

Clinical significance of plasma levels of brain natriuretic peptide and cardiac troponin T in patients with sepsis

JIFENG WANG, WENLI JI, ZHENGQIN XU and TAO PAN

Department of Intensive Care Medicine, Xiangyang Hospital Affiliated to Hubei University of Medicine, Xiangyang, Hubei 441000, P.R. China

Received September 10, 2015; Accepted November 12, 2015

DOI: 10.3892/etm.2015.2863

Abstract. Sepsis is a systemic inflammatory response of the body to an antigen and can become a life-threatening condition by triggering a cascade of changes leading to multiple organ failure such as heart failure. The aim of the present study was to examine the changes of the plasma levels of N-terminal of the prohormone brain natriuretic peptide (NT-proBNP) and cardiac troponin T (cTnT) in patients with sepsis and to analyze their prognostic significance. A total of 38 hospitalized patients with sepsis were included in the present study. The patients were divided into the survival and death groups, based on their prognosis. The plasma levels of NT-proBNP and cTnT for the two groups were measured for all the patients on the 1st, 3rd and 7th day of admission. The plasma levels of NT-proBNP and cTnT between the two groups were compared and their association with prognosis were analyzed. The plasma levels of NT-proBNP and cTnT in the death group were significantly higher than those in the survival group ($P < 0.05$). Additionally, a positive association of the plasma levels of NT-proBNP and cTnT was identified ($P < 0.05$). In conclusion, the plasma levels of NT-proBNP and cTnT may be used as routine clinical biomarkers to assess the prognosis of patients with sepsis.

Introduction

Sepsis is a systemic inflammatory response of the body to an antigen (1) caused by infection. Severe sepsis can lead to 27 organ dysfunction and/or tissue perfusion, and even shock (2). It can become a life-threatening condition by triggering a cascade of changes leading to multiple organ failure. Sepsis has a relatively high incidence in intensive care unit (ICU) in Poland (3). The majority of deaths associated with sepsis

are incurred by organ failures, especially heart failures (4,5). However, there is a lack of effective biomarkers that facilitate prognosis. N-terminal of the prohormone brain natriuretic peptide (NT-proBNP) and cardiac troponin T (cTnT) are myocardial injury markers. These markers are used as a screening tool for the diagnosis of cardiovascular complications (6). Different levels of NT-proBNP and cTnT in the plasma of patients with sepsis may play different roles on the prognosis of the disease (7-9).

In the present study, 38 cases of hospitalized patients having sepsis were investigated to examine the plasma levels of NT-proBNP and cTnT and to investigate their prognostic significance. The results showed that the plasma levels of NT-proBNP and cTnT may be used as routine clinical biomarkers to assess the prognosis of patients with sepsis.

Materials and methods

Patients. A total of 38 cases were identified from the ICU of the Xiangyang Hospital Affiliated to Hubei University of Medicine (Hubei, China). Patient diagnosis was confirmed as per the criteria issued in 2001, by the American College of Chest Physicians or Society of Critical Care Medicine (10). Any patients with acute coronary syndrome, congestive heart failure and increasing levels of NT-proBNP and cTnT incurred by cardiopulmonary resuscitation, cardiothoracic surgery, hepatic and renal dysfunction within one month, were excluded. Of the 38 cases, 21 cases were male and 17 cases were female, with an age of 52-71 years. Following admission, the patients were administered early fluid resuscitation and bundle treatment in accordance with the guidelines (2). The levels of NT-proBNP and cTnT as well as organ functions were monitored. Based on their prognosis, the patients were divided into the survival and death groups. The survival group comprised 22 cases, 13 cases were male and 9 cases were female, with an average age of 57.96 ± 13.66 years. The infection sites identified were as follows: 13 cases, lung; 5 cases, abdomen; 1 case, urinary tract and 3 cases, other sites. The death group included 16 cases with 8 cases being male and 8 cases being female, with an average age of 60.94 ± 10.03 years. The infection sites for this group were: 11 cases, lung; 3 cases, abdomen; 1 case, urinary tract and 1 case, other site. Differences regarding age, gender, and infection site between the two groups were not statistically significant ($P > 0.05$).

Correspondence to: Dr Wenli Ji, Department of Intensive Care Medicine, Xiangyang Hospital Affiliated to Hubei University of Medicine, 15 Jiefang Road, Xiangyang, Hubei 441000, P.R. China
E-mail: 1366346747@qq.com

Key words: N-terminal of the prohormone brain natriuretic peptide, cardiac troponin T, sepsis

Table I. Comparison of the level of NT-proBNP between the survival and death groups on the 1st, 3rd and 7th day of admission.

