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血清 IL-6、IL-8、IgM 抗体及 T 细胞亚群水平对新生儿先天性梅毒的诊断价值*

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摘要 目的:探讨血清白介素-6(IL-6)、白介素-8(IL-8)、IgM 抗体及 T 细胞亚群对先天性梅毒新生儿的诊断价值。**方法:**选择 2015 年 5 月至 2017 年 5 月在我院进行临床治疗的先天性梅毒新生儿 81 例为观察组,另选同期来我院进行健康体检 81 例新生儿为对照组。比较两组患者血清 IL-6、IL-8、T 细胞亚群中 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 细胞及 IgM 抗体的阳性率。**结果:**治疗后,观察组血清 IL-6、IL-8 水平均明显高于对照组($P<0.05$),T 细胞亚群中 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 明显低于对照组,而 CD8⁺T 细胞比例高于对照组($P<0.05$)。19S-IgM-TP ELISA 法检测出 IgM 的阳性率 92.59%,明显高于 TRUST 法(74.07%)及 TP-ELSA 法(70.37%)($P<0.05$)。ROC 曲线中,血清 IL-8 特异度为 88.34%明显高于血清 IL-6 特异度 81.48%、IgM 抗体特异度 60.13%、T 细胞亚群特异度 65.34%;IgM 抗体的曲线面积 88.91 cm² 明显大于 IL-6 的曲线面积 45.09 cm²、IL-8 的曲线面积 76.19 cm²、T 细胞亚群的曲线面积 77.35 cm²;T 细胞亚群准备性 67.89%明显高于 IL-6 准确性 60.39%、IL-8 准确性 51.09%、IgM 抗体准确性 50.12%;IgM 抗体的灵敏度 60.13%高于 IL-6 灵敏度 59.19%、IL-8 灵敏度 42.35%、T 细胞亚群灵敏度 59.37%。具有比较意义($P<0.05$)。**结论:**血清 IL-6、IL-8 水平、T 细胞亚群中 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 及 IgM 抗体阳性率是诊断先天性梅毒新生儿的重要指标。

关键词:血清白介素-6(IL-6);白介素-8(IL-8);CD3⁺;CD4⁺;CD4⁺/CD8⁺;IgM 抗体;先天性梅毒

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Diagnostic Value of IL-6 IL-8 IgM Antibody and T Cell Subsets in Congenital Syphilis Neonates*

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ABSTRACT Objective: To study the diagnostic value of IL-6, IL-8, IgM antibody and T cell subsets for the congenital syphilis neonates. **Methods:** 81 cases of children with congenital syphilis neonatal in our hospital from May 2015 to May 2017 were selected as the observation group, and 81 cases of healthy newborns were selected as the control group. The percentages of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ cells, positive rate of IgM and serum IL-6, IL-8 levels were compared between the two groups before and after treatment. **Results:** After treatment, the levels of serum IL-6 and IL-8 in the observation group were significantly higher than those in the control group ($P<0.05$), CD3⁺, CD4⁺/CD8⁺T cell subsets were significantly lower than those in the control group ($P<0.05$). The positive rate of IgM was 92.59%, which was significantly higher than that of TRUST (74.07%) and TP-ELSA (70.37%) ($P<0.05$) by 19S-IgM-TP ELISA. In the ROC curve, the specificity of serum IL-8 was 88.34%, which was significantly higher than that of serum IL-6 specificity of 81.48%, IgM antibody specificity of 60.13%, T cell subgroup specificity of 65.34%; IgM antibody curve area of 88.91 cm² was significantly larger than The curve area of IL-6 was 45.09 cm², the curve area of IL-8 was 76.19 cm², the curve area of T cell subsets was 77.35 cm², the preparation rate of T cell subsets was 67.89%, which was significantly higher than that of IL-6 60.39% Accuracy of 51.09%, IgM antibody accuracy of 50.12%; IgM antibody sensitivity of 60.13% higher than IL-6 sensitivity of 59.19%, IL-8 sensitivity of 42.35%, T cell subpopulation sensitivity of 59.37% ($P<0.05$). **Conclusion:** The percentages of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ cells, positive rate of IgM and serum IL-6, IL-8 levels were important indexes for the diagnosis of neonatal syphilis.

