




Neutrophil Gelatinase-Associated Lipocalin Profile in Critically Ill Patients with Decreased of Consciousness

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Abstract

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BACKGROUND: Neutrophil gelatinase-associated lipocalin (NGAL) is an early marker of renal tubules damage. In critically ill patients, there are significant oxygenation disruptions to many organs particularly the kidneys and the brain. The early recognition of renal abnormalities in patients with a decreased of consciousness may improve the outcomes of these patients.

AIM: The objective of this study was to observe the profile of NGAL in critically ill children with a decreased level of consciousness in Hasan Sadikin Hospital Bandung.

METHODS: A cross-sectional study was performed on critically ill children with a decreased of consciousness in Hasan Sadikin Hospital, Bandung.

RESULTS: Fifty-nine patients aged 2–15-years-old were included in the study. There were 37 males (62.7%) and 22 females (37.2%). In this study, all critically ill patients had elevated urinary NGAL levels with an average value of 606.95 ng/mL (1.20–24629.59 ng/mL). We found that 30% of these patients developed sepsis caused by various etiologies which mostly were malignancy in 22 patients (37.3%) and pneumonia in 14 patients (23.7%). Of all the patients, 16.9% showed clinical improvement.

CONCLUSION: NGAL level is elevated in critically ill patients with a decreased of consciousness.

Introduction

Acute renal impairment/acute kidney injury (AKI) is a sudden kidney dysfunction resulting in the inability acids bases, electrolytes, metabolic waste, and water disposal management. AKI known as acute kidney disorder that is often associated with morbidity and mortality in infants and children, and increased length of stay in intensive care for four times. Delay in treatment of renal disorders in infants and children can be fatal [1], [2], [3], [4]. Nowadays, AKI prevalence is increasing and potentially leads to various complications in patients who are hospitalized [1], [2], [3], [5].

Endogenous markers or biomarkers in serum or urine that can identify early kidney function are very useful, especially in children sepsis, so that the management of a given can be done earlier. The ideal endogenous marker for impaired kidney function is a molecule that increases in urine and serum from several minutes to hours after kidney involvement, which remains elevated for the damage that is still ongoing and quantitatively correlated with the extent of the damage and decreases when the repair process. Some endogenous markers that have been widely used among other creatinine, cystatin C, and neutrophil

gelatinase-associated lipocalin (NGAL). Cystatin C and NGAL are an early biological marker that is sensitive, specific, and are predictive in diverse disease processes [6].

NGAL appears in very low concentrations in various body tissues, including the kidneys, lungs, and gastrointestinal tract, and are produced in increased amounts of epithelial cells that undergo injury. This substance is produced in large quantities in the renal proximal tubular epithelial cells after ischemia, and from several preclinical studies previously showed that NGAL can be easily detected in the urine. NGAL is released from the granules of activated neutrophils, the levels are elevated in infections and inflammation, especially bacterial infections. Plasma NGAL (pNGAL) levels significantly increased in patients with acute renal insufficiency compared to creatinine, whereas urine NGAL (uNGAL) is more sensitive and specific than pNGAL in detecting acute renal disorders in patients after cardiac surgery [6], [7].

At present, research on the endogenous marker of AKI in the pediatric population is limited in patients undergoing cardiopulmonary bypass procedures, and partly on neonates. 17 (29) Research Mc Caffrey, 2015 in 49 patients PICU, showed new biomarker cystatin C serum, pNGAL as well as

uNGAL and kidney injury molecule-1 urine in the early detection of acute kidney disorders, although in patients with acute renal insufficiency due to sepsis, uNGAL better than pNGAL. Cystatin C levels > 0.91 mg/L (sensitivity 75% and specificity 82%) and pNGAL > 258 ng/mL (sensitivity 88% and specificity 62%) are the cut-off point for the early detection of acute kidney disorders. The combination of cystatin C and pNGAL examination will enhance the specificity of up to 92.9% compared to checks only cystatin C alone, or pNGAL only [8].