Group	NT-proBNP (pg/ml)		
	Day 1	Day 3	Day 7
Survival group	1839.14±1060.27	2786.21±1206.23	2074.08±970.43
Death group	3965.74±1462.65	6268.56±1825.49	5384.46±1049.62
P-value	<0.05	<0.05	<0.05

NT-proBNP, N-terminal of the prohormone brain natriuretic peptide.

Blood sampling. Venous blood (3 ml) was collected from patients under quiescent condition every morning on the 1st, 3rd and 7th day of admission. The blood samples were placed into test tubes with EDTA to prevent anticoagulation and were immediately sent for analysis to determine NT-proBNP and cTnT levels.

Analysis for NT-proBNP and cTnT. The NT-proBNP detector was provided by Roche Diagnostics GmbH (Mannheim, Germany), combined with electrochemiluminescence for detection of plasma levels. Detection was carried out strictly by a specially-assigned pathologist. The normal reference value was taken as <900 pg/ml. Electrochemiluminescence was applied to measure the level of serum cTnT. A detector was produced using the kit provided by Roche Diagnostics GmbH. The normal reference value was considered as 0.1 ng/ml.

Statistical analysis. SPSS 20.0 statistical software (IBM SPSS, Armonk, NY, USA) was used for statistical analysis. Measurement data were presented by mean ± standard deviation, and the t-test was applied to make comparisons between groups. The linear correlation analysis was performed to determine any correlations between NT-proBNP and cTnT. P<0.05 was considered to indicate a statistically significant difference.

Results

As shown in Table I, the level of NT-proBNP in the death group was significantly higher than that in the survival group and the difference was statistically significant (P<0.05). Similarly the levels of cTnT were significantly higher than those in the survival group (P<0.05) (Table II).

The correlation analysis between NT-proBNP and cTnT showed that the blood levels of NT-proBNP and cTnT in patients with sepsis showed a significantly positive correlation ($r=0.756$, P<0.05). Thus, NT-proBNP and cTnT levels are increased in the plasma collectively in a directly proportional manner.

Discussion

Sepsis is a type of systemic inflammatory response syndrome resulting from infection. Myocardial damages incurred by sepsis, also known as pyemic cardiomyopathy or pyemic myocardial dysfunction, likely increases the mortality risk of sepsis (7,8). At least one half of mortalities associated with

Table II. Comparison of the level of cTnT between survival and death groups on the 1st, 3rd and 7th day of admission.

Group	cTnT (pg/ml)		
	Day 1	Day 3	Day 7
Survival group	0.53±0.21	0.68±0.17	0.62±0.23
Death group	1.03±1.04	1.57±0.86	1.38±0.53
P-value	<0.05	<0.05	<0.05

cTnT, cardiac troponin T.

sepsis were caused by the impairment of the cardiovascular system (10). During sepsis, regional blood flows abnormally, leading to microcirculation disturbance and resulting in the ischemia of various organs, including the heart as well as mitochondrial structural change on myocardial cells. This condition eventually results in cell metabolic dysfunction and eventually death (11,12). In clinic, NT-proBNP and cTnT are usually used as markers to reflect myocardial injury.

Sepsis usually concurs with cardiac insufficiency (13-15). Under sepsis condition, a large amount of fluids or media produces a toxic effect on the heart. When the entire body becomes affected by a strong inflammatory reaction, the homeostasis of cardiovascular system changes, leading to cardiac insufficiency. Early ventricular systolic dysfunction has been proven in patients with sepsis (16). NT-proBNP mainly primarily stems from ventricle. Patients with cardiac failures showed higher levels of NT-proBNP in plasma, suggesting an important indication for heart failure diagnosis, treatment and prognosis. Current investigations have confirmed that the level of NT-proBNP on patients with sepsis is likely to increase (17-19). However, myocardial function impairment was not the only factor likely to result in the increase of NT-proBNP. Charpentier and other authors (20-22,28) have determined that the increase of certain NT-proBNP was associated with the increased secretion or reduced inactivation of NT-proBNP under an inflammatory response. Therefore, the basic pathophysiological changes of sepsis may be a reason for the increase of the NT-proBNP level (23-25). The results of our study have shown that the plasma level of NT-proBNP in patients with sepsis was significantly increased and that of the death group was significantly higher in comparison to

the survival group. The result was consistent with the above-mentioned study results.