Key words: IL-6; IL-8; CD3⁺; CD4⁺; CD8⁺; CD4⁺/CD8⁺; IgM antibody; Congenital syphilis

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前言

先天性梅毒又称为胎传梅毒,是母体经胎盘传染给胎儿导致的梅毒螺旋体^[1],近年来发病率逐渐增高。梅毒可损害新生儿

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全身各器官,造成各器官的衰竭,甚至引起其他严重疾病的发生^[2]。因此,积极做好产前检查以预防先天性梅毒疾病的发生非常重要。先天性梅毒的临床症状一般表现为肝脾肿大、胎盘增厚、胎儿水肿、血小板减少、早产等^[3]。大多数新生儿临床表现多样化,且与其他疾病容易混淆,早期确诊对治疗先天性梅毒具有重要的临床作用^[4]。T 细胞亚群具有协调体液免疫和细胞免疫的作用,与各亚群互相约束和互相辅助;IL-6 和 IL-8 是反映机体免疫功能的重要指标,具有抑制梅毒的重要作用^[5]。IgM 抗体是在机体感染后,体内最早出现的免疫功能,在感染的两周内可以从血清检测出,且只要有活的梅毒螺旋体出现,造成抗原刺激,IgM 抗体就会维持在一定的水平,因此 IgM 抗体是早期检测感染的一个重要指标^[6,7]。本研究旨在探讨血清 IL-6、IL-8、IgM 抗体及 T 细胞亚群对先天性梅毒新生儿的诊断价值研究,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 5 月至 2017 年 5 月在我院进行临床治疗的先天性梅毒新生儿 81 例作为观察组,纳入标准:符合先天性梅毒诊断标准。排除标准:患者家属不配合者。其中,男 61 例,女 20 例,早产儿 30 例;足月儿 26 例,足月小样儿 25 例。同期选

择在我院接受健康体检 81 例新生儿为对照组,其中男 51 例,女 30 例,均无先天性梅毒病史,且体检各项指标均为正常。两组患者性别、年龄等一般资料相比差异均无统计学意义($P>0.05$),具有可比性。

1.2 方法

抽取两组静脉血 3 mL,置于 4℃ 冰箱静置半个小时至一小时,分离血清,避免反复冻融,在检测前进行样本稀释,取 20 μ L 血清加入 1 mL 分析缓冲液中进行 1:51 比例稀释备用,采用酶联免疫吸附法检测其血清 IL-6、IL-8 水平及 T 细胞亚群中 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 水平。IgM 抗体采用 19S-IgM-TP ELISA 法、TRUST 法、TP-ELSA 法三种方法检测对比,比值是指样品 OD 平均值,比值 >0.01 为阳性,比值 <0.09 为阴性。

1.3 统计学分析

本研究数据选择 SPSS18.0 进行统计,计量资料比较采用 t 检验,计数资料比较采用 χ^2 检验,当 $P<0.05$ 时表示差异具有统计学意义。

2 结果

2.1 两组患者血清 IL-6、IL-8 水平的比较

治疗前,观察组血清 IL-6、IL-8 水平显著高于对照组,差异具有统计学意义($P<0.05$),见表 1

表 1 两组患者治疗前血清 IL-6、IL-8 水平的比较[($\bar{x} \pm s$)mg/L]

Table 1 Comparison of the serum IL-6 and IL-8 levels between two groups of patients before treatment[($\bar{x} \pm s$)mg/L]

Group	n	IL-6	IL-8
Observation group	81	15.18 $\pm$ 2.19 ^a	18.39 $\pm$ 2.56 ^a
Control group	81	9.27 $\pm$ 1.38	13.21 $\pm$ 2.11

Note: compared with the control group, ^a $P<0.05$.

