ISSN 0303 - 7932

FOLIA MEDICA INDONESIANA

Vol. 46 No. 2 April – June 2010

International Online Distribution by ProQuest™
www.proquest.com

Folia Medica Indonesiana	Vol.46	No. 2	Page 78-160	Surabaya Apr-Jun 2010	ISSN 0303 - 7932

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Folia Medica Indonesiana Vol. 46 No. 2 April– June 2010 : 125-131

CORRELATION BETWEEN BLOOD SEROTONIN LEVEL WITH CONSCIOUSNESS LEVEL AND DEPRESSION SYMPTOMS IN MODERATE BRAIN INJURY PATIENTS

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ABSTRACT

To analyze a correlation between blood serotonin level, level of consciousness after resuscitation, and depression symptoms to reveal pathological neurobiochemistry level on moderate brain injury patients. This study uses analytical prospective with cross sectional design. Blood sample was taken using disposable spuit approximately 5 cc and was kept in the closed container and centrifuged. The temperature was kept at -200C. Serum was used to determine serotonin level in the blood. Blood sample was taken twice: before 24 hrs after brain injury and less than 1 month afterwards. To examine depression level Hamilton Rating Scale for Depression (HAM-D) was used to figure out whether there is depression symptoms after brain injury. Glasgow Coma Scale was used to examine level of consciousness. The statistical analysis using Spearman correlation resulted in rs = 0,295 and p=0,090 (p>0,05), which means that there is no association between consciousness level and serotonin level before 24 hrs after brain injury. The statistical analysis using Spearman correlation resulted in rs = 0,309 and p=0,075 (p>0,05), which means that there is no association between serotonin level one month after injury and depression level. The last, the statistical analysis using Phi coefficient resulted in Phi = 0,342 and p=0,046 (p<0,05), which means that there is correlation between serotonin level one month after injury and occurrence of depression, which means that people with lower level of serotonin have higher occurrence of depression than people with higher level of serotonin. There is no significant correlation between level of consciousness and serotonin level in the blood under 24 hrs after brain injury. There is significant correlation between serotonin level one month after injury and occurrence of depression..

Keywords: *serotonin, Glasgow Coma Scale, depression.*

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INTRODUCTION

At the beginning of this 21st century, brain injury is still a public health problem that is very serious about the incidence and degree of severe brain injury is increasing in line with technological developments and increased population mobility, which is not accompanied by improvements in discipline and compliance activities of the highway and where other. Of the total brain injury, 75% to 80% classified as mild brain injuries the rest, including medium and heavy (Arifin 2002).

On dr. Soetomo, the average number of patients with brain injuries is 2043 cases per year, with mortality rates in the year 1998 as many as 57 patients (32%) of 174 severe brain injury who were treated (Balafif 1999). Almost 100% of people with severe brain injury and brain injury was 66%, causing permanent disability and will not return to the level of initial function (Shepard 2001). Brain injury in the United States approximately 1.4 million per year, 235 000 hospitalized, 50,000 die and 1.1 million are treated and out of the emergency room. Approximately 90 000 leaving a permanent disability every year. Approximately 439 000 treated in the psychiatric space, and 89 000 undergoing outpatient (Ashman & Gordon 2006).

Brain injury associated with known psychiatric disorders, ranging from the disruption process of thinking up with emotional disturbances. Changes in cognitive, behavioral, and several other psychiatric symptoms was found after brain injury. Depression is the most psychiatric symptoms is estimated that between 14-77%, 60% found some time after brain injuries, and 20% was found several months later. Other symptoms include stress 3-27% and anxiety 3-28% (Ashman 2006).

The degree of brain injury are assessed from the GCS (Glasgow Coma Scale). Level of consciousness as measured by the GCS is the most widely used evaluation to measure the degree of severity of brain injuries (Krauss 1996).

Neurotransmitter that is often associated with neuropsychiatric disorders is serotonin, noradrenaline,

dopamine and GABA. Among these neurotransmitters, serotonergic dysfunction is the neurotransmitter most often associated with various mental disorders (Suparno 2006). Serotonin is found in neuronal cell bodies in the midbrain raphe nucleus that play a role in emotion regulation and cognitive as well as the hippocampus and limbic system and the frontal cortex. The variation of the serotonin receptor 5 HT1a, 5HT2b, 5HT2c, 5HT3, and 5HT4 associated with emotion regulation in limbic systems such as the amygdala, and hippocampus girus singulatum (Zenab & Turhan 2005).In experimental animals rats found an increase in serotonin levels in the cortex as a whole on one side of the hemisphere injury. Serotonergic system is thought to play a role in conditions such trauma (Ramesh 1998). Twenty-four hours after brain injury is, will increase blood levels of serotonin, whereas serotonin levels 15-22 days later it will decrease (Ninel et al. 2000).

