2%)		p
	mean±SD	min-max	mean±SD	min-max	
pH	7.40±0.04	7.27-7.69	7.37±0.05	.16-7.50	0.000*
pCO2 (mmHg)	39.01±5.71	23.8-64.1	40.48±7.54	24.7-67.9	0.178
pO2 (mmHg)	38.55±13.31	13.2-74.3	39.53±14.46	13.2-82.2	0.613
HCO3(act) (mmol/L)	23.86±2.75	16.8-33.0	23.25±3.38	14.5-34.7	0.081
HCO3(std) (mmol/L)	23.16±2.43	1.8-28.6	22.3±2.44	15-28.2	0.006*
BE (b) (mmol/L)	-0.61±2.39	-8.8-5.10	-1.67±3.05	-11.8-6.10	0.003*
BE (ecf) (mmol/L)	-0.74±3.33	-9.6-26.4	-1.83±3.57	-11.8-8.7	0.013*
Lactate (mmol/L)	1.71±0.69	0.61-5.53	1.98±0.80	0.50-4.46	0.002*

*Statistically Significant
pCO2: Partial Carbon Dioxide Pressure, pO2: Partial Oxygen Pressure, HCO3 (act): Actual Bicarbonate, HCO3 (std): Standard Bicarbonate, BE (b): Blood Base Excess, BE (ecf): Extracellular Fuild Base Excess, SD: Standard Deviation

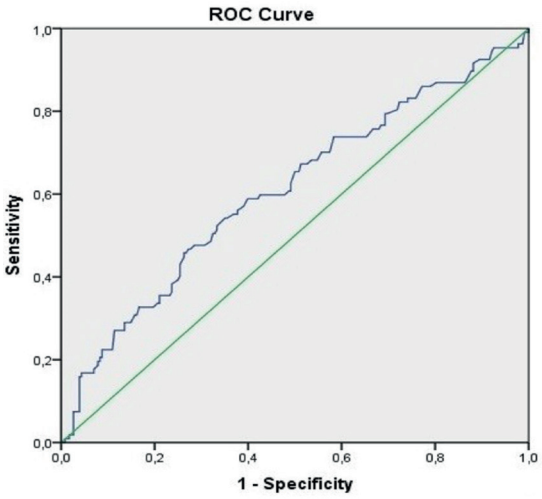

Figure 3. Receiver operating characteristic (ROC) curve analysis according to initial disability

The Association Lactate Levels with Clinical Improvement
Patients were divided into two groups according to NIHSS difference and groups were compared. One hundred and fifty-six (43.2%) patients had clinical improvement, 205 (56.8%) patients had no clinical improvement. There was no statistically significant difference between clinical improvement groups and lactate level (p=0.989). In addition, other blood gas parameters were equal in clinical improvement groups (p> 0.05). Lactate and other blood gas parameters were summarized in clinical improvement groups (Table 4).

The Association Lactate Levels with In-hospital Mortality
In-hospital mortality rate was 16.6% (n=60) in patients with ischemic stroke treated with IVT. Lactate value was equal between mortality and non-mortality groups (p=0.149). There was no difference between other blood gas parameters in these groups (p> 0.05). Lactate and other blood gas parameters were summarized in mortality groups (Table 5).

Table 4. Blood gas parameters according to clinical improvement. Data are shown as mean±standard deviation and min-max

Blood gas parameters	Clinical improvement (-) (n=205, 56.8%)		Clinical improvement (+) (n=156, 43.2%)		p
	mean±SD	min-max	mean±SD	min-max	
pH	7.39±0.04	7.24-7.49	7.40±0.05	7.16-7.69	0.409
pCO2 (mmHg)	39.8±6.64	23.8-67.9	39.07±6.02	23.8-58.0	0.586
pO2 (mmHg)	39.37±14.11	13.2-82.2	38.18±13.09	13.2-77.5	0.565
HCO3(act) (mmol/L)	23.78±3.04	14.5-34.7	23.5±2.88	15.6-32.0	0.530
HCO3(std) (mmol/L)	22.9±2.66	1.8-28.6	22.8±2.17	15.0-28.4	0.571
BE (b) (mmol/L)	-0.89±2.68	-9.5-6.1	-1.04±2.66	-11.8-4.6	0.683
BE (ecf) (mmol/L)	-0.93±3.69	-11.3-26.4	-1.3±3.08	-11.8-6.5	0.596
Lactate (mmol/L)	1.79±0.72	0.61-4.93	1.80±0.76	0.50-5.53	0.989

pCO2: Partial Carbon Dioxide Pressure, pO2: Partial Oxygen Pressure, HCO3 (act): Actual Bicarbonate, HCO3 (std): Standard Bicarbonate, BE (b): Blood Base Excess, BE (ecf): Extracellular Fuild Base Excess, SD: Standard Deviation

