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HIGH ARTERIAL BLOOD LACTATE AS SIRS PREDICTOR IN PATIENTS WITH SEVERE HEAD INJURY

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Objectives: Lactate is one of the prognostic factor for evaluation of clinical severe head injury patients outcome. Lactate is also known as a factor to support diagnostic and prognosis of SIRS cases. Severe head injury is a head traumatic case frequently found in Emergency Units, where some cases result in mortality. Based on Glasgow Coma Scale (GCS), severe head injury is define as a head injury with GCS score between 3 and 8. This study aims to determine whether high arterial blood lactate can be used as predictor that causes the occurrence of SIRS. **Method**. A Cohort prospective study applied in this research to determine arterial blood lactate as a predictor that causes the occurrence of SIRS. This study was conducted at Sanglah General Hospital Bali-Indonesia from May 2013 to July 2013 with 40 patients who fulfilled the inclusive criteria. Data were presented in tables and analyzed by applying Chi Square Test with CI 95% and p <0.05 was considered significant. **Results**: From 40 samples, 27 were male (62.5%) and 17 female (37.5%) at the age of 0-10, 2 people (5%), 10-20 years 7 people (17.5%), 20-40 years 14 people (35%), 40-60 years 12 people (30%) and over 60 years 5 people (12.5%). On the first day, patients with normal level blood arterial lactate 2 (5%), and high 38 (95%) causing SIRS (+) 39 (97.5%) and SIRS (-) 1 (2.5%) samples to occur. Using bivariate analysis between arterial blood lactate level and the amount occurrence of SIRS, we obtain $p < 0.05$ and variable control using multivariate analysis we obtained variable of liver dysfunction that give significant value with level arterial blood lactate with $p < 0.05$). **Conclusion:** From 40 samples of Severe head injury, there were 38 (95%) whose blood arterial lactate level increased on the first day, 2 (5%) in normal limit and 39 (97.5%) with SIRS on the third day when $p < 0.05$) so that high level arterial blood lactate can be used as predictor that causes SIRS to occur.

Keywords: **Severe head injury, Glasgow coma scale, high arterial blood lactate, Systemic inflammatory response syndrome.**

INTRODUCTION

The incidence of head injury have never been diminished in developed or developing country especially Indonesia. Head injury was the most common cause of death to the people under 45 years old group.[1,2]

Head injury leads to pathological changes either in cerebral vascularization and cerebral metabolism systems. Cerebral metabolism was highly dependent to the component contained within cerebral vascular.[3,4] Inflammation response, endothelial cell activation, and inflammation mediator release in head injury will increase the number of leucocyte. Head injury was connected to acute response phase characterized by leucocytosis caused by epinefrin and cortisol enhancement. SIRS is a systemic inflammation response caused by severe inflammation response to critical incidence such as burns, trauma, pancreatitis.[6-8]

There were many theories explained the pathophysiology of SIRS such as mediator theory, microvascular failure theory, two hit theory and integrated theory. The most adopted theory was microvascular failure theory. One of the parameter to determine microvascular disturbance was blood

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lactate concentration which described tissue hypoperfusion or hypoxia.[5,6]

Lactate was a sensitive marker for changes in cerebral metabolism, even though its mechanism had not fully understood yet. Previous studies stated that ischemia following head injury was responsible for blood lactate concentration enhancement. In contrary, another studies stated that majority of patients with head injury did not have periodic ischemia, instead of secondary ischemia which lead to lactate accumulation. Another explanation was ion changes as physiologic response in head injury.[8,9]

Lactate is additional product from glycolysis. Through glycolysis, anaerobic process occurs in cytosol, two Adenosine Three Phosphate (ATP) molecule was produced along with pyruvic for every glucose molecule hydrolysed. There are two things could occur to the assembled piruvate. First, if sufficient oxygen is available then pyruvic would be involved in Kreb's cycle inside mitochondria and produced another ATP. Second, under hypoxia condition, pyruvic will not be involved in Kreb's cycle instead converted into lactate. Pyruvic into lactate conversion is a reversible process which be catalyzed by Lactate Dehyrogenase enzyme inside the cytosol. Nicotinamide Adenine Dinucleotide ($NADH/NAD^+$) cofactor would be interconnected or exchanged with H^+ ion.[10,11]