Cardiac troponin is an important protein that could adjust the contraction of striated muscle (17,26,27). When the myocardium cell membrane of heart is intact, cTnT is unable to get into the blood circulation. Thus, the plasma in healthy individuals usually has no or a low level of cTnT. The mechanism for the increasing level of cTnT in patients with sepsis remains to be determined. It was estimated that myocardial damage in patients with plasma may be associated with the direct damage on myocardial cells incurred by the release of a large amount of cytokines and reactive oxygen species and the toxic effect of bacterial endotoxin on myocardial cells subsequent to bacterial infection (28). Sepsis is always accompanied with microcirculation disturbance, which results in the ischemia of myocardial cells and reperfusion damage. When myocardial cells are impaired, the cytomembrane suffers damage and therefore cTnT is released into the blood, and becomes evident as higher levels in plasma. The increasing level of troponin may reflect a worse myocardial function, and is potentially associated with the patient prognosis (29). The results of our study have shown that the change of level of myocardial injury markers was significantly different between the survival and death groups. The level of cTnT in the death group was significantly higher than that in the survival group, indicating that the myocardial troponin level in patients with sepsis was positively associated with the severity of disease. There are currently no reports confirming that the level of troponin may be used as an independent predictor for prognosis of patients with sepsis. Therefore, this aspect remains to be investigated.

The result of the correlation analysis showed that the plasma levels of NT-proBNP and cTnT in the death group were significantly higher than those in the survival group, and the plasma levels of NT-proBNP and cTnT were positively correlated, indicating that the increasing levels of NT-proBNP and cTnT exert a predictive effect on the prognosis of patients with sepsis.

In conclusion, monitoring of the levels of NT-proBNP and cTnT is crucial and can demonstrate the status of cardiac health with a potential to circumvent the severity of disease.