Children who experience a critical illness can experience a variety of organ disorders. Rate critically ill children need to be detected as early as possible. A variety of tools to detect them is the Pediatric Early Warning Sign (PEWS), Pediatric-Multiple Organ Dysfunction Score, a score of Pediatric Logistic Organ Dysfunction (PELOD), modified Sequential Organ Failure Assessment scores for children, and others. PELOD score is one disease severity scoring system critically ill children which more common [9], [10]. The easiest screening method which done by health workers is PEWS. PEWS consists of three components, namely, ratings behavioral, cardiovascular, and respiratory [10], [11], [12].

When there is a decline in the flow of oxygen toward, the kidney will be accompanied by an impairment of central nervous system. This needs to be detected early to reduce organ damage more severe that patients become better outcomes. This study aims to observe NGAL level in critically ill children with impaired consciousness. Earlier detection in kidney abnormalities will expect better outcomes better.

Methods

All critically ill patients with loss of consciousness' NGAL was checked without waiting for symptoms of kidney impairment. The patient characteristics such as gender, age, and types of diseases were recorded. An examination of uNGAL was performed in the laboratory. At present, there was no cut-off uNGAL level which used to categorize as dangerous. However, when levels of urinary NGAL were detected, its present showed there had been damage in the renal tubules. All data will be processed by SPSS 22.

Results

There were 59 children with impaired consciousness enrolled in this study. Characteristics

Table 1: Characteristics of patients

Characteristics	N
Age	
<5 years	22
5–10 years	31
>10 years	6
Gender	
Male	37 (62.7%)
Women	22 (37.2%)
Types of Diseases	
Sepsis	30%
Malignancy	37.2%
Pneumonia	23.7%
Outcome	
Clinically improved	16.9%
Not improved	83.1%

of subjects as explained in Table 1 showed that all participants had severe condition dan poor outcome.

Table 2 showed that impaired of consciousness caused an increase of urinary NGAL levels but not related to the degree of consciousness itself. Condition of somnolence, soporous, and comatose cause kidney disorders that characterized by an increased of urinary NGAL.

Table 2: Level of NGAL

Consciousness Impairment	N	NGAL Urine ng/mL (min)	NGAL Urine ng/mL (max)	Average NGAL Urine ng/mL
Somnolen	38	1	2000	148,31
Sopor	20	6	24630	1507,76
Coma	1	19	19	19,1

Discussion

AKI in children incidence is high. Approximately 5% of inpatients and up to 30–50% of patients in intensive care were diagnosed as AKI. It was proved that case of AKI was in a high level of vigilance [8]. The early identification of AKI was a vital process which then guides the early intervention to prevent disease progression to ESRD in children, adolescents, and young adults with severe morbidity and mortality [9], [13]. Critically ill children were very risky exposure to a number of conditions that can aggravate the work of the kidneys. These circumstances include: Hypovolemia, hypoxia, inflammation, thrombosis caused by sepsis, systemic inflammation caused by trauma, large-scale operations, as well as medicine.

NGAL appears in very low concentrations in various body tissues, including the kidneys, lungs, and gastrointestinal tract, and is produced in increased amounts of epithelial cells that undergo injury. This substance is produced in large quantities in the renal proximal tubular epithelial cells after ischemia. Several studies showed NGAL can be easily detected in the urine. NGAL is released from the granules of activated neutrophils, the levels are elevated in infections and inflammation, especially bacterial infections. pNGAL levels significantly increased in patients with acute renal insufficiency

compared to creatinine, whereas uNGAL is more sensitive and specific than pNGAL in detecting acute renal disorders in patients after cardiac surgery [6], [7]. This study showed that there were increased NGAL levels in critically ill patients who experience loss of consciousness. The degree of loss of consciousness was not related to the rise in urinary NGAL levels, this might happen due to the effect of the underlying disease.

