Research Article

Assessment of PCSK9 in Infants and Children with Sepsis

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Introduction

Sepsis is a systemic life-threatening syndrome characterized by the development of multi-organ dysfunction in the context of systemic infection. The simplistic view in which pathogen overgrowth and infection are the only factors involved in the cascade of pathological sepsis-related events has been replaced by a more complex theory in which a global dysregulation of the host response to infection might be causative (Singer et al., 2016).

Significant changes in cholesterol levels during inflammation and infection have been frequently reported, which may have also some prognostic impact (Lee et al., 2015).

In addition, cholesterol and pathogen's lipids play an essential role in generating intracellular signals, and consequently in the regulation of the systemic inflammatory response to different septic agents. (Oliveira-Nascimento et al., 2012).

Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9), a molecule mainly expressed by hepatocytes, is involved in the degradation of the low-density lipoprotein receptor (LDLR) and in the modulation of intracellular and plasma cholesterol levels. Gain-of-function mutations of the PCSK9 gene are associated with significant elevations of plasma LDL cholesterol and cardiovascular risk, whereas loss-of-function mutations of the PCSK9 gene are associated with reduced LDL-cholesterol levels and reduced cardiovascular risk. In 2015, two human anti-PCSK9 monoclonal antibodies received FDA and EMA approval (Seidah et al., 2016).

In vitro and in vivo studies in both animals and humans have shown that PCSK9, which is strictly linked to HMGCoAR and LDLR pathways, can play a central role in sepsis. Indeed, there is substantial evidence that LDLR participates in the clearance of pathogen's lipids (e.g., lipopolysaccharide, LPS), thus limiting their deleterious pro-inflammatory effect (Seidah et al., 2016).

Aim of the Work

To evaluate serum level of PCSK9 in infants and children with sepsis and severe sepsis.

Subjects and Methods

The present was conducted on 60 infants and children were admitted to PICU of Minia University Children Hospital, El-Minia. The study was conducted during the period of October 2016 till February 2017.

Also, 20 apparently healthy children included as control group, they were age and sex matched with the children of the 2 septic groups.

Laboratory investigations were done at bacteriology and clinical pathology departments of faculty of medicine Minia University.

The studied children were divided into three groups: -

Group 1 (Sepsis group):

This group included 30 children, they were 19 boys and 11 girls, with a mean age of 26.6± 32.6 months. They were diagnosed with sepsis according to international pediatric sepsis consensus conference criteria, 2005.

Group 2 (Severe sepsis group):

This group included 30 children, they were 19 boys and 11 girls, with a mean age of 19.04±28.96 months. They were diagnosed with severe sepsis according to international pediatric sepsis consensus conference criteria, 2005.

Group 3 (control group):

This group included 20 apparently health children. They were 13 boys and 7 girls, with mean age of 32.12±25.44 months. They were

age and sex matched with the previous two groups.

Exclusion criteria:
1- Congenital diseases.
2- Metabolic diseases.

Table: Serum PCSK9 level in children in the sepsis and severe sepsis groups according to different organs dysfunction.

Organ dysfunction	Total n=60 n (%)	PCSK9 (ng/ml) mean ± SD	p
Cardiovascular	21 (35%)	352.29±136.8	<0.001
Respiratory	25 (41.7 %)	353.3±132.3	<0.001
Hematological	12 (20%)	400.2±163.7	<0.001
Renal	4 (6.7 %)	453.1±161.3	<0.004
Hepatic	10 (16.7 %)	370.2±122.8	<0.008

*significant at P <0.05 **Highly significant at p < 0.01

Table showed that children with sepsis or severe sepsis who developed any organ dysfunction had higher PCSK9, when compared to children with sepsis and severe sepsis who did not suffer that organ dysfunction, (p <0.001) in all, except for renal and hepatic dysfunction, (p < 0.004 and 0.008) respectively.

Discussion

Sepsis is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs *(*Singer et al., 2016).

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an enzyme encoded by the PCSK9 gene on chromosome 1 in humans *(*Seidah et al., 2003).

Our study showed that the severe sepsis group had significantly lower length than the control group. Also, it showed that the sepsis and severe sepsis groups had significantly higher temperature, heart rate and respiratory rate than the control group. This can be attributed to infection that leads to increase in body temperature which leads to increase in heart rate and respiratory rate ,and the respiratory distress and the heart failure which happened as a cause or a result of sepsis, may cause an increase in heart rate and respiratory rate (Edwards et al., 2013).

This study showed that severe sepsis group had significantly lower blood pressure than the other two groups. This can be explained by that when bacteria enter the bloodstream, they release a toxin that leads to severe vaso-dilatation of vessels which leads to a dangerous drop in blood pressure *(*Surviving Sepsis Campaign Guidelines Committee., 2013), which may be aggravated in severe sepsis by an enzyme secreted called phosphor-lipase A2 which causes further vasodilatation and more profound hypotension (Cicala et al., 1993) (Table 1).

The current study showed that most frequent cause of admission in the sepsis and severe sepsis groups were severe chest infection followed by gastroenteritis. Also, from table 2, the most frequent complication encountered in the sepsis group was respiratory distress (56.7%) and dehydration (40%), while in the

severe group, the most frequent complication was apnea (20%) and respiratory distress (20%).

Recommendations

Any children with sepsis should measure PCSK9 level and they should receive PCSK9 inhibitors to avoid developing organ failure.

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