2.2 两组治疗前 T 细胞亚群检测结果的比较

观察组 T 细胞亚群中细胞 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 均显著低于对照组 T 细胞亚群 CD3⁺、CD4⁺、CD4⁺/CD8⁺ ($P<0.05$); 而观

察组 T 细胞亚群细胞 CD8⁺ 则明显高于对照组 T 细胞亚群 CD8⁺ ($P<0.05$), 见表 2。

表 2 两组治疗前 T 细胞亚群检测结果的比较[($\bar{x} \pm s$)%]

Table 2 Comparison of the T cell subset between two groups before treatment[($\bar{x} \pm s$)%]

Group	n	CD3 ⁺	CD4 ⁺	CD8 ⁺	CD4 ⁺ /CD8 ⁺
Observe group	81	55.23 $\pm$ 6.49 ^a	33.28 $\pm$ 4.54 ^a	33.28 $\pm$ 4.11 ^a	1.01 $\pm$ 0.19 ^a
Control group	81	66.19 $\pm$ 9.13	44.27 $\pm$ 5.38	27.39 $\pm$ 3.18	1.61 $\pm$ 0.27

Note: compared with control group, ^a $P<0.05$.

2.3 三组方法检测先天新生儿梅毒螺旋体 IgM 抗体阳性率的比较

19S-IgM-TP ELISA 法检测先天新生儿梅毒螺旋体 IgM 抗体

的阳性率为 92.59%, 显著高于 TRUST 法阳性率 (74.07%) 及 TP-ELSA 法阳性率 (70.37%), 差异具有统计学意义 ($P<0.05$)。见表 3。

表 3 三组方法检测先天新生儿梅毒螺旋体 IgM 抗体的比较($\bar{x} \pm s$)

Table 3 Comparison of the positive rate of neonatal Treponema pallidum IgM antibodies among three methods($\bar{x} \pm s$)

Group	n	Positive number	Positive rate(%)
19S-IgM-TP ELISA	81	75	92.59
TRUST	81	60	74.07 ^a
TP-ELSA	81	57	70.37 ^a

Note: Compared with 19S-IgM-TP ELISA, ^a $P<0.05$.

2.4 血清 IL-6、IL-8、IgM 抗体及 T 细胞亚群的 ROC 曲线分析 (见图 1)

ROC 曲线越靠近左上角,则是错误最少的准确性,表明有诊断价值,四个指标对先天性梅毒新生儿的诊断性见表 4。

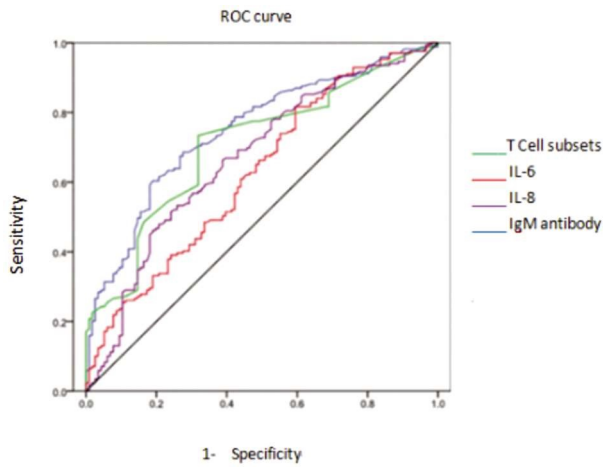


图 1 先天性梅毒新生儿血清中 IL-6、IL-8、IgM 抗体及 T 细胞亚群的 ROC 曲线

Fig.1 ROC curve of serum levels of IL-6, IL-8, IgM antibodies and T cell subsets

表 4 IL-6、IL-8、IgM 抗体及 T 细胞亚群对先天性梅毒新生儿的诊断性能指标

Table 4 Diagnostic performance indicators of IL-6, IL-8, IgM antibodies and T cell subsets in congenital syphilis neonatal

	IL-6	IL-8	IgM antibody	T Cell subsets
Area under the curve(cm^2)	45.09	76.19	88.91	77.35
Accuracy(%)	60.39	51.09	50.12	67.89
Specificity(%)	81.48	88.34	83.45	65.34
Sensitivity(%)	59.19	42.35	60.13	59.37

作用的关键。CD3⁺T 细胞是一种蛋白质复合物,存于 T 细胞和胸腺细胞的表面,可通过将其抗原信号传递到细胞内^[20,21]。CD4⁺T 细胞是辅助性 T 细胞,协助分化抗体中的 B 细胞;CD8⁺T 细胞具有抑制作用,可有效控制 B 淋巴细胞的活性,抑制抗体的合成、分泌及增值作用^[22,23]。

