



Correlation of insulin resistance extent with systemic inflammatory response and target organ damage in children with sepsis

Min Liu 

Department of Pediatrics, Xindu Hospital of Traditional Chinese Medicine in Chengdu Sichuan Province, Chengdu 610500, China

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ABSTRACT

Objective: To explore the correlation of insulin resistance (IR) extent with systemic inflammatory response and target organ damage in children with sepsis. **Methods:** A total of 70 patients with sepsis who were treated in our hospital between June 2013 and July 2016 were collected as observation group, 50 healthy children who received vaccination in our hospital during the same period were selected as normal control group, the insulin resistance index (HOMA-IR) of two groups of children were determined, the median of HOMA-IR of observation group was referred to further divide them into high HOMA-IR group and low HOMA-IR group, 35 cases in each group. The systemic inflammatory response and target organ damage extent were compared between sepsis children with different HOMA-IR levels. **Results:** HOMA-IR level in observation group was significantly higher than that in normal control group. Serum inflammatory factors PCT, IL-1 β , IL-8 and IL-10 contents in high HOMA-IR group were significantly higher than those in low HOMA-IR group; serum myocardial injury indexes CK, CK-MB and LDH contents were significantly higher than those in low HOMA-IR group; serum liver injury indexes ALT, AST and TBIL contents were significantly higher than those in low HOMA-IR group while ALB content was lower than that in low HOMA-IR group; serum renal injury indexes Cr, BUN and CysC contents were significantly higher than those in low HOMA-IR group. **Conclusion:** HOMA-IR level in children with sepsis is higher than that in normal people, and HOMA-IR level is positively correlated with systemic inflammatory response and target organ injury.

1. Introduction

Sepsis is the systemic inflammatory response syndrome caused by infection, it can lead to multiple organ tissue damage once it occurs, and severe cases can die in a short time[1,2]. The immune system development is not yet complete in children, they develop sepsis more easily than adults after the pathogen infection, and the prognosis is poor if early appropriate treatment is not taken. Sepsis severity judgment is crucial for the establishment of therapy and the obtaining of final treatment effect, numerous current studies have shown that sepsis can cause endocrine and glucose metabolism disorders, severe cases can lead to insulin resistance

(IR) and increase patients' mortality, and therefore, the degree of IR in patients with sepsis is expected to become the new means for the illness severity judgment[3,4]. In the study, the levels of IR were compared between children with sepsis and the normal children, and the internal link between IR levels and sepsis severity was further determined, now reported as following.

2. Information and methods

2.1 Case information

A total of 70 patients with sepsis who were treated in our hospital between June 2013 and July 2016 were collected as observation group, 50 healthy children who received vaccination in our hospital during the same period were selected as normal control group, and the family members of enrolled children signed informed consent. Observation group included 27 male cases and 23 female cases

Corresponding author: Min Liu, Department of Pediatrics, Xindu Hospital of Traditional Chinese Medicine in Chengdu Sichuan Province, Chengdu 610500, China.

Tel: 02883971817; 13438966317

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that were 3-11 years old; normal control group included 27 male cases and 23 female cases that were 2-10 years old. The gender and age distribution of the two groups of children were not statistically significant ($P>0.05$), and the study was approved by the hospital ethics committee.

Inclusion criteria: (1) conforming to the diagnostic criteria for sepsis; (2) the interval between onset and admission was 24 h; (3) sepsis was developed for the first time. Exclusion criteria: (1) associated with congenital diseases of important organs such as heart, liver and kidney; (2) associated with type 1 diabetes; (3) dead within 24 h after admission.

2.2 Insulin resistance indexes

Immediately after admission, 1.0 mL peripheral venous blood was extracted from two groups of children, and glucose meter (Shanghai Junrui Biotechnology Co., LTD, the article number UFWD0228) was used to measure insulin resistance index (HOMA-IR).

2.3 Observation indexes

Immediately after admission, 2.0 mL peripheral venous blood was extracted from observation group again, put in anticoagulant tube and centrifuged at low speed to get upper serum, which was stored in a cryogenic environment. ELISA kit (Roche Company in the United States) instructions were followed to detect the contents of inflammatory cytokines, including procalcitonin (PCT), interleukin-1 β (IL-1 β), interleukin-8 (IL-8) and interleukin-10 (IL-10). Myocardial enzyme spectrum instrument (Jinan Hanfang Medical Instrument Co., LTD., the article number HF240-300) was used to detect the serum contents of myocardial enzyme spectrum, including creatine kinase (CK), creatine kinase isoenzyme (CK-MB) and lactate dehydrogenase (LDH). Automatic biochemical analyzer (Shanghai Utrao Medical Instrument Co., Ltd., the article number SA808) was used to determine the serum contents of liver

and kidney function indexes, including liver function indexes alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB) and total bilirubin (TBIL) as well as renal function indexes serum creatinine (Cr), blood urea nitrogen (BUN) and cystatin C (CysC).