Table 5. Blood gas parameters according to in-hospital mortality. Data are shown as mean±standard deviation and min-max

Blood gas parameters	Mortality (-) (n=301, 83.4%)		Mortality (+) (n=60, 16.6%)		p
	mean±SD	min-max	mean±SD	min-max	
pH	7.39±0.04	7.16-7.69	7.39±0.04	7.31-7.48	0.249
pCO2 (mmHg)	39.35±6.51	23.8-67.9	40.14±5.68	27.4-23.04	0.310
pO2 (mmHg)	38.85±13.57	13.2-77.5	38.96±14.31	18.3-82.2	0.859
HCO3(act) (mmol/L)	23.62±3.00	14.5-34.7	23.9±2.86	14.5-29.8	0.284
HCO3(std) (mmol/L)	22.89±2.51	1.8-28.6	23.04±2.18	16.3-27.3	0.479
BE (b) (mmol/L)	-0.97±2.68	-11.8-6.1	-0.86±2.64	-9.5-3.6	0.444
BE (ecf) (mmol/L)	-1.11±3.52	-11.8-26.4	-1.0±3.06	-11.3-4.3	0.372
Lactate (mmol/L)	1.75±.70	0.5-5.53	1.98±0.87	0.81-4.93	0.149

pCO2: Partial Carbon Dioxide Pressure, pO2: Partial Oxygen Pressure, HCO3 (act): Actual Bicarbonate, HCO3 (std): Standard Bicarbonate, BE (b): Blood Base Excess, BE (ecf): Extracellular Fuild Base Excess, SD: Standard Deviation

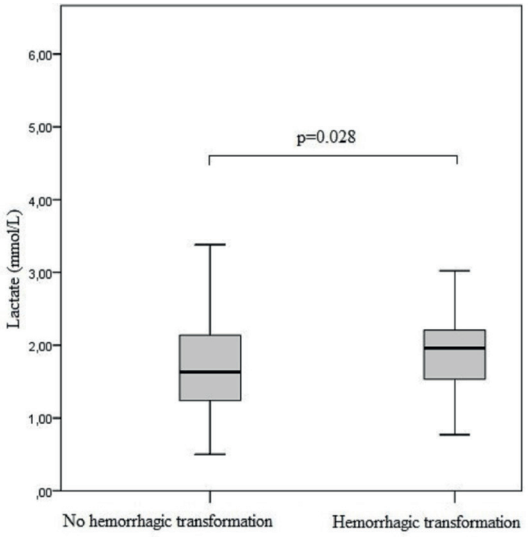

Figure 4. Box plot graph: lactate levels according to cerebral hemorrhagic transformation groups

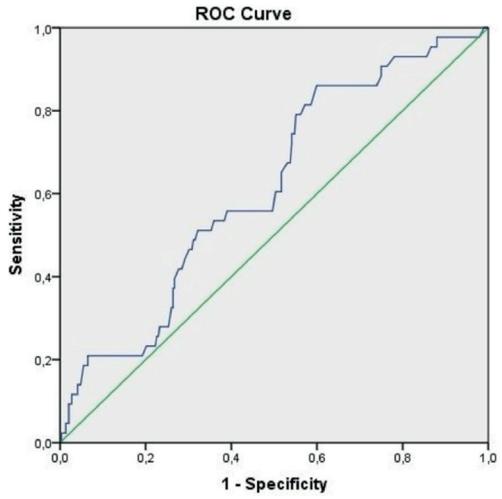

Figure 5. Receiver operating characteristic (ROC) curve analysis according to cerebral hemorrhagic transformation

The Association Lactate Levels with Cerebral Hemorrhagic Transformation

All cerebral hemorrhagic transformation rate was 11.9% (n=43) in patients with ischemic stroke treated with IVT. A total of 16 of 361 (4.4%) patients experienced symptomatic intracerebral hemorrhage. Serum lactate level was higher in patients with cerebral hemorrhagic transformation (p=0.028) (Figure 4). There was no difference between other blood gas parameters in these groups (p> 0.05). Lactate and other blood gas parameters were summarized in cerebral hemorrhagic transformation groups (Table 6).

