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The Dynamic Measurement of Procalcitonin in Neonatal Purulent Meningitis

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Abstract

Neonatal purulent meningitis is a significant cause of neonatal disability and death. The early diagnosis and effective treatment are critical for neonatal purulent meningitis. Procalcitonin (PCT) is currently used as a clinical diagnosis marker of inflammation and infection, such as sepsis. Due to the lower immunity of neonates and the atypical symptoms of neonatal purulent meningitis, it is challenging to obtain reliable information of the development, diagnosis, treatment and prognosis of neonatal purulent meningitis. This study monitored the dynamic change of the PCT levels in 48 neonatal patients after the standard treatment and found out that the PCT level may not be a distinguish diagnosis marker but a useful indicator for efficacy of the treatment and prognosis specifically in neonatal purulent meningitis.

Keywords: Neonatal purulent meningitis; Procalcitonin; Diagnosis; Prognosis

Introduction

Neonatal purulent meningitis usually happens in infants within three months old and caused by varies bacterial spread and rapid multiplying in the subarachnoid space of the meninges. It is a severe infection leading to a high mortality and disabling. The common clinical signs of neonatal purulent meningitis, including fever, poor feeding, lethargy and seizure, are commonly shown up in other pathological conditions such as bacterial infection and pneumonia [1,2]. Procalcitonin (PCT), a precursor of the calcitonin is a 13 kDa protein with 116 amino acids, synthesized in the parafollicullar cells of the thyroid, and the neuroendocrine cells in the lung and the intestine. Blood PCT level in a healthy adult is relatively low and even below the common clinical detection limitation. In normal newborns the PCT level increased up to 41 ng/ml during the first 12-23 hours after birth and came back to lower level around 9 ng/ml at the 48 hours after birth [3]. PCT level usually is elevated in an individual with a bacterial infection, but not with a viral infection [1,4]. Therefore, PCT level has been reported as a biomarker for early diagnosis of bacterial infection with a sensitivity of 76% and specificity of 70% [1,5,6]. In a cluster randomized clinical trial the level of PCT was successfully used to guide antibiotic therapy in a pneumonia treatment [7] while in another study it was reported with limited prognostic value [8]. To clarify whether PCT can be used as a clinical iagnosis/prognosis marker for neonatal purulent meningitis, we conducted this study that comprised 48 neonatal patients with purulent meningitis.

Subjects and Methods

Total 48 neonatal patients were included in this study, including 37 male and 11 female hospitalized at Department of Neonatology in First People's Hospital during the period from February 2011 to November 2013, with the age ranging from three to 30 days. The standard treatment was applied immediately after diagnosis confirmed following standard criteria and protocols [9]. Briefly antipyretics were applied when the body temperature was above 38.5°C, anti-seizures and antibiotic therapy based on the patients' condition and pathogen detected. All the patients had been screened to eliminate viral meningitis and other comorbidities. After treatments, 29 of the patients recovered without complication, 14 of the patients improved with varied complications along with five death. In this study the subjects were divided into two groups, the first group (A) composed the patients recovered without complication (29 patients) and the second group (B) composed the patients with complications, including death (19 patients). There were no significant difference of treatments between group A and B (Table 1).

Groups	n	gender	Age (days)	Median age (days)	WBC2 in CSF3	pathogen
A	29	21M/8F	3-30	19	>20x109/L	Bacteria4
B	19	16M1/3F	4-29	20	>20x109/L	Bacteria4

Table 1: The information of the patients and the grouping; 1:The five death are all male. 2: WBC--white blood cell; 3: CSF--cerebrospinal fluid; 4: E.coli, group B streptococci, and Staphylococci were detected.

In this study, three ml vein blood after three hour fasting was collected for centrifuge (3,500 rpm for five minutes) and the serum was used for PCT detection. The elecsys BRAHMS PCT assay kit were used to measure the serum PCT level on the Roche Cobas E601 analyzer according to the manufacturer's protocol (elecsys BRAHMS PCT, Roche, Mannheim, Germany). Besides PCT, cerebrospinal fluid (CSF) were collected through Lumbar puncture (LP) and used for microscopic smear, microbial culture, white blood cell (WBC) counting, protein and glucose measurement. Bacteria, including *E.coli*, group *B streptococci*, and Staphylococci were detected in CSF of all the patients and the distribution of the individual bacterial species did not

show significant difference between group A and B. The WBC counts were elevated, mostly above 20x109/L. Protein levels were in the range of 1.3-5.1 g/L and glucose levels were in the range of 1.8-2.2 mmol/L. All these CSF parameters were measured before treatment and showed no significant difference between group A and B.