2.4 Statistical processing

Personnel who had statistical qualification recorded and calculated the data in the study, and statistical software was SPSS 20.0. HOMA-IR, inflammatory factors, myocardial injury indexes, liver injury indexes, renal injury indexes and other measurement data were in terms of mean \pm standard deviation, and comparison between groups was by grouping t test. $P<0.05$ was the standard of statistical significance in differences.

3. Results

3.1 HOMA-IR

HOMA-IR level in normal control group was (4.57 \pm 0.56), HOMA-IR level in observation group was (5.89 \pm 0.64), HOMA-IR level in observation group was significantly higher than that in normal control group, and the differences were statistically significant ($P<0.05$). Median HOMA-IR in observation group was 5.72 and used as boundary to divide the children with sepsis into high HOMA-IR group and low HOMA-IR group, 35 cases in each group.

3.2 Inflammatory factors

Comparison of serum contents of inflammatory factors PCT (μ g/L), IL-1 β (pg/mL), IL-8 (pg/mL) and IL-10 (pg/mL) between sepsis children with different HOMA-IR was as follows: serum inflammatory factors PCT, IL-1 β , IL-8 and IL-10 contents in high HOMA-IR group were significantly higher than those in

Table 1.

Relationship between different HOMA-IR and inflammation.

Groups	<i>n</i>	PCT	IL-1 β	IL-8	IL-10
Low HOMA-IR group	35	0.93 \pm 0.16	0.17 \pm 0.03	20.37 \pm 3.16	34.37 \pm 4.82
High HOMA-IR group	35	1.54 \pm 0.18	0.32 \pm 0.05	41.92 \pm 5.48	71.28 \pm 9.53
<i>T</i>		7.281	6.483	10.293	9.826
<i>P</i>		<0.05	<0.05	<0.05	<0.05

Table 2.

Relationship between different HOMA-IR and myocardial injury (U/L).

Groups	<i>n</i>	CK	CK-MB	LDH
Low HOMA-IR group	35	89.27 \pm 9.11	12.36 \pm 1.89	163.28 \pm 25.79
High HOMA-IR group	35	145.83 \pm 17.62	34.17 \pm 4.52	275.45 \pm 30.18
<i>T</i>		9.231	7.382	14.382
<i>P</i>		<0.05	<0.05	<0.05

Table 3.

Relationship between different HOMA-IR and liver injury.

Groups	n	ALT	AST	ALB	TBIL
Low HOMA-IR group	35	73.27±8.19	102.32±14.78	37.48±4.19	10.38±1.75
High HOMA-IR group	35	118.63±14.73	141.24±17.88	24.75±3.11	19.68±2.53
T		15.381	13.092	11.273	14.372
P		<0.05	<0.05	<0.05	<0.05

Table 4.

Relationship between different HOMA-IR and renal injury.

Groups	n	Cr	BUN	CysC
Low HOMA-IR group	35	24.37±3.19	9.21±0.95	0.73±0.09
High HOMA-IR group	35	35.84±4.27	12.17±1.85	1.21±0.15
T		10.928	8.362	6.483
P		<0.05	<0.05	<0.05

low HOMA-IR group. Differences in serum inflammatory factors PCT, IL-1 β , IL-8 and IL-10 contents were statistically significant between the two groups ($P<0.05$), shown in Table 1.

3.3 Myocardial injury indexes

Comparison of serum contents of myocardial injury indexes CK, CK-MB and LDH between sepsis children with different HOMA-IR was as follows: serum myocardial injury indexes CK, CK-MB and LDH contents in high HOMA-IR group were significantly higher than those in low HOMA-IR group. Differences in serum myocardial injury indexes CK, CK-MB and LDH contents were statistically significant between the two groups ($P<0.05$), shown in Table 2.

3.4 Liver injury indexes

Comparison of serum contents of liver injury indexes ALT (U/L), AST (U/L), ALB (g/L) and TBIL ($\mu\text{mol/L}$) between sepsis children with different HOMA-IR was as follows: serum liver injury indexes ALT, AST and TBIL contents in high HOMA-IR group were significantly higher than those in low HOMA-IR group while ALB content was lower than that in low HOMA-IR group. Differences in serum liver injury indexes ALT, AST, ALB and TBIL contents were statistically significant between the two groups ($P<0.05$), shown in Table 3.