Lactate that has already converted back into pyruvic would enter Kreb's cycle inside mytochondria for further metabolism or being used in gluconeogenesis process. Pyruvic is used in aerob tissue through two oxydative process. The first oxydative process is conversion of pyruvic into Acetyl-CoA by Pyruvic Dehyrogenase Enzyme (PDH). Thiamin is a cofactor for PDHb so thiamine deficiency would cause disturbance in lactate metabolism. The second oxydative process is usage of pyruvic in gluconeogenesis process. Head injury will cause hypoxia that brought consequences of mitochondria metabolism dysfunction which would result in lactate accumulation.[9,13,14]

Inflammation processes after head injury are characterized by activation of vasodilatation mediator, decrease of blood flow and increase of capiller permeability. These lead to fluid and leucocyte accumulation in trauma site. The leading role cell in inflammation process was phagocyte cell, especially PolyMorphoNuclear (PMN) Cell, which being accumulated within 30-60 minutes in necrotic tissue. If the causes of inflammation process are occurred exceeded this time then within 5-6 hours, there would be mononunclear leucocyte cell, macrophage and lymphocyte infiltration. These macrophages would support PMN cell activity in phagocytosis process.[15-18]

The purpose of this study was to determine high artery blood lactate concentration as a predictor for SIRS in patients with head injury based on Glasgow Coma Scale (GCS). We assumed that the severity of head injury was correlated to artery blood lactate concentration

METHOD

A Cohort prospective study was applied in this research to determine that high level blood arterial lactate as a predictor of SIRS. This study was conducted at Sanglah General Hospital Bali-Indonesia from May 2013 to July 2013 with 40 patients who fulfilled the inclusive criteria. Data is presented in tables and is analyzed using Chi Square Test to CI 95% and $p<0.05$.

RESULT

This research is conducted on severe head injury patients with GCS 3-8 who visited Sanglah General Hospital, Bali-Indonesia emergency unit for medical treatment between May 2013 and July 2013.

A number of 40 patients in each group was recruited in this study. The patients consisted of 27 male (62.5%) and 13 female (37.57%). The level of blood arterial lactate of the whole samples on the first day was observed. The results indicate 2 normal samples (5%), and 38 samples of high level blood arterial lactate (97.5%). Then on the third day, the occurrence of SIRS were evaluated to the whole samples in which we found 39 SIRS samples occurred and 1 SIRS samples failed as presented in Table 1 and 2.

DISCUSSION

Inflammation responses, caused by trauma were dynamic processes that result from inflammatory mediator release. Head injury induced immune response that activated by endogen signals as response to stress, tissue or cell injury and systemic inflammatory response through changed in stress hormone, metabolic mediator, immunology and hemodynamic response that result in organ system damage. There had been an evidence that in head injury, hyperglycolysis caused lactate enhancement inside extra-cell chamber which would be used as an energy source.[15,18]

Forty participants were followed during this study. Arterial lactate concentration was performed in first day and SIRS evaluation was performed in third day. Arterial lactate concentration will reach its maximum level after first twenty four hours.

Significant higher arterial lactate concentration during first day was found in cohort group ($p<0.05$). This findings are similar to previous study by Terry and suistomaa which stated highest enhancement of

arterial lactate concentration was obtained during first day.[19,20] Mean arterial lactate concentration in severe head injury is higher compared to in mild head injury. In this study, we found arterial lactate concentration enhancement in severe head injury during first day was observed in 38 to 40 patients (95%).

Pallerin and Magistreti had shown that astrocyte used glucosa during stress environment and transformed it into lactate which through specific transporter was sent to neuron and blood circulation. Recent in vivo rat study by Aurbert described lactate kinetic through lactate dynamic evaluation in brain tissue during hypocampal stimulation. In summary these study had shown lactate which came from astrocyte through *monocarboxylic acid transporter* (MC1 and MC 4) acted as substrate to fulfill neuron energy required.[21]

Table 1
Study Sample Characteristics

Variable	SIRS occurrence in severe head injury patients on 3rd day		Total	*p*
	SIRS occur	SIRS not occur		
Sex				
Male	26	1	27	0.482
Female	13	0	13	
	39	1	40	
Age				0.305
0-10 years	2	0	2	
11-20 years	6	1	7	
21-40 years	14	0	14	
41-60 years	12	0	12	
>60 years	5	0	5	
	39	1	40	
Hs-CRP level				
Normal	1	1	2	0,001*
High	38	0	38	
	39	1	40	

**Significant if p-value < 0.05*

Based on table Chi-Square Test we find grade p-value 0,000 with numerical calculation 19,487 (df=2). Since grade p-value < α (0,000 < 0.05), we conclude that there has been an increase blood arterial lactate can be used as predictor of SIRS occurrence in patients with severe head injury.

