# THE EFFECTIVITY OF PIRACETAM AND CITICOLIN AMONG INPATIENT HEAD INJURY WITH GLASGOW COMA SCALE (GCS) AT PKU MUHAMMADIYAH YOGYAKARTA HOSPITAL

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### **Abstract**

**Background.** The use of nootropic agent to regulate cerebral function and to improve cognitive impairement in patient with head injury is still controversial. The other fact, piracetam and citicolin as nootropic agent in patient with head injury at RS PKU Muhammadiyah Yogyakarta is used in a great numbers.

**Objective.** This research is aimed to know the profile of the use and to evaluate the effectivity of piracetam and citicolin as a single agent or combination among head injury inpatient at RS PKU Muhammadiyah Yogyakarta during

**Method.** Research conducted with cross sectional analytical study by intake data prospectively, then analyzed patient outcome or clinical response patient qualitatively. The clinical outcome of head injury was measured by Glasgow Coma Scale (GCS).

Result and Conclusion. From 59 head injury patients inclusive, 37,3% was given piracetam, 49,2% was given citicolin, 5,1% was given combination, and 8,5% was given nothing. All of the head injury patients who was given piracetam and citicolin as a single agent or combination and who was not given piracetam and citicolin showed the improvement of consciousness. Based on statistical test, the different mean between the first treatment and the last treatment on the group of piracetam and the group of citicolin was showed statistical significantly difference.

**Keywords:** piracetam, citicolin, head injury, GCS.

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#### **BACKGROUND**

Nootropic agent was first introduced by CE. Guirgea at 1972 (Balaraman and Shingala, 2002). This drug has been used in many countries and claimed to regulate cerebral function by improving cognitive impairement in the brain decreased (Keil et al, 2006).

Piracetam (2-oxo-1-pyrolidine acetamide) is nootropic agent was first discovered and has been used as therapy in stroke and cognitive impairement (Balaraman and Shingala, 2002). Piracetam work at neuronal and vascular level. At the neuronal level, piracetam can improve the fluidity of cell membranes, improving neurotransmission, and stimulate adenylate kinase which catalyzes the conversion of ADP to ATP. At the vascular level, piracetam can increase deformability of erythrocytes so that increase cerebral blood flow, decrease platelet hyperagregation and improve vascular microsirculation (Misbach et al., 2004).

The effectivity of piracetam in various pathological conditions such as brain injury (head injury), stroke, dementia, myoclonus epilepsy, vertigo is controversial (Keil et al., 2006). Piracetam known to have an effect on cerebral blood flow by decreasing the adhesion, aggregation, and erythrocyte deformability, thus improving blood perfusion to the brain (Mahapatra et al., 2008). RCT studies on post-trauma patients showed that low doses piracetam can increase cerebral blood flow and restore perfusion to the brain abnormalities (Agrawal and Gowda, 2007).

Besides piracetam, the other nootropik agent are often used is citicolin. Citicolin (cytidine-5-diphosphocholine) works at neuronal and vascular level. The primary mechanisms in neuronal level is increases the formation of choline and inhibits destruction phosphatidilcholine (inhibiting phospholipase). At the vascular level, citicolin can increase blood flow to the brain, increases oxygen consumption, and lower vascular resistance (Misbach et al., 2004).

The use of citicolin among head injury patients is still controversial. RCTs study in patients with head injuries, showed that citicolin can not decrease patients working days lost and can not improve the quality of life of patients (Aniruddha et al., 2009). At another trial double-blind trials, citicolin can improve cognitive skills, coordination skills, and shorten length of stay in patients with head injury (Anonymous, 2002).

Based on several studies of piracetam and citicolin on head injuries is still controversial, it is necessary to evaluate the effectiveness of its use. The use of piracetam and citicolin in PKU Muhammadiyah Hospital based on data from the last three months is quite a lot, while the price is quite expensive. Piracetam total usage is 1401 (oral dosage), 1178 (injectable preparations), and 932 (intravenous preparation). While the amount of use is citicolin 999 (oral dosage), 3611 (injectable preparation). This fact become one of the reasons why the research was conducted.

#### **METHOD**

The research was conducted with a cross sectional analytic study design, by intake data prospectively and then analyzed patients outcome (clinical response) that occurs after administration piracetam and citicolin. The clinical outcome in patients with head injury was measured by GCS (Glasgow Coma Scale).

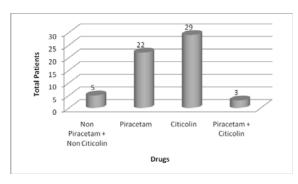
#### RESULT AND DISCUSSION

## 1. Profile of the Use Piracetam and Citicolin

From the result of this study, there are 59 cases of head injury patients in PKU Muhammadiyah Yogyakarta Hospital.

