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Human neutrophil peptide (HNP) in deteriorate sepsis patients[☆]



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KEYWORDS

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Abstract

Objective: The objective of this study was analyzed HNP1 and HNP3 level of deteriorating sepsis patients.

Methods: It was a cross-sectional study that observed HNP and sepsis level, samples size were 40 patients taken by consecutive random sampling. Analysis of HNP serum level use enzyme-linked immunosorbent assay (ELISA), data analyzed used independent T-test and presented in tables with mean, standard deviation, mean difference and probability value.

Results: Results show that when patients become deteriorate or shock sepsis, HNP1 levels increase dramatically, which is 356.2 pg/ml higher than sepsis patients and statistically significant ($p=0.016$, $p \leq 0.05$). It is similar to HNP3 level which is 2.04 ng/ml higher than with sepsis patients and statistically significant ($p=0.021$, $p \leq 0.05$).

Conclusion: This study reveals that HNP1 and HNP3 level increases dramatically in deteriorate sepsis patients. Level of HNP1 and HNP3 of sepsis patient is higher than nonsepsis patient, shock sepsis patient is higher than sepsis patient and both HNP1 and HNP3 level is higher in die patient compare to alive patient.

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Introduction

Although medicine progressed rapidly, the incidence of sepsis continues to exist and leads to high mortality. It is still a priority to clinicians worldwide, especially related organ dysfunction.^{1,2} Organ dysfunction is often used to show the severity of sepsis and mortality.^{3,4}

The immune system has an essential role in sepsis because it is defined as a systemic inflammatory response syndrome (SIRS) after severe microbial infection.^{5,6} One of mediator innate immune is endogen antimicrobial peptide human alpha-defensin, defensin supposed as a natural antibiotic that released by neutrophil degranulation related to Independent killing oxygen mechanism.⁷⁻⁹ Defensin is classified according to its structure as α defensin (3.5–4 kDa) and β defensin (4–6 kDa).¹⁰ Produced by certain leukocyte cells and epithelial cells lining the gastrointestinal tract, urinary tract, respiratory tract, and skin.^{7,10}

Activation of neutrophil during sepsis increased alpha defensin (α -defensin) or human neutrophil peptide (HNP).⁷ Expression of human beta defensin 2 (hBD2) is significantly decreased in a patient with severe sepsis compared to healthy control and nonseptic critically ill patients while plasma level of sepsis patients was significantly higher compared to healthy control and critically ill non-septic patients.¹¹

Some studies have showed increased of HNP in sepsis, HNP has to target as a potential target in the therapy of many diseases such as coronary disease, leishmania, and hypercholesterolemia.¹²⁻¹⁴ The potential use of HNP in predict prognosis or deteriorate sepsis patient is a consideration to prevent severe sepsis or mortality caused by sepsis, but study about it still rare. The objective of this study was analyzed HNP1 and HNP3 level of deteriorating sepsis patients.

Methods

It was a cross-sectional study that observed HNP and sepsis level in Wahidin Sudirohusodo hospital sepsis patients from April to July 2017. Samples size were 49 patients taken by consecutive random sampling. Ethical clearance

has been approved by the ethical committee of Medical Faculty, Hasanuddin University.

Sepsis was defined as an infectious patient accompanied by life-threatening organ dysfunction caused by the dysregulation of the host response to infection based on the consensus results of 2016 sepsis-conference. Organ dysfunction is an acute change characterized by an increase in Sequential Organ Failure Assessment (SOFA) score ≥ 2 points as a consequence of infection. The baseline SOFA score = 0. In an unknown patient had previous organ dysfunction. The SOFA score ≥ 2 points reflects a 10% mortality risk in the hospital's suspect infection population.

Analysis of HNP level use enzyme-linked immunosorbent assay (ELISA), the sample was 3 ml of venous blood samples were taken from every patient within 24 h after the diagnosis of sepsis was established using a gel separator gel. Serum was isolated after blood was centrifuged at $1000 \times g$ for 20 min and stored at -80°C for further analysis. ELISA procedure uses the instruction of the LSBio ELISA kit product.

Results

Characteristics of the subject showed that subject sepsis and nonsepsis patient have a significant difference in age. Sepsis patient was older than nonsepsis patient. There was no difference in gender, but almost blood routine check was significant difference except lymphocytes. Leucocytes and neutrophils of sepsis patient are higher as much as 6496 cells/mm^3 and 7850 cell/mm^3 respectively. Hemoglobin and platelets were lower as much as 3.86 g/dl and 151 cel/mm^3 respectively. The lymphocyte of sepsis patient also lower 246 cel/mm^3 insignificantly (Table 1).

The data in Table 2 show that HNP1 levels differed significantly ($p = 0.000$, $p \leq 0.05$) between sepsis and non-sepsis patients, sepsis patients had higher HNP1 levels of 900.15 ng/ml . HNP3 levels also differed significantly ($p = 0.000$, $p \leq 0.05$) and sepsis patients had higher levels of HNP1 5.37 pg/ml compared with nonsepsis patients.

The data show that when patients become deteriorate or shock sepsis, HNP1 levels increase dramatically, which

Table 1 Characteristic of subject.