In ROC analysis, lactate cut off value was calculated as 1.79 with 56.0% sensitivity and 61.0% specificity (p=0.014, AUC=0.616, CI=0.53-0.70) (Figure 5).

DISCUSSION

In this study, the relationship between blood lactate level and prognosis was evaluated in patients treated with IVT. In literature review, there was no other study evaluating the relationship between prognosis and lactate level in patients with ischemic stroke treated with IVT.

Lactate occurs with increased anaerobic metabolism and indicates hypoperfusion. Hyperlactatemia occurs when the lactate production and elimination balance is disturbed (21). Increased blood lactate level is an indicator of peripheral hypoperfusion and organ dysfunction in patients with acute heart failure. In addition, hyperlactatemia is associated with poor prognosis in these patients (22). Hyperlactatemia is an independent risk factor for poor discharge prognosis in intensive care patients after cardiac surgery (23).

In acute cerebral diseases (such as ischemic and hemorrhagic stroke), lactate increases with anaerobic metabolism and it is metabolized as an energy source for brain tissue (24). This is confirmed with increased CSF lactate dehydrogenase level in patients with ischemic stroke (25). In experimental ischemic stroke models, local lactate injection to ischemic area reduces the volume of ischemia and positively contributes to prognosis.

Lactate is an important energy source for axons and oligodendrocytes. It has neuroprotective effect especially in strokes (26). In addition, hyperlactatemia is associated with mortality and poor functional outcome at 3 months in ischemic stroke (16). Increased lactase is associated with impaired cerebral autoregulation and penumbral edema in patients with more than 50% ischemia in the middle cerebral artery perfusion area (27). In our study, patients with high lactate levels had higher initial disability scores and more cerebral hemorrhagic transformation. These results are consistent with recent published studies. Cerebral hemorrhagic transformation is more common in patients with severe stroke. Therefore, hyperlactatemia may be an indirect indicator of cerebral hemorrhagic transformation and severe disability in ischemic stroke patients treated with IVT.

In a study, 2737 patients treated in neurointensive care were evaluated and blood tests of these patients were taken within the first 6 hours. Sixty-three (2.3%) patients died due to neurological disease. It was determined that the initial lactate level was associated with 90-day mortality due to neurological disease (28). Low blood bicarbonate and pH levels are associated with disability severity and long-term mortality in patients with acute ischemic stroke (29). In our study, there was no relationship between initial lactate level and in-hospital mortality. It was detected that low blood pH and bicarbonate level; high base excess values were associated with disability.

LIMITATIONS

There are several limitations of our study. First; it is a retrospective study in only one center. Second; disability, in-hospital short-term clinical improvement, mortality and cerebral hemorrhagic transformation were evaluated. There are no data on long-term prognosis. Third, it has been demonstrated that lactate level is associated with cerebral hemorrhagic transformation after IVT in ischemic stroke. However, its relationship with other factors has not been evaluated.

CONCLUSION

Increased blood lactate level is associated with disability and cerebral hemorrhagic transformation in patients with AIS treated with IVT. Lactate level is not associated with in-hospital mortality and short-term clinical improvement.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The study was approved by University of Health Sciences Turkey, Konya Training and Research Hospital, Ethics Committee (08/05/2020; 38-14).