At Table 3, we can analyze degree of consciousness with level of severity renal dysfunction. Based on RIFLE criteria, our research found that in the early consciousness impairment, there was already failure in the renal (76%). Although in coma stage, we also found failure in the renal but the subject was limited. Our conclusion are NGAL level will be increases in critically ill patients with a decreased of consciousness and we can predict renal injury in the early stage of consciousness impairment. The limitation of this study is limited subject and we suggest to evaluate NGAL periodically.

Table 3: Association between renal injury and consciousness

Consciousness Impairment	n	RIFLE criteria n (%)		
		Injury	Failure	Normal
Somnolen	38	1 (2.6%)	29 (76%)	8 (21.1%)
Sopor	20	3 (15%)	7 (35%)	10 (50%)
Coma	1	0	1 (100%)	0

Chi-square test $P < 0.03$. RIFLE (risk, injury, failure, loss, and end stage renal diseases).

Conclusion

We have to check kidney function earlier in critically ill children with decreased level of consciousness. Long term follow up for neuro development must be done routinely.

References

- Zappitelli M, Goldstein SL. Acute kidney injury: General aspects. In: Kiessling SG, Goebel J, Somers MJ, editors. Pediatric Nephrology in the ICU. Berlin Heidelberg: Springer; 2009. p. 85-97.
- Andreoli SP. Acute kidney injury in children. *Pediatr Nephrol*. 2009;24(2):253-63. <https://doi.org/10.1007/s00467-008-1074-9> PMID:19083019
- Hoste EA, Kellum JA. Acute kidney dysfunction and the critically ill. *Minerva Anesthesiol*. 2006;72(3):133-43. PMID:16493389
- Al-Ismaili Z, Palijan A, Zappitelli M. Biomarkers of acute kidney injury in children: Discovery, evaluation, and clinical application. *Pediatr Nephrol*. 2011;26(1):29-40. <https://doi.org/10.1007/s00467-010-1576-0> PMID:20623143
- Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Acute Dialysis Quality Initiative Workgroup. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: The second international consensus conference of the acute dialysis quality initiative (ADQI) group. *Crit Care*. 2004;8(4):R204-12. <https://doi.org/10.1186/cc2872> PMID:15312219
- Amardiyanto R, Trihono PP, Rundjan L. Acute kidney injury in asphyxiated neonates. *Paediatr Indones*. 2013;53(4):232-8. PMID:16208054
- Nouri S, Mahdhaoui N, Zakhama SB. Acute renal failure in full term neonates with perinatal asphyxia. Prospective study of 87 cases. *Arch Pediatr*. 2008;15(3):229-35. <https://doi.org/10.1016/j.arcped.2008.01.011>
- Nguyen MT, D. P. Biomarkers for the early detection of acute kidney injury. *Pediatr Nephrol* 2008;23:2151-7. <https://doi.org/10.1097/MOP.0b013e328343f4dd> PMID:21252674
- Briguori C, Visconti G, Rivera N. Cystatin C and contrast-induced acute kidney injury. *Circulation*. 2010;121:2117-22. <https://doi.org/10.1161/CIRCULATIONAHA.109.919639> PMID:20439784
- Oldroyd C, Day A. The use of pediatric early warning score in emergency department. *J Emerg Nurs*. 2011;37:374-6.
- Gold DL, Mihalov LK, Cohen DM. Evaluating the pediatric early warning score system too admitted patients in pediatric emergency department. *A Cad Emerg Med*. 2015;21(11):1249-56. <https://doi.org/10.1111/acem.12514> PMID:25377402
- Xun N, Bradley T, Elizabeth D, Hitomi K, Kelley R, Mindi J. Feasibility and reability pediatric early warning sign in the emergency department. *J Emerg Nurs*. 2016;31(2):161-6. <https://doi.org/10.1097/NCQ.000000000000162> PMID:26855268
- Schwartz G, Dana F. Measurement and Estimation of GFR in Children and Adolescents. New York: American Society of Nephrology; 2009.