### 2. The Effectivity of Piracetam and Citicolin

In this study, effectiveness of piracetam and citicolin among head injury patients is measured by GCS (Glasgow Coma Scale). The initial measurements was first measured at the time of hospital admission. The measurement is limited in patients who admitted to the hospital



Picture 1. Profile of the Use Piracetam and Citicolin among Head Injury Inpatient at PKU Muhammadiyah Yogyakarta Hospital

24 hours after the patient is hospitalized. The baseline characteristics of patients who received piracetam and citicolin therapy at the time of hospital admission was showed at Table 1.

Clinical manifestation of head injury that

The main conditions among head injury patients is an increase of intracranial pressure. Increased intracranial pressure can cause irreversible brain cell death due to lack of oxygen supply. The earliest sign of increased intracranial pressure is the change of consciousness, dysphasia, decreas of verbal response, and abnormalities of motor response (Rosjidi and Nurhidayat, 2008).

From the observation patients clinical condition at the time of initial hospital admission, most of patients become agitated, confused, and sleepy. This conditions is an important sign of brain compression due to oedema haemorrhage. Some patient loss their consciousness and can not talk (coma). According to Rosjidi and Nurhidayat (2008), worsening of consciousness is a sensitive and

Table 1. Baseline Characteristics of Piracetam and Citicolin among Head Injury Inpatients at PKU
Muhammadiyah Yogyakarta Hospital

Characteristics	Non piracetam + non citicolin	Piracetam	Citicolin	Piracetam+citicolin	
Total of Patients (n)	5	22	29	3	
Age	24,8±19,8	35,0±18,9	33,8±16,1	35,3±31,8	
Length of Stay (days)	5,6±2,3	10,6±8,5 7,9±5,6		9,3±3,1	
Sex (% men)	60,0	63,6	55,2	33,3	
Baseline GCS					
Average 11,2±5,2		11,2±4,3	13,2±2,9	11,7±3,1	
13-15 (%)	60,0	54,5	72,4	33,3	
9-12 (%)	0,0	13,6	20,7		
0-8 (%)	40,0	31,8	6,9	0,0	

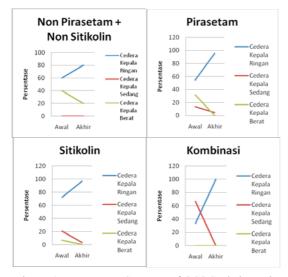
often occurs is the change of consciousness, which is measured using the GCS (Glasgow Coma Scale). The average value of the baseline GCS in citicolin group was 13.2 (mild head injury), while the other group is being in moderate category. However, based on statistical tests of independent T-test, each group did not give significant differences. However, in this study, initial baseline imbalances of GCS give an impact on the overall efficacy in head injury patients.

reliable ratings to identify a possible worsening of neurological condition. So it is necessary to monitor the GCS (Glasgow Coma Scale) to know the patients state of consciousness.

The evaluation of GCS scale has three categories, mild head injury, moderate head injury, and severe head injury. The percentage of each category of GCS in patient with head injury at the time of initial hospitalization and discharge hospital may indirectly indicate the patients GCS development. Picture 2 showed the development

of GCS in each group of drugs among inpatient at PKU Muhammadiyah Yogyakarta Hospital at the time of initial hospitalization and at hospital discharge.

In all groups of head injury patients, the percentage of mild head injury categories when



Picture 2. Percentage Category of GCS Scale in Each Group of Drugs among Inpatient PKU Muhammadiyah Yogyakarta Hospital at the Time of Initial Hospitalization and at Hospital Discharge

experienced improvement of awareness. Although the final percentage of all groups close to 100%, but the slope of the curve in each group are different due to the initial baseline in each group are different. Therefore, the differences in each group can not be evaluated from the slope of the curve.

Table 2 showed the development condition of improved consciousness patient to change the patients consciousness.The patient have improved conditions is the GCS scale shows an increase score, and the patient have worsening conditions if the GCS scale shows decrease score.

Picture 3 presented the average value of GCS at the time of initial hospitalization and at discharge hospital. This picture can evaluate the development of GCS condition among inpatient head injury.

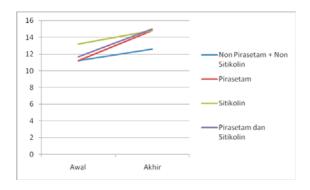
Picture 3 presented that all head injury patients are given piracetam and citicolin as a single agent or combination and who was not given piracetam and citicolin showed the improvement of consciousness. Statistical analysis paired T-Test of each groups. Based on

Table 2. Percentage of GCS Scale Changes at the Time of Hospital Discharge among Inpatient Head Injury at PKU Muhammadiyah Yogyakarta Hospital

	Initial Condition (Total of Patient)				Last Condition [Percentage (%)]		
Drugs	Mild	Moderate	Severe	Total	Improveme nt Condition	No Improveme nt	Worsening Condition
Piracetam	12	3	7	22	54,5	45,4	0,0
Citicolin	21	6	2	29	44,8	51,7	3,4
Piracetam and Citicolin	1	2	0	3	66,7	33,3	0,0
Non Piracetam + Non Citicolin	3	0	2	5	80,0	0,0	20,0

the patient discharge from the hospital are increase almost 100%. It means that the patients

statistical test, the different mean between the first treatment and the last treatment on the group



Picture 3. The Average of GCS (Glasgow Coma Scale) among Inpatient Head Injury at the Time of Initial Hospitalization and Hospital Discharge at PKU Muhammadiyah Yogyakarta Hospital

of piracetam and the group of citicolin was showed statistical significantly difference.