References

- Bentzer P, Russell JA and Walley KR: Advances in sepsis research. *Clin Chest Med* 36: 521-530, 2015.
- Guidelines for treatment of severe sepsis/septic shock in China. *Crit Care Med* 6: 401-426, 2015 (In Chinese).
- Kübler A, Adamik B, Ciszewicz-Adamiczka B and Ostrowska E: Severe sepsis in intensive care units in Poland - a point prevalence study in 2012 and 2013 *Anaesthesiol Intensive Ther* 47: 315-319, 2015.
- Zhang D, Li H and Li J: The change of cardiac troponin I on patients with sepsis and septic shock as well as its clinical significance. *J Pract Med* 27: 49-51, 2011.
- Wang X, Wei S and Li T: The application of coagulation-fibrinolysis dynamic graph on the detection of sepsis coagulation fibrinolytic imbalances. *Chongqing Med J* 37: 1706-1708, 2008.
- Altintas Z, Fakanya WM and Tothill IE: Cardiovascular disease detection using bio-sensing techniques. *Talanta* 128: 177-186, 2014.
- Jiang Z and Ye GY: 1:4 matched case-control study on influential factor of early onset neonatal sepsis. *Eur Rev Med Pharmacol Sci* 17: 2460-2466, 2013.
- Mahmoudi L, Mohammadpour AH, Ahmadi A, Niknam R and Mojtahedzadeh M: Influence of sepsis on higher daily dose of amikacin pharmacokinetics in critically ill patients. *Eur Rev Med Pharmacol Sci* 17: 285-291, 2013.
- Liu YJ, Du P and Rao J: Procalcitonin as a diagnostic and prognostic marker for sepsis caused by intestinal infection: a case report. *Eur Rev Med Pharmacol Sci* 17: 1311-1313, 2013.
- Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL and Ramsay G; International Sepsis Definitions Conference: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definition Conference. *Intensive Care Med* 29: 530-538, 2003.
- Jozwiak M, Persichini R, Monnet X and Teboul JL: Management of myocardial dysfunction in severe sepsis. *Semin Respir Crit Care Med* 32: 206-214, 2011.
- Pulido JN, Afessa B, Masaki M, Yuasa T, Gillespie S, Herasevich V, Brown DR and Oh JK: Clinical spectrum, frequency, and significance of myocardial dysfunction in severe sepsis and septic shock. *Mayo Clin Proc* 87: 620-628, 2012.
- Zhang XH, Dong Y, Chen YD, Zhou P, Wang JD and Wen FQ: Serum N-terminal pro-brain natriuretic peptide level is a significant prognostic factor in patients with severe sepsis among Southwest Chinese population. *Eur Rev Med Pharmacol Sci* 17: 517-521, 2013.
- Celik IH, Demirel G, Oguz SS, Uras N, Erdevi O and Dilmen U: Compassionate use of voriconazole in newborn infants diagnosed with severe invasive fungal sepsis. *Eur Rev Med Pharmacol Sci* 17: 729-734, 2013.
- Shen ZG, Guo JL and Li DS: Screening of differentially expressed genes related to severe sepsis induced by multiple trauma with DNA microarray. *Eur Rev Med Pharmacol Sci* 18: 734-739, 2014.
- Werdan K, Schmidt H, Ebel H, Zorn-Pauly K, Koidl B, Hoke RS, Heinroth K and Müller-Werdan U: Impaired regulation of cardiac function in sepsis, SIRS, and MODS. *Can J Physiol Pharmacol* 87: 266-274, 2009.
- Zhou FJ, Zhou CY, Tian YJ, Xiao AJ, Li PL, Wang YH and Jia JW: Diagnostic value of analysis of H-FABP, NT-proBNP, and cTnI in heart function in children with congenital heart disease and pneumonia. *Eur Rev Med Pharmacol Sci* 18: 1513-1516, 2014.
- Ding YJ, Han B, Yang B and Zhu M: NT-proBNP plays an important role in the effect of ibuprofen on preterm infants with patent ductus arteriosus. *Eur Rev Med Pharmacol Sci* 18: 2596-2598, 2014.
- Russo A, Scagliusi A, Scarano A, Bevilacqua F, Di Stasio E, Polidori L and Marana E: Influence of pneumoperitoneum on left ventricular filling pressures and NT-proBNP levels. *Eur Rev Med Pharmacol Sci* 16: 1570-1575, 2012.
- Kara S, Tonbul A, Karabel M, Akca H, Uras N and Tatli M: The role of serum N-terminal pro-brain natriuretic peptide in transient tachypnea of the newborn. *Eur Rev Med Pharmacol Sci* 17: 1824-1829, 2013.
- Chen K, Jiang RJ, Wang CQ, Yin ZF, Fan YQ, Cao JT, Han ZH, Wang Y and Song DQ: Predictive value of plasma galectin-3 in patients with chronic heart failure. *Eur Rev Med Pharmacol Sci* 17: 1005-1011, 2013.
- Shao N and Xie M: The impairment influence of sepsis on myocardial mitochondria. *China Med Her* 5: 23-24, 2008.
- Chagnon F, Bentourkia M, Lecomte R, Lessard M and Lesur O: Endotoxin-induced heart dysfunction in rats: assessment of myocardial perfusion and permeability and the role of fluid resuscitation. *Crit Care Med* 34: 127-133, 2006.
- Post F, Weilemann LS, Messow CM, Sinning C and Münzel T: B-type natriuretic peptide as a marker for sepsis-induced myocardial depression in intensive care patients. *Crit Care Med* 36: 3030-3037, 2008.
- Ji X, Duan M and Li: Diagnostic value of NT-PROBNP detection on pyemic myocardial damage. *Mol Cardiol Chin*: 207-209, 2010.
- Xu R, Lu R, Jiang H, Li QF, Sun Y, Xu H and Huang Y: Meta-analysis of protective effect of sevoflurane on myocardium during cardiac surgery. *Eur Rev Med Pharmacol Sci* 18: 1058-1066, 2014.
- Casagrande I and Lauritano EC: Diagnostic and prognostic significance of high sensitive troponin in chest pain. *Eur Rev Med Pharmacol Sci* 15: 695-700, 2011.
- Charpentier J, Luyt C-E, Fulla Y, Vinsonneau C, Cariou A, Grabar S, Dhainaut JF, Mira JP and Chiche JD: Brain natriuretic peptide: A marker of myocardial dysfunction and prognosis during severe sepsis. *Crit Care Med* 32: 660-665, 2004.
- Li T, Liu JJ, Du WH, Wang X, Chen ZQ and Zhang LC: 2D speckle tracking imaging to assess sepsis induced early systolic myocardial dysfunction and its underlying mechanisms. *Eur Rev Med Pharmacol Sci* 18: 3105-3114, 2014.