Statistical analysis was conducted with software SPSS 17.0 and the Student's t-test was used to compare the PCT level after the treatment with its level before the treatment. The statistical significance is set at *: $p<0.05$, ** $p<0.01$.

Results

The serum PCT level was measured at three time points: before the treatment, 48 hours after the initiation of treatment, 72 hours after the treatment. Before the initiation of treatment, all the patients had elevated PCT levels that were not significantly different from other pathological conditions such as neonatal sepsis and neonatal bacterial pneumonia (unpublished observation). After the initiation of treatment, the PCT levels changed in different ways in group A and B. In group A, all the patients had significantly decreased PCT levels after 48 hours of the initiation of treatment, and kept low after 72 hours of treatment ($p = 0.007$ and 0.004 respectively, Figure 1). In group B, the average of PCT levels of most patients were kept high along with the treatment. Four of the 19 patients in group B had decreased PCT levels at 48 hours ($p=0.054$) after the treatment, but their PCT levels elevated again at 72 hours after the treatment. There were five death in group B that were all male, and the PCT level in these five patients were kept high all the time during the treatment. The average of PCT level in group A and B had no significant difference before the treatment, but had significant difference after treatment at 48 hours and 72 hours ($p = 0.005$ and 0.003 respectively, Figure 1).

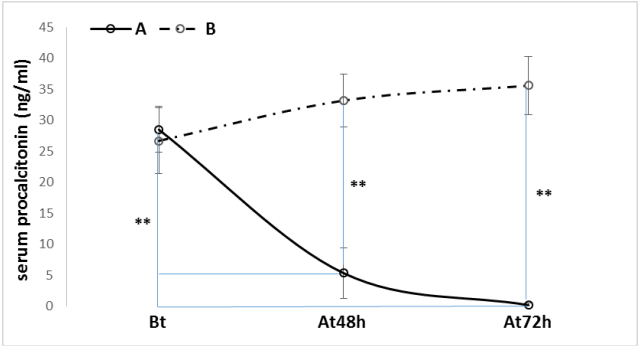

Figure 1: The dynamics of serum procalcitonin level in neonatal purulent meningitis

Before the treatment the procalcitonin level in group A and B were similar. After the initiation of treatment, PCT levels in group A decreased significantly at 48 hours ($p =0.007$) and 72 hours ($p = 0.004$) compared with that before treatment. Meanwhile, the PCT levels in group A and B showed significant difference at 48 hours ($p =0.005$) and 72 hours ($p = 0.003$) after treatments. A: the group of patients recovered well after treatment, in solid line; B: the group of patients improved with complications or death, in dash line. Bt: before the treatment; At 48h: 48 hours after treatments; At 72h: 72 hours after treatments. **: $p<0.01$.

Discussion

Among several infectious conditions including neonate purulent meningitis the PCT level was a more sensitive indicator than C-reactive protein (CRP), although the increased range of the PCT levels in neonate purulent meningitis was overlapped with systemic inflammatory response syndrome (SIRS) and neonatal sepsis [10]. PCT levels were found significantly higher in patients with bacterial meningitis and other CSF parameters, such as blood leukocytes, and CRP showed overlapping values [11]. Other reports indicated that PCT levels with proper cutoff value could be used in early diagnosis of bacterial meningitis but they did not do the prognosis evaluation [12]. PCT level was also reported as biomarker in diabetic ulcer with combination of other markers like WBC, CRP and erythrocyte sedimentation rate (ESR) while the prognosis value of PCT level was not studied[13]. Interestingly, PCT level was used as a biomarker to guide antibiotic therapy in pneumonia treatment for prognostic purpose [7].

In our study we found that the dynamic measurement of serum PCT levels is more reliable than a single point measurement. For example, there were four patients in group B showed deceased PCT levels at 48 hours but increased levels at 72 hours after the treatment. Thus the dynamic measurement of serum PCT levels is a substantial indicator to evaluate the efficacy of the treatment and predicate prognosis. It is clear that the significantly decreased serum PCT level along with an improved pathological condition lead to a full recovery. On the other hand, the increased PCT level, or temporally decreased PCT level indicates varied complications and even death. By our knowledge this study is the first report of the dynamic PCT measurement in neonatal purulent meningitis. The dynamic observation of PCT level would be important for clinical evaluation of treatment and prognosis at least in neonatal purulent meningitis. Nevertheless, more patients, more time points and thoroughly analysis of PCT associate factors such as CRP, polymorphonuclear leukocytes and corresponding pathogens would greatly enhance the conclusion.

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