High lactate circulation enables astrocyte to compensate for energy requirement enhancement in order to maintain synaps function and minimize neuron damage caused by ischemia. These can be shown by sudden and brief enhacement of brain glycolysis process, ATP synthesis, lactate, and oxygen consumption during first hour after head injury. Some studies had shown that head injury affected mitochondrial function through free radical enhancement, calcium influx, mitochondrial permeability transposition pores (mPTP) and caused mitochondria swelling and microcirculation changes. Arterial lactate concentration will change accordingly with the severity of head injury. These can be caused by brain parenchym damage therefore result in lactate production enhancement by astrocyte which means diminished aerobic ATP production accordingly with neuron cell and astrocyte mitochondria damage.[15]

SIRS is a general body response to bacterial infection and tissue trauma. These inflammation response is caused by microorganism invasion into the tissue which in turn cause sepsis.[22,23,24] In this study we found that all patients with arterial lactate concentration enhancement will suffered from SIRS although in normal arterial lactate concentration group, we found one patients suffered from SIRS (P<0,005).This findings was similar to recent theory that stated after head injury, there will be an inflammation process characterized by activation of substance mediator that lead to vasodilatation, reduced blood flow and capillary hyper-permeability.

Table 2
Grade p-value each variable control with High level arterial blood lactate

Variable	Arterial blood lactate level on 1st day		Total	*p*
	Normal	High		
Alcohol				0.236
Yes	0	16	16	
No	2	22	24	
	2	38	40	
Diabetes Mellitus				0.504
Yes	0	7	7	
No	2	31	33	
	2	38	40	
Cardiovascular diseases				0.542
Yes	0	1	1	
No	2	37	39	
	2	38	40	
Cancer				0.816
Yes	0	1	1	
No	2	37	39	
	1	38	40	
Liver diseases				0.003
Yes	1	1	2	
No	1	37	38	
	2	38	40	
Treatment (terbutalin, achetaminophen)				
Yes	1	12	13	0.816
No	1	26	27	
	2	38	40	

Based on multivariate test found in pneumonia $p < 0.05$ so liver diseases influences rate of SIRS occurrence.

In patients who suffer from severe head injury, there will be enhancement of neuroinflammation characterized by microglia cell and astrocyte activation, disruption of blood brain barrier, enhancement of inflammation cytokine and free radical production.Freen radical will injure cell membrane ;cytokine (IL 1, IL6 and TNα) will ruin blood brain barrier and in the end will lead to neuron damage.The systemic effects of severe brain injury were as a result from inflammation mediator that begun SIRS.[25,26]

There were a hidden process that preceding macrovascular disruption such as microvascular disruption, endotel cell damage,coagulation cascade activation and mitochondrial distress syndrome.The ineffective phagocytosis process by neutrofill had lead to survival of the undigested bacteria which would result in inflammation and microvascular disturbance.[5,27,28] Under hypoxia condition after head injuy,glucosa proceed into anaerob metabolism that produce lactate acid. Blood Lactate concentration will increase and therefore induce intracellular-

extracellular acidosis. Ischemia in brain tissue will damage neuron, glia tissue and vascular tissue.[29-31]

This study found two of forty samples (5%)had liver dysfunction in which one of them (2.5%) had high arterial lactate concentration and the other one had normal arterial lactate concentration so we concluded that there was a significant correlation between liver dysfunction and arterial lactate concentration in patients who suffered from severe head injury. Patient with liver dysfunction would have lactate production enhancement that caused by excessive glycolysis as a response to stresses organ.[32]

The main goal of handling SIRS is to prevent source of infection, repair and retrieve perfusion tissue, repair and maintain ventricle function and other supportive efforts.[33-35]

CONCLUSION

From forty samples of severe head injury, there were thirty eight to forty (95%) whose blood arterial lactate level in blood were increased and two to forty (5 %) whose Hs-CRP were within normal range at the first day. There was significant correlation between SIRS event and blood arterial lactate correlation in patients who suffered from head injury ($P < 0.05$), so that high level lactate in blood can be used as predictor that causes SIRS to occur.

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