Depression is the most neuropsychiatric sequelae of brain cedra case, as shown by outpatients and inpatients. Although in most case studies on moderate and severe brain injury, but patients with mild brain injury also have a risk of depression (Jesse & Jay 2000). At one month after the brain injury, evaluation of the Hamilton rating scale for depression (HAM-D) obtained 26% of patients experiencing depression (Simon & Olive 2007).

Serotonin is the neurotransmitter most often associated with depression. There are changes in serotonin levels in patients with depression, which can be measured in urine, blood or cerebrospinal fluid (CSS) (Saddock & Alcott 2003). Along with lots of organic brain dysfunction as a result of brain injuries that are temporary or permanent, forcing us to consider more thoroughly all aspects and degrees of injury, premorbid factors, prognosis and rehabilitation (Susanto & Mawardi 1994).

MATERIALS AND METHODS

This study is a prospective cross sectional analytic design. Brain injury patients admitted in Neurosurgery space dr. Soetomo view the provisions of appropriate research criteria. What is meant here is the blood sampling using a needle as much as 5 cc disposibel and stored in sealed bottles, serum used for the examination of blood serotonin levels. After the centrifuge and stored in a temperature-200C.

Blood samples were taken in less than 24 hours after brain trauma and within one month after the brain injury at the same hour.

RESULTS

Patients who become the subjects of this study were 34 people divided into two groups: 17 people undergoing surgery and 17 people did not have surgery. From the collection of data was conducted during the period May to July 2007 as the data obtained are listed in the table below.

Table 1 Mean, Standard Deviation, the Age of the Youngest and Oldest Patient was Brain Injury

Group	$\bar{x}$	SD	Min	Maks
Operation	27.47	11.48	16	50
Nonoperation	26.12	7.19	17	39
All patient	26.79	9.46	16	50

For all sampled patients found that mean age of 26.79 years with a standard deviation of 9.46 years. However, if the fall in both categories, namely surgery and non surgery found that mean each of 27.47 years and 26.12 years.

Table 2 Age Group of Patients was Brain Injury

Group of Age	Operation	Non Operation	Total
- 20	7 (41.2%)	5 (29.4%)	12 (35.3%)
21-30	5 (29.4%)	8 (47.1%)	13 (38.2%)
31-40	1 (5.9%)	4 (23.5%)	5 (14.7%)
41-50	4 (23.5%)	0 (0.0%)	4 (11.8%)
Total	17 (100.0%)	17 (100.0%)	34 (100.0%)

From the table above, the data showed that patients with brain injuries are the most who come to the dr. Atopic Dermatitis is a nonoperation of the age group 21-30 years as many as eight people (47.1%), while group operating under the age of 20 years as many as seven people (41.2%).

This research will see the presentation of sex that gets a brain injury is and to see the possibility of connection with the incident was received brain injuries.

Table 3 Sex Brain Injury Patients Are

Sex	Operation	Non Operation	Total
Male	15 (88.2%)	13 (76.5%)	28 (82.4%)
Female	2 (11.8%)	4 (23.5%)	6 (17.6%)
Total	17 (100.0%)	17 (100.0%)	34 (100.0%)

Of the samples taken showed that the presentation of male sex as much as 15 people (88.2%) in group operations and 13 people (76.5%) in non-operation group. While in the female sex, get as many as two people (11.8%) in group operations and four people (23.5%) in nonoperation group.

Assessment of level of consciousness using the GCS score in patients with brain injury is.

Table 4 Distribution 0f Classification Based on the Awareness of Operating - Non-Operating

Group	Median	Min	Maks
Operation	10	9	12
Nonoperation	11	9	12
All Group	10	9	12
Wilcoxon – Mann Whitney (p>0.05)		z=-1.337	p=0.181

From non-parametric Wilcoxon test, Mann Whitney test, showed p> 0.05, which means no significant difference was found from the level of awareness of non-operating group with operations.

Initial blood serotonin levels were taken in less than 24 hours, while the final blood serotonin levels were taken in less than one month after the brain injury was.