#### **CONCLUSION**

From 59 head injury patients inclusive, 37,3% was given piracetam, 49,2% was given citicolin, 5,1% was given combination, and 8,5% was given nothing. All of the head injury patients who was given piracetam and citicolin as a single agent or combination and who was not given piracetam and citicolin showed the improvement of consciousness. Based on statistical test, the different mean between the first treatment and the last treatment on the group of piracetam and the group of citicolin was showed statistical significantly difference

### REFERENCE

- Agrawal, D., and Gowda, N.K., 2007, Piracetam in Postconcussion Syndrom: preliminary results of a randomized study using SPECT, *In. J*, 4. 2. pp. 109-114.
- Aniruddha, T. J., Pillai, S., Devi, I., Sampath, and Chandramouli, 2009, Role of Citicolin in the Management of Mild Head Injury, *Ind J.*. 6. 1, pp. 49-52.
- Anonimous, 2002, *Citicolin Research*, Immortality Institute-Advocacy & Research for Unlimited Lifespan.

- Balaraman, R., and Shingala, J. 2002., Molecule of the Millenium, *Ind. J Pharmacol*: 34: 439-440.
- Beeker, D., P., Dietrich, W., D., McIntosh, T., K., Marion, D., W., Robertson, C., and Bulluck, R., 2002, *Traumatic Brain Injury: Hope Through Research*, National Institute of Neurological Disorders and Stroke, National Institute of Health (NINDS).
- Dipiro, J., T., Talbet, R., L., Yee, G., C., Matzke, G., R., Wells, B., G., and Posy, L., M., 2008, *Pharmacotherapy: a Patophysiologic Approach* Seventh Ed., Mc Graw Hill Medical, United State.
- Gualtieri, F., Manetti, D., Romanelli, M., N., dan Ghelardini, C., 2002, Design and Study of Piracetam-like Nootropics, Controversial Members of the Problematic Class of Cognition-Enhancing Drugs, *Curr Pharmaceut Design*, 8: 125-138.
- Keil, U., Scherping, I., Hauptmann, S., Schuessel, K., Eckert, A., and Muller, W.E., 2006, Piracetam Improves Mitochondrial Dysfunction Following Oxidative Stress, Br. J Pharmacol; 147 (2): 199-208.
- Koda-Kimble, M., A., Young, L., Y., Alldredge, B., K., Corelli, R., L., Guglielmo, B., J., Kradjan, W., A., and Williams, B., R., 2009, *Applied Therapeutics The Clinical Use of Drugs, Ninth Edition*, Lippincorts Williams and Wilkins.
- Lacy, C., Amstrong, L., Goldman, M., Lance, L., 2009, *Drug Information Handbook*, Lexi Comp Drug Reference Handbooks.
- Mahapatra, A. K., Agrawal, D., and Kumar, R., 2008, Review Article: Minor Head Injury, *Ind J.*. 5 2. pp. 59-62.
- Mahoney, F., I., and Barthel, D., W., 1965, Functional Evaluation: The Barthel Index", Maryland State *Med J.* 14: 56-61.
- Medic8, no year (www.medic8.com).

- Priharjo, R., 2005, *Pengkajian Fisik Keperawatan Edisi 2*, EGC : Jakarta.
- Riyanto, W. B., 2002, Penatalaksanaan Fase Akut Cedera Kepala, *Cermin Dunia Kedokteran* No, 77. Hal: 52-55.
- Rosjidi, C., H., and Nurhidayat, S., 2008, *Buku Ajar Perawatan Cedera Kepala dan Stroke*, Ardana Meia: Yogyakarta.
- Secades, D., D., and Lorenzo, J., L., 2006, Citicolin: Pharmacological and Clinical Review, 2006 Update, PubMed.
- Supraptiningsih, Lamsudin, R., Was'an, M., and Sutanto, 2002, Reliabilitas Modifikasi

- Ideks Barthel pada Penderita Stroke, B. *Neurosains*, 3.: 2: 1-10,
- Wibowo, S., and Gofir, A., 2001, *Farmakoterapi* dalam Neurologi, Jakarta: Salemba Medika.
- Wotton, C., and Phillips, B., 1999, *Stroke:* Piracetam had no Clear Effect on Death or Dependency, The Cochrane Library Issue 2, Oxford.
- Zasler, N., D., and Serio, D., C., tanpa tahun, *Traumatic Brain Injury*, Clinical Neuropsychologist, Rehabilitation of the Injured Combatant. Volume 1.