Medical Hypotheses 94 (2016) 77–80

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

In the diagnosis of neonatal sepsis importance of gelsolin and relationship with mortality and morbidity

Hülya Halis [a,*], Tamer Gunes [a], Sabriye Korkut [a], Berkay Saraymen [b], Ahmet Şen [b], Osman Bastug [a], Adnan Öztürk [a], Selim Kurtoğlu [a]

[a] Erciyes University Medical Faculty, Department of Pediatrics, Division of Neonatology, Talas Street, 38039 Kayseri, Turkey
[b] Erciyes University Medical Faculty, Department of Biochemistry, Talas Street, 38039 Kayseri, Turkey

ARTICLE INFO

Article history:
Received 27 January 2016
Accepted 13 June 2016

Keywords:
Neonatal sepsis
Gelsolin

ABSTRACT

In spite of advances in neonatal care and the new generation of antibiotics, neonatal sepsis is still a major cause of morbidity and mortality. Early diagnosis of neonatal sepsis is difficult because clinical signs are non-specific. Thus, new biomarkers are still needed for diagnosis. Gelsolin is an actin-binding plasma protein. Furthermore, extracellular gelsolin binds lipopolysaccharide and lipoteichoic acid, which are major virulence factors of Gram-negative and Gram-positive bacteria. The result of this binding is the inhibition of gelsolin's F-actin depolymerizing activity. Thus, gelsolin inhibits the release of IL-8 from human neutrophils subjected to lipoteichoic acid, lipopolysaccharide and heat-inactivated bacteria treatment. Our hypothesis is that pGSN levels decrease in neonatal infants with sepsis and this decrease might be used as a reliable biological marker. Forty patients who were diagnosed with severe sepsis at a neonatal intensive care unit were enrolled in the sepsis group. Twenty patients who were followed for prematurity were enrolled in the control group. The pGSN level at the time of diagnosis in the sepsis group was 33.98 ± 11.44 μg/ml, which was significantly lower than that of control group (60.05 ± 11.3 μg/ml, $P < 0.001$) and after treatment (53.38 ± 31.26 μg/ml, $P = 0.003$). Area under ROC curve was 0.96 (p: 0.0001, 95% CI; 0.90–0.99). Sensitivity was 90.32 (95% CI; 74.2–97.8), specificity was 95 (95% CI; 75.1–99.2). Plasma gelsolin significantly decreased in septic patient and recovery of decreased gelsolin levels correlated with clinical improvement. Thus, plasma gelsolin may be a usable marker for severe sepsis.

© 2016 Elsevier Ltd. All rights reserved.

Introduction

Gelsolin is a multi-functional Ca^{+2} dependent actin-regulating protein that circulates in healthy human plasma [1]. Gelsolin has 3 isoforms two of which are cytoplasmic and one is secretory extracellular plasma isoform. These are namely mature plasma (secretory) gelsolin (pGSN), cytoplasmic gelsolin (cGSN) and gelsolin-3 which is non-secretory minor form [2]. Actin has a role in regulation of dynamics, cell motion, phagocytosis, apoptosis regulation, thrombocyte modulation and signal transmission as well as showing anti-inflammatory and transcriptional cofactor activity [3]. Although the normal level of gelsolin in human being is between 190 and 300 mg/L (in average 250 mg/L), some variety about pGSN levels due to different methods had been reported previously [4–6].

Gelsolin is found in amniotic and cerebrospinal fluid in second trimester [7,8]. Plasma form composes one of the two proteins of extracellular actin-cleaning system and makes depolymerization and separation of actin which enters the circulation after cell damage and cell death [9]. cGSN is with Fc-receptors and has a role in integrin-mediated phagocytosis. pGSN has an actin-cleaning function. Plasma gelsolin tears off and clears the actin filaments secreted by the cells during inflammation and infection period [10,11]. Various organ injuries and diseases cause long duration decrease in pGSN levels. It was reported that degree of this decrease in gelsolin levels is inversely proportional to duration of mechanic ventilation, intensive care unit staying and duration of hospitalization period [4,5,12]. It was demonstrated in animal

* Corresponding author.
E-mail addresses: drhhalis@yahoo.com (H. Halis), trgunes@yahoo.com (T. Gunes), sabriyeyaman@hotmail.com (S. Korkut), berkaysaraymen@gmail.com (B. Saraymen), ahmet369@yahoo.com (A. Şen), drosman76@hotmail.com (O. Bastug), adozturk@erciyes.edu.tr (A. Öztürk), selimchief@gmail.com (S. Kurtoğlu).

http://dx.doi.org/10.1016/j.mehy.2016.06.017
0306-9877/© 2016 Elsevier Ltd. All rights reserved.

models that the recombinant gelsolin infusion in moderate doses decreases mortality and prevents the damage due to hyperoxia, burn and sepsis conditions [13–15].

We designed this study in preterm infants with sepsis, in order to investigate the change in plasma gelsolin levels and re-evaluation of this change after treatment and its relation to mortality. Also searched whether pGSN levels may be a new biomarker for neonatal sepsis or not.

Hypothesis

Gelsolin may be used in various diseases as a marker detected in peripheric blood. Considering the present knowledge, gelsolin concentration is sensitive; for instance the direct sequence of gelsolin confirms the diagnosis of amyloidosis. Gelsolin determines the metastatic potential in cancer through actin remodeling. Gelsolin is also important in cardiovascular diseases, an increase might be a sign of chronic heart failure whereas its decrease in acute myocardial infarct may be a marker of the severity of acute disease [3]. Our hypothesis is that pGSN levels decrease in neonatal infants with sepsis and this decrease might be used as a reliable biological marker.