Table 5 Initial Blood Serotonin Levels

Group	$\bar{x}$	SD	Min	Maks
Operation	148.54	59.52	25.6	256.2
Nonoperation	158.10	135.13	55.6	590.1
All Patient	153.32	102.93	25.6	590.1

T test: t = -0.267 p = 0.791 (p>0.05)

From analysis using unpaired t test can be found that there was no significant difference in mean levels of serotonin between surgery and non surgery group. Surgery group showed a value of 148.54 and 158.10 nonoperation. Thus we can conclude that in conditions of less than 24 hours post-injury levels of serotonin showed no difference of mean between the two treatment groups.

Table 6 Final Blood Serotonin Levels

Group	$\bar{x}$	SD	Min	Maks
Operation	91.24	30.18	46.4	153.4
Nonoperation	74.11	40.89	27.6	161.1
All Patient	82.67	36.44	27.6	161.1

T test: t = 1.389 p = 0.174 (p>0.05)

Table 7 Comparison of Blood Serotonin Levels Beginning with the End

Examination	$\bar{x}$	SD	t-test
Begining	153.32	102.93	t = 3.957
End	82.67	36.44	p = 0.000

From analysis using unpaired t test can be seen that there was no significant difference in the mean serotonin levels between sample groups operating with non operational. Surgery group showed a value of 91.24 and 74.11 non-operation. Thus we can conclude that in the final condition, serotonin levels did not show differences between both treatment groups mean it.

From the analysis, p value = .000 which means p <0.05, so it was concluded that there are differences in the initial and final levels of serotonin (serotonin is lower end than the beginning)

Table 8 Levels of Blood Serotonin in the Control Group

Sex	$\bar{T}$otal	×	SD	Min	Max	Range
Male	8	102,225	35.6421	71.7	187.5	115.8
Female	3	76.800	17.534	57.1	90.7	33.6
Total	11	100.382	34.3531	57.1	187.5	130.4

The above data show that groups of men have average levels of serotonin by 102.225 and women's groups at 76.8. In the control group numbered 11 people found normally distributed data by using Kolmogorov-Smirnov test (Z = 0.789 and p = 0.562). With normally distributed data, the parametric analysis will be used for dissecting.

The table below shows the comparative levels of serotonin in patients with the control (no brain injury) using one sample t test.

Level of depression was measured using the HAM-D score after brain injury is post.

Table 9 Comparison of Patients with Controls Serotonin Levels

Serotonin Level	T	df	Signification (2 tails)	Confidens Interval 95%	
				Bottom Score	Above Score
<24 hours	2.870	44	0.006	11.906	68.090
<30 days	-2.467	44	0.018	-24.308	-2.451

From the below data indicate that the group had a median of 19 operational and non operational at 15. By using the Wilcoxon - Mann Whitney p value = 0.182 (p> 0.05) so there was no significant difference from the

mean level of depression among the treatment groups operating with non operational.

Table 10 Level of Depression in the Operations Group and the Nonoperating

Group	Median	Min	Maks
Operation	19	7	29
Nonoperation	15	8	24
All Patient	17.5	7	29

Wilcoxon – Mann Whitney z = -1.334 p = 0.182 (p>0.05)

Once conditions improved, and met the inclusion criteria, patients were examined with the Hamilton rating scale for depression (HAM-D) When classified in several categories such as depressed levels of distribution found in Table 11. In the operation group showed that incidence of depression with the most severe category of 7 people (41.18%), whereas the non-surgery group were mostly suffering from mild depression category as much as eight people (47.06%).

Table 11 Distribution of Level of Depression

Depression Level	Operation	Non Operation	Total
Normal	1 (5.88%)	0 (0.0%)	1 (2.94%)
Low	3 (17.65%)	8 (47.06%)	11 (32.35%)
Average	4 (23.53%)	3 (17.65%)	7 (20.59%)
Severe	7 (41.18%)	4 (23.53%)	11 (32.35%)
Serious	2 (11.76%)	2 (11.76%)	4 (11.76%)
Total	17 (100.00%)	17 (100.0%)	34 (100.0%)

Spearman correlation analysis results obtained with rs = 0.295 and p = 0.090 (p> 0.05), which means there is no correlation between the level of awareness with early blood serotonin levels.

Analysis results obtained with Phi Phi coefficient = 0.342 and p = 0.046 (p <0.05), which means there is a correlation between final blood serotonin levels and the occurrence of depression, where patients with subnormal levels of serotonin have a higher incidence of depression than patients with higher levels of serotonin than normal.