REFERENCES

1. Johnson CO, Nguyen M, Roth GA, et al. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the global burden of disease study 2016. Lancet Neurol 2019;18:439-58.
2. Liu L, Wang D, Wong KS, et al. Stroke and stroke care in China: huge burden, significant workload, and a national priority. Stroke 2011;42:3651-4.
3. PowersWJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American heart association/ American stroke association. Stroke 2018;49:46-110.
4. Cheripelli BK, Huang X, MacIsaac R, et al. Interaction of recanalization, intracerebral hemorrhage, and cerebral edema after intravenous thrombolysis. Stroke 2016;47:1761-7.
5. Eren F, Ongun G, Yildogan AT, et al. Intravenous thrombolytic therapy in acute ischemic stroke: Clinical Evaluation. General Med J 2019;29:169-74.
6. Whiteley W, Chong WL, Sengupta A, et al. Blood markers for the prognosis of ischemic stroke: a systematic review. Stroke 2009;40:380-9.
7. Gundogdu OL, Bilge N, Yalcin A, et al. Association between biomarkers in the long-term prognosis of ischemic stroke. Ann Med Res 2019;26:1875-9.
8. Bruhn H, Frahm J, Gyngell ML, et al. Cerebral metabolism in man after acute stroke: new observations using localized proton NMR spectroscopy. Magn Reson Med 1989;9:126-31.
9. Graham GD, Hwang JH, Rothman DL, et al. Spectroscopic assessment of alterations in macromolecule and small-molecule metabolites in human brain after stroke. Stroke 2001;32:2797-802.
10. Berger C, Schabitz WR, Georgiadis D, et al. Effects of hypothermia on excitatory amino acids and metabolism in stroke patients: a microdialysis study. Stroke 2002;33:519-24.
11. Schneweis S, Grond M, Staub F, et al. Predictive value of neurochemical monitoring in large middle cerebral artery infarction. Stroke 2001;32:1863-7.
12. Khosravani H, Shahpori R, Stelfox HT, et al. Occurrence and adverse effect on outcome of hyperlactatemia in the critically ill. Crit Care 2009;13:90.
13. Cerović O, Golubović V, Spec-Marn A, et al. Relationship between injury severity and lactate levels in severely injured patients. Intensive Care Med 2003;29:1300-5.
14. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004;32:1637-42.
15. Brouns R, Sheorajpanday R, Wauters A, et al. Evaluation of lactate as a marker of metabolic stress and cause of secondary damage in acute ischemic stroke or TIA. Clin Chim Acta 2008;397:27-31.
16. Jo S, Jeong T, Lee JB, et al. Initial hyperlactatemia in the ED is associated with poor outcome in patients with ischemic stroke. Am J Emerg Med 2012;30:449-55.
17. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American heart association/ American stroke association. Stroke 2018;49:46-110.

18. Adams HP Jr, Davis PH, Leira EC, et al. Baseline NIH stroke scale score strongly predicts outcome after stroke: a report of the trial of org 10172 in acute stroke treatment (TOAST). Neurology 1999;53:126-31.
19. Juneja D, Singh O, Dang R. Admission hyperlactatemia: causes, incidence, and impact on outcome of patients admitted in a general medical intensive care unit. J Crit Care 2011;26:316-20.
20. Nichol AD, Egi M, Pettila V, et al. Relative hyperlactatemia and hospital mortality in critically ill patients: a retrospective multi-centre study. Crit Care 2010;14:25.
21. Groeneveld AB, Kester AD, Nauta JJ, et al. Relation of arterial blood lactate to oxygen delivery and hemodynamic variables in human shock states. Circ Shock 1987;22:35-53.
22. Zymliński R, Biegus J, Sokolski M, et al. Increased blood lactate is prevalent and identifies poor prognosis in patients with acute heart failure without overt peripheral hypoperfusion. Eur J Heart Fail 2018;20:1011-8.
23. Hajjar LA, Almeida JP, Fukushima JT, et al. High lactate levels are predictors of major complications after cardiac surgery. J Thorac Cardiovasc Surg 2013;146:455-60.
24. Wyss MT, Jolivet R, Buck A, et al. In vivo evidence for lactate as a neuronal energy source. J Neurosci 2011;31:7477-85.
25. Parakh N, Gupta HL, Jain A. Evaluation of enzymes in serum and cerebrospinal fluid in cases of stroke. Neurol India 2002;50:518.
26. Berthet C, Lei H, Thevenet J, et al. Neuroprotective role of lactate after cerebral ischemia. J Cereb Blood Flow Metab 2009;29:1780-9.
27. Dohmen C, Bosche B, Graf R, et al. Identification and clinical impact of impaired cerebrovascular autoregulation in patients with malignant middle cerebral artery infarction. Stroke 2007;38:56-61.
28. Oh TK, Song IA, Bae HJ, et al Serum lactate level upon admission to the neuro-intensive care unit and 90-day mortality: A retrospective study. J Clin Neurosci 2019;70:173-7.
29. Ganti L, Gilmore RM, Weaver AL, et al. Prognostic value of complete blood count and electrolyte panel during emergency department evaluation for acute ischemic stroke. ISRN Stroke 2013.