Characteristic	Patient		Difference	p-value
	NonSepsis	Sepsis		
Age (year), mean \pm SD	34 \pm 13	52 \pm 15	18	0.000 ^a
Gender, n(%)				
Male	14 (35.0%)	12 (30.0%)	2	0.819 ^b
Female	7 (17.5%)	7 (17.5%)	0	
Hematology, mean \pm SD				
Leucocytes (cell/mm^3)	9984 \pm 5.41	16 480 \pm 8.92	6496	0.008 ^a
Hemoglobin (g/dl)	12.80 \pm 2.73	8.94 \pm 1.69	3.86	0.000 ^a
Platelets ($\times 10^3 \text{ cell/mm}^3$)	306 \pm 8.30	155 \pm 1.13	151	0.000 ^a
Neutrophils (cell/mm^3)	6365 \pm 3.72	14215 \pm 8.48	7850	0.001 ^a
Lymphocytes (cell/mm^3)	1899 \pm 8.34	1653 \pm 2.12	246	0.639 ^a

^a Independent samples T-Test.

^b Chi Square T-Test.

Table 2 Comparison HNP1 and HNP3 level in sepsis and nonsepsis patients.

HNP	Nonsepsis (n=19)	Sepsis (n=21)	Mean difference	p-value
HNP1 (ng/ml)	370.39 ± 2.22	1271.34 ± 3.17	900.95	0.000 ^a
HNP3 (pg/ml)	2.75 ± 1.30	8.12 ± 1.88	5.37	0.000 ^a

^a Independent samples T-Test.

Table 3 HNP1 and HNP3 level in deteriorate patients.

HNP	n	Mean ± SD	Mean difference	p-value
HNP1 (pg/ml):				
Sepsis	15	1169.57 ± 29.66	356.2	0.016 ^a
Shock sepsis	6	1525.77 ± 21.65		
HNP3 (ng/ml):				
Sepsis	15	7.53 ± 1.75	2.04	0.021 ^a
Shock sepsis	6	9.57 ± 1.43		

^a Independent samples T-Test.

Table 4 HNP1 and HNP3 level in surviving and mortal patients.

HNP	Survive n (30) Mean ± SD	Mortal n (10) Mean ± SD	Mean difference	p-value
HNP1 (pg/ml)	690.82 ± 4.89	1301.08 ± 3.73	610.254	0.001 ^a
HNP3 (ng/ml)	4.665 ± 2.914	8.279 ± 2.212	3.614	0.001 ^a

^a Independent samples T-Test.

is 356.2 pg/ml higher than sepsis patients and statistically significant ($p=0.016$, $p \leq 0.05$). It is similar to HNP3 level, which is 2.04 ng/ml higher than with sepsis patients and statistically significant ($p=0.021$, $p \leq 0.05$) (Table 3).

Data show that patients who died had higher levels of HNP1 and HNP3, Level of HNP1 increase 610.254 pg/ml while HNP3 increase 3.614 ng/ml from both HNP1 and HNP3 level of mortal patients significantly differ with surviving patients (Table 4).

Discussion

Level of HNP1 and HNP3 of sepsis patient is higher than nonsepsis patient, shock sepsis patient is higher than sepsis patient and both HNP1 and HNP3 level is higher in die patient compare to alive patient. Majority of sepsis patient is older than nonsepsis patient. Author has been check microbe culture of patient and found that majority of sepsis and die patients did not have microbial growth based on culture examination. It is suggested that their worsening condition may be due to systemic inflammatory response syndrome (SIRS) or immune response becomes or the immune response becomes unfavorable to the host.

Antimicrobial peptide itself such as human neutrophil peptide (HNP) 1–3 recently use as new strategies against infection like tuberculosis and this peptide has benefit in infection condition, HNP inhibits proteolytic cleavage of von

Willebrand factor (VWF).^{15–19} It is a danger when antimicrobial reactions are not able to cope with microbes so that they escape from the process of elimination or this immune response injures host cells themselves.²⁰

The pathogenesis of sepsis is closely related to the immune response system and the coagulation-fibrinolysis system as a genetic predisposing element, which interacts mutually to form a network.²¹ HNP Stored in large quantities (30–50%) and released from neutrophil granules during infection and inflammation.²²

This study can be a basic data to calculate predictor of sepsis and shock sepsis using HNP as a biomarker. It is very important because clinician will make a decision based on HNP calculation. They should aware a warning to try a balance HNP 1 and HNP 3 when HNP 1 increase from 1169 pg/ml or HNP3 9 ng/ml.

HNP also can be a consideration for patients monitoring during sepsis condition. Usually physiologic measurements, laboratory and scoring system parameter such as heart, respiratory rate, blood pressure, platelet count, sodium serum used as sepsis monitoring.^{23,24}

Conclusion

This study reveals that HNP1 and HNP3 level increases dramatically in deteriorate sepsis patients. Level of HNP1 and

HNP3 of sepsis patient is higher than nonsepsis patient, shock sepsis patient is higher than sepsis patient and both HNP1 and HNP3 level is higher in mortal patient compare to survive patient.

Conflict of interest

The authors declare no conflict of interest.

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