Table 12 Relationship of Blood Serotonin Levels and the Occurrence of Depression End

		Comparation of Serotonin Level in the End and Normal		Total
		Above Average	Below Average	
Prosentasion of Depression	No	0 (0%)	1 (14.3%)	1 (2.9%)
	Yes	27 (100%)	6 (85.7%)	33 (97.1%)
Total		27 (100%)	7 (100%)	34 (100%)

Incidence of depression in serotonin levels in the top end of the normal mean as many as six people (85.7%). while only one person who did not experience depression. Incidence of depression in serotonin levels in the lower end of the normal mean as many as 27 people (100%). and no single person who did not experience depression.

DISCUSSION

From the results, the mean age of study subjects to pasienyang surgery amounted to 27.47 ± 11.48 years, while pasienyang not undergo surgery amounted to 26.12 ± 7.19 years. Pasientermuda aged 16 years, while the oldest 50 years old.

It was found that patients with brain injuries were mostly occur in the productive age group (age group 20-30 years). This is due to the mobility of this age group is higher than other age groups. The incidence and degree of severe brain injury is increasing in line with technological developments and increased population mobility, which is not accompanied with the improvement of discipline and obedience on the road and where other activities (Arifin M 2002).

Also found that patients who suffered a brain injury is largely male-sex. The incidence of brain injury on men more than women possibly due to the mobility of men higher than women in daily activity.

Non-parametric test of Wilcoxon-Mann Whitney found that measuring the level of awareness of patients using GCS scores showed no statistically significant difference with p = 0.181 (p> 0.05) between groups of patients who performed the operation with non operational. In patients with brain injury is coming on days 0 (day in which the injury occurred) showed a median value for GCS score was 10 for group pasienoperasi is to group the median value obtained operating pasiennon 11. From these data we can conclude that patients with surgery and non surgery group had a level of consciousness that is not much different when the patient is examined on the day of injury.

At the beginning of the measurement of serotonin levels in patients with brain injury were taken as sample measurement operation today showed that at the time of the injury showed a mean value of 148.54 with a standard deviation of 59.52. Then the minimum value of the measurement subject to obtain the maximum value 25.6 and 256.2. As for the sample of non operation today showed that at the time of the injury measurements showed mean values with standard

deviation 158.10 135.13. Then the minimum value of the measurement subject to obtain the maximum value of 55.6 and 590.1.

From analysis using unpaired t test where p = 0.791 (p> 0.05) can be seen that there was no significant difference in the mean serotonin levels between sample groups operating with the non-operation. Thus we can conclude that in conditions of less than 24 hours post-injury levels of serotonin showed no difference of mean between the two groups.

At the end of the measurement of serotonin levels on brain injury patients were taken as sample measurement operation today showed that at the time of the injury showed a mean value of 91.24 with a standard deviation of 30.18. Then the minimum value of the measurement subject to obtain the maximum values 46.4 and 153.4. While for the sample of non operation today showed that at the time of the injury measurements indicated a mean value of 74.11 with a standard deviation of 40.89.

Then the minimum value of the measurement subject to obtain the maximum value of 27.6 and 161.1. From analysis using unpaired t test where p = 0.174 (p> 0.05) can be seen that there was no significant difference of mean serotonin levels between sample groups with the non-surgery operations. Thus it can be concluded that in the final condition, serotonin levels did not show differences in mean between the two groups.

At the beginning of the comparison analysis of serotonin levels by the end, using the t test, P = 0.000 result. It means that there are significant differences between early treatment with serotonin levels serotonin levels end of the treatment. Will tend to be high levels of serotonin after injury and will increasingly decreases its value at the end of treatment. Reduced serotonin levels are also correlated with the improvement in patient awareness. This is consistent with research that never existed, which mentions that twenty-four hours after brain injury is serotonin levels in the blood will increase, while the 15-22 days and then serotonin levels would decrease (Ninel et al. 2000).

Normal serotonin levels are shown here as a comparison to the levels of serotonin is a brain injury group. In distribution, the manifold data normal control group. There were limitations on the number-two sampling due to differences in patients where the condition of these patients has improved conditions. Serotonin in the blood can be produced in places such as in the gastroinstestinal cells in the midbrain and the nucleus of the brain raphae. In this study there are limitations in estimating intake of serotonin before the accident therefore required additional examination by anamnesis of food intake in the family.