Evaluation of the hypothesis

We designed a prospective cohort study to test this hypothesis and collected pilot data. Blood samples of all infants born between January 2013 and December 2013 at our university hospital were collected after parental consent. The study included 60 preterm infants with gestational age between 24 and 34 weeks. Sepsis study group included 40 of them and control group included 20 of them. All infants presenting of the clinical signs of sepsis such as hypothermia or fever, tachypnea, cardiorespiratory instability, lethargy, feeding intolerance were evaluated for sepsis with a complete blood count, peripheral blood smear, C-reactive protein and cultures. According to Töllner score which is often used in diagnosis of sepsis [16] the cases with scores >5 were detected and empirical antibiotic treatment was initiated following blood sample taken for plasma gelsolin detection. The gestational age, birth weight, postnatal age and weight during sepsis diagnosis, mechanical ventilation support, existence of BPD were recorded in sepsis study group. Blood samples for plasma gelsolin detection were again obtained when stopping antibiotic treatment was considered in sepsis study group. Because the relationship between normal plasma gelsolin levels and gestational age, birth weight, postnatal age, postnatal weight was unknown in especially preterm infants, the control group was composed of 20 preterm infants considering the gestational age, birth weight, postnatal age and weight, mechanical ventilation support and bronchopulmonary dysplasia (BPD) existence of the study group patients. Following the detection of negativity of infection markers during the inclusion phase, blood samples were obtained for plasma gelsolin measurement.

The blood samples (2 ml) were immediately placed into sterile EDTA-containing test tubes and centrifuged at 1500*g* for 10 min at 4 °C to collect plasma. Plasma was stored at −80 °C until assayed. Plasma gelsolin levels were measured using an enzyme-linked immunosorbent assay, in accordance with the manufacturer's instructions (Wuhan EIAab Science Co., LTD, China). The blood samples were run in duplicate. Researchers running ELISAs were blinded to all subjects' details.

All statistical analysis was performed by using IBM's SPSS (Chicago IL, USA), version 21.0. The hospital based ethics committee approved the study. The study was supported by the University of Erciyes Research Fund (TSA-2013-4647).

Results

Of the 40 patients with severe sepsis enrolled in this study, nine patients in the sepsis group (six patients due to sepsis, two patients due to pneumothorax and one patients due to multiorgan failure following opening of patent ductus arteriosus (PDA) for sepsis) and one infant in the control group died due to perforated necrotizing enterocolitis (NEC) during subsequent follow-up. The underlying diseases associated with the development of severe sepsis were late neonatal sepsis, early neonatal sepsis related to early ruptures of the membranes and infection related to peripheral venous line. The demographic and clinical data for the patients are presented in Table 1. No difference was observed in gestational age, sex, birth weight, intrauterine growth restriction (IUGR), postnatal age and weight at the onset of sepsis, and presence of RDS, BPD, early membrane rupture (EMR), intraventricular hemorrhage (IVH) and requirement for mechanical ventilation (MV) between the control and the sepsis group (Table 1).

The mean pGSN level at the time of diagnosis in the sepsis group was 33.98 ± 11.44 μg/ml, which was significantly lower than that of the control group (60.05 ± 11.3 μg/ml, $p < 0.001$) and after treatment in the survivors (53.38 ± 31.26 μg/ml, $p = 0.003$). In this study, although level of C-reactive protein (CRP) and number of white blood cells (WBC) of five patients were normal, we started ampyric antibiotic because of higher Töllner scores. pGSN level of these patients was 35.51 ± 9.26 μg/ml. However, CRP increase occurred later.

The Töllner scores in the sepsis group were 12.3 ± 4. pGSN levels were negatively correlated with Töllner scores, although the association did not have statistical significance ($rho = -0.34$, $p = 0.06$). In addition, a correlation was not detected between postnatal age and pGSN level in either the sepsis or control group. Also, gestational age, birth weight, gender, RDS, EMR, BPD and IUGR did not affect pGSN level at onset of sepsis (Table 2; $p > 0.05$). Although, pGSN levels were higher in survivors than in non-survivors, this result did not have statistical significance ($p = 0.74$).

ROC analysis of pGSN and sepsis is shown in Fig. 1. pGSN levels found strong predictive ability with an area under the ROC curve of 0.96 ($p = 0.0001$ 95% confidence interval of 0.90–0.99). Using a cut-off of 44.97 μg/ml, there was 90.3% sensitivity and 95% specificity for predicting sepsis.

Discussion

In spite of advances in neonatal care and the new generation of antibiotics, neonatal sepsis is still a major cause of morbidity and

Table 1
Demographic and clinical data of sepsis and control group.

	Sepsis group Mean ± SD	Control group Mean ± SD	P
GW (weeks)	29.4 ± 2.3	29.5 ± 2.4	0.7
Birth weight (g)	1376 ± 382	1202 ± 321	0.44
Sex	22 F/18 M	12 F/8 M	0.71
IUGR (n)	12	4	0.16
Postnatal age (day)	16.2 ± 12	15.5 ± 12.8	0.85
Postnatal weight (g)	1522 ± 336	1347 ± 319	0.78
RDS (n)	24	13	0.83
EMR (n)	11	7	0.92
BPD (n)	13	6	0.34
NEC (n)	14	3	**0.03**
IKK (n)	10	4	0.38
MV during sepsis (day)	15	5	0.08
O_2 during sepsis (day)	23	7	**0.005**
Exitus (n)	9	1	**0.035**

F: Female, M: Male.

Download English Version:

https://daneshyari.com/en/article/5810390

Download Persian Version:

https://daneshyari.com/article/5810390

Daneshyari.com