3.5 Renal injury indexes

Comparison of serum contents of renal injury indexes Cr ($\mu\text{mol/L}$), BUN (mmol/L) and CysC (mg/L) between sepsis children with different HOMA-IR was as follows: serum renal injury indexes Cr, BUN and CysC contents in high HOMA-IR group were significantly higher than those in low HOMA-IR group. Differences in serum renal injury indexes Cr, BUN and CysC contents were statistically significant between the two groups ($P<0.05$), shown in Table 4.

4. Discussion

The metabolism is in disorder after the occurrence of sepsis, increase liver glycogenolysis and impaired glucose utilization, etc., can all lead to hyperglycemic state in the body, and meanwhile, IR appears easily in patients with acute stage disease and further stimulates the increase of blood sugar levels[5]. IR is that the ability of peripheral target tissues of insulin to take in glucose is weakened and the body's sensitivity to insulin decreases, pediatric sepsis can cause the sympathetic - adrenal medulla axis and the hypothalamus - pituitary - adrenal cortex axis excitement, a lot of stress hormones are secreted and promote gluconeogenesis, and it is the core cause of the IR[6,7]. Animal experiment results show that there is significant IR in mice with sepsis, and IR extent is closely associated with the ultimate mortality rate, suggesting that IR could advance the progression of the disease. In the study, IR levels were compared between children with sepsis and the normal children, and it was found that HOMA-IR level in observation group was significantly higher than that in normal control group, verifying that there is IR in children with sepsis, but the correlation between IR degree and disease severity remains to be confirmed in following study.

Systemic inflammatory response is a typical manifestation of sepsis patients, and a large number of inflammatory mediators are release and form cascade reaction with each other, which is the important pathologic basis of later tissue viscera damage[8,9]. PCT is a new popular inflammatory factor closely associated with severe infection, its content is consistent with the degree of infection, and many studies suggest that is diagnostic specificity for infection is higher than that of CRP[10]. IL-1 β , IL-8 and IL-10 are the most commonly studied clinical inflammatory mediators, and they are massive produced after pathogenic bacteria stimulate the mononuclear macrophages, then enter into the circulating blood and spread to various tissues to further induce neutrophils to aggregate in vital organs and produce damage, which is the basis for the occurrence and development of sepsis[11,12]. The contents of inflammatory mediators can accurately diagnose sepsis, serum contents of above

inflammatory mediators were compared between sepsis children with different levels of HOMA-IR in the study, and it was found that serum inflammatory factors PCT, IL-1 β , IL-8 and IL-10 contents in high HOMA-IR group were significantly higher than those in low HOMA-IR group, confirming that the HOMA-IR level in children with sepsis is consistent with the degree of inflammation.

Most patients with sepsis can develop heart, liver, kidney and other important tissue organ damage with disease progression, and the heart injury is with the highest incidence and furthest influences the children[13,14]. Severe myocardial damage can cause the specific factors to be secreted from myocardial cells into the blood, which are called the "myocardial enzyme spectrum"[15]. CK, CK-MB and LDH are the most typical myocardial enzyme spectrum indexes, serum contents of above myocardial enzyme spectrum indicators were compared between sepsis patients with different HOMA-IR levels in this study, and it was found that serum myocardial injury indexes CK, CK-MB and LDH contents in high HOMA-IR group were higher than those in low HOMA-IR group, confirming that HOMA-IR level is positively correlated with the degree of myocardial injury. Liver and kidney injury are the complications with the highest incidence second to after myocardial injury in children with sepsis, ALT, AST, ALB and TBIL are the typical liver function indexes, ALT and AST are massively released from cells into the blood after the liver cell damage, and the liver's ability to produce ALB reduces and the ability to metabolize TBIL is weakened, which lead to the decrease of the ALB content and the increase of the TBIL content in the circulating blood[16,17]. Cr, BUN and CysC are the factors that are closely related to kidney function, and blood Cr and BUN contents rise when the glomerular filtration rate falls; kidney is the only organ to filtrate and metabolize CysC, mild glomerular injury can cause sharp increase in serum CysC levels, and therefore, to detect the contents of CysC can early and sensitively reflect kidney state[18,19]. In the study, serum contents of liver and kidney function indexes were compared between sepsis children with different levels of HOMA-IR, and it was found that serum liver injury indexes ALT, AST and TBIL contents in high HOMA-IR group were higher than those in low HOMA-IR group while ALB content was lower than that in low HOMA-IR group; serum renal injury indexes Cr, BUN and CysC contents were higher than those in low HOMA-IR group, which confirm that liver and kidney damage are aggravated with the increase of IR levels.

IR levels increase in children with sepsis, and IR levels are closely related to the degree of systemic inflammatory response as well as heart, liver and kidney injury. Detecting IR levels can be used as an easy and accurate way to determine the disease severity in children with sepsis, and it is worthy of popularization and application in clinical practice in the future.

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