In measuring the degree of depression as incurred head injuries showed a median value of 19. Then the minimum value of the measurement subject to obtain the maximum value of 7 and 29. As for the sample of non operation today showed that at the time of the injury measurements indicated a mean value of 15. Then, from the minimum value of the subject obtained the maximum value of eight and the value 24.

By using the Wilcoxon-Mann Whitney test showed P = 0.182, so there was no significant difference from the mean level of depression between the group and nonoperasi operation.

Seen that 97.1% incidence of depression in brain injury pasienpasca was depressed. This gives a higher incidence of depression when compared with previous research that says that the depression

Seen that 97.1% incidence of depression in brain injury pasienpasca was depressed. This gives the incidence of depression is higher when compared with previous research that says that most psychiatric symptoms of depression are estimated at between 14-77%, 60% found some time after brain injuries, and 20% found in a few months later (Ashman 2006). Other research also mentions that at one month after the brain injury, with HAM-D evaluation found 26% patients experiencing depression (Simon 2007).

When you see the level of depression sufferers, can be seen that the sample groups operating in the most severely depressed, while in the sample group of non operation ever experienced mild depression.

Differences in level of depression is caused by the sample group who had surgery the mass effect of a brain hemorrhage and has caused brain damage that may damage the more severe monoamine path (Susanto & Mawardi 1994).

Spearman correlation analysis results obtained with rs = 0.295 and p = 0.090 (p> 0.05), which means there is no correlation between the level of awareness with early blood serotonin levels. This suggests that changes in level of consciousness is not directly caused only by changes in blood serotonin levels, but there are several other factors that may cause changes in the level of awareness among the factors before injury (age, psychology, alcohol use, nutrition, drug use) , primary brain damage, secondary brain damage, intracranial factors, acute intervention (resuscitation, the normalization of ICT, fluid and electrolyte hemostasis),

and Extracranial injuries, all play a role in influencing the level of consciousness (Kelly 1996).

Analysis results obtained with the phi coefficient phi = 0.342 and p = 0.046 (p <0.05), which means there is a correlation between final blood serotonin levels and the occurrence of depression, where pasiendengan serotonin levels below normal had a higher incidence of depression compared with levels pasiendengan Serotonin is higher than normal.

Platelets can retrieve, store and 5HT release by a mechanism similar to the central nerve. In patients with head injuries was almost 65% -75% gave a significant decrease in the levels of serotonin than normal people. The reduced value of the platelet and plasma levels have been reported by several researchers. Decreased activity of the serotonergic system may result in a depression (Maes 2000). This shows that in the first three months post-injury emotional symptoms of depression and post-brain injury can disrupt social lives next. Additionally complaints were also found memory loss, impaired concentration and attention (Fenny 2006).

Serotonin is believed play a role in the biochemistry of depression, migraine, and anxiety and sexual disorders and appetite. In brain injury, physical and mental condition of the patient's sudden change, so fair if the patient has many complaints. Certain brain injuries can also be a predisposing factor to incidence of depression. (Susanto &Mawardi 1994).

Depression is the most neuropsychiatric sequelae of brain injury cases, as shown by outpatients and inpatients. Although in most case studies on moderate and severe brain injury, but patients with mild brain injury also have a risk of depression (Jesse & Jay, 2000). Starkstein and Robinson's hypothesis in 1989 stating that the lesion area frontal cortex and basal ganglia in the anterior left hemisphere, will break the monoamine path, so that neurotransmitter receptor regulation decreased or interrupted, resulting in depression (Susanto & Mawardi 1994).

According to a recent study, a closed head injury alleged coup and contra coup cut axonal and contribute significantly to depression through reduction of receptor and termination of the relationship between dorsal and ventral areas of such centers in the hypothalamus, amygdala, and cortical areas (Kathryn 1999).

CONCLUSION

Patients who suffered a brain injury are mostly suffered by the productive age group (21-30 years) as many as 13 people (38.2%) with male sex as many as 28 people (82.4%). This relates to the high mobility of this age group. This incident indicates a higher risk factor in this age group to experience injury than other groups.

There was no significant relationship between the level of consciousness was observed by a score of GCS with serotonin levels in the blood in patients with brain injury is an injury occurred on the day (<24 hours) (P = 0.090).

There is significant correlation between final blood serotonin levels and the occurrence of depression, where patients with below normal levels of serotonin have a higher incidence of depression than patients with higher levels of serotonin than normal (p = 0.046).

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