IgM 抗体是患者感染梅毒机体后最早出现的反映体液免疫功能的指标^[24]。一旦胎儿血液中检测出 IgM 抗体,表明其在子宫内已经感染^[25]。当机体检测出阳性结果,则提示发生先天性梅毒感染几率大^[26,27]。IgM 抗体最常用的三种方法为 19S-IgM-TP ELISA 法、TRUST 法及 TP-ELISA 法,19S-IgM-TP ELISA 法对评定梅毒具有独特的作用,治疗后新生儿梅毒机体内的 IgM 抗体可有效反映病理情况。TRUST 法检测的是 TP 非特异性的抗心磷脂抗体,新生儿免疫系统尚未成熟,对梅毒的感染反应很弱,导致检测出的阳性均低于母亲,对检测结果有一定的干扰;TP-ELISA 法要在新生儿 4~12 周才能检测出感染情况,已经错过诊断的最佳时机,还可导致病情的加重,该方法不能有效区分现症感染和既往感染,失去临床诊断意义^[28]。19S-IgM-TP ELISA 法检测准备率比其他两种高,具有明显优势,可以作为早期诊断新生儿先天性梅毒基础性检测方法^[29]。

本研究结果先天性梅毒新生儿的血清 IL-6、IL-8 水平明显

3 讨论

梅毒在新生儿出生后的几周或几个月内发病^[8]。通过血源传播引起胎传梅毒可导致全身器官受损,包括皮肤、呼吸道、肝脾肿大及脑炎等^[9,10]。先天性梅毒的危险性大,严重者甚至造成患者死亡。大部分患者都是由于孕妇未经过正规治疗或者治疗疗程不够引起的梅毒,因此产前正规检查及治疗可降低先天性梅毒的发生率^[11,12]。

IL-6 是机体内的炎症介质,是天然免疫的细胞因子^[15]。在局部和全身可与各自特异性受体结合,可激活 T 细胞及活化 B 细胞,刺激肝细胞合成急性反应 C 蛋白。血清 IL-6 水平升高提示患者感染梅毒后,机体免疫体统应答,细胞因子发挥起相应的生物活性作用。IL-8 也属于机体内的炎症介质,是趋化因子家族的一种,可调节人类生殖生理及病理过程,具有促进血管再生作用,趋化炎症部位的中性粒细胞、嗜酸细胞及淋巴细胞^[16,17]。因此,通过检测血清 IL-6、IL-8 水平变化有助于判断先天性梅毒严重程度,是检测先天性梅毒严重程度的重要参考指标。

T 细胞亚群中 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 水平可反映 T 和 B 淋巴细胞的免疫功能^[18,19]。先天性梅毒病原进入新生儿机体后,能迅速引起免疫功能改变,T 细胞亚群就是发挥重要

高于健康新生儿,T 细胞亚群中 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 明显低于健康新生儿,而 CD8⁺ 细胞则明显高于健康新生儿 CD8⁺ 细胞,19S-IgM-TP ELISA 法的阳性率 92.59%结果明显高于 TRUST 法阳性率 74.07 及 TP-ELISA 法阳性率 70.37%。由此可见,血清 IL-6、IL-8 水平及 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 细胞是检测先天性梅毒患者的重要指标;通过检测指标水平变化,有效掌握病情数据及治疗是新生儿性梅毒的关键。19S-IgM-TP ELISA 法可以作为早期检测 IgM 抗体阳性率的重要参数,与其他两种方法比较,准备性更高,数据更精确。IL-8 中特异度 81.48%,明显高于其 IL-6、IgM 抗体、T 细胞亚群的特异度;IgM 抗体的曲线面积 88.91 cm^2 大于 IL-6、IL-8、T 细胞亚群的曲线面积;T 细胞亚群诊断准备性 67.89%高于 IL-6、IL-8、IgM 抗体准确性;IgM 抗体的灵敏度 60.13%高于 IL-6、IL-8、T 细胞亚群灵敏度。ROC 曲线是将灵敏度、特异性相结合起来综合评价诊断试验正确程度的一种方法,根据曲线的形状和曲线下面积分析,提高先天性梅毒新生儿的诊断和病情判断的准确性,利于指导治疗,降低死亡率。

综上所述,检测血清 IL-6、IL-8 水平及 T 细胞亚群中 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 的变化,19S-IgM-TP ELISA 法检测 IgM 抗体阳性数的变化均有助于新生儿先天性梅毒的诊断。

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