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降钙素原、IL-6 及 CRP 诊断新生儿宫内细菌感染的临床价值

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摘要 目的：探讨降钙素原、IL-6 及 CRP 对新生儿宫内细菌感染诊断的临床价值。**方法：**采用回顾性分析方法，对 121 例疑似宫内细菌感染的新生儿的相关临床资料进行比较分析。通过影像学或细菌学方法对患儿进行检查判定感染类型，并检测患儿脐血中的降钙素原、C- 反应蛋白（CRP）和白细胞介素 -6（IL-6）的水平。**结果：**在 121 例患儿中 41 例确定为细菌感染，IL-6（>100ng/L）与 CRP（>10mg/L）联合对诊断新生儿宫内细菌感染的敏感性为 90.1%，特异性为 76.9%，阴性预测率为 91.7%，阳性预测率为 71.9%；与 PCT 结合后，诊断新生儿宫内细菌感染的敏感性升高至 98.3%，特异性为 67.8%，阴性预测率为 99.2%，阳性预测率为 57.0%。**结论：**脐血 PCT 可作为新生儿宫内细菌感染诊断的有效指标，可明显提高 IL-6 与 CRP 诊断新生儿宫内细菌感染的阴性预测值和敏感性，指导临床治疗。

关键词：降钙素原；C- 反应蛋白；白介素 -6；新生儿宫内细菌感染

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Effect of Procalcitonin Combined With IL-6 and C-reactive Protein in Diagnosis of Intrauterine Bacterial infection in Neonates

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ABSTRACT Objective: To evaluate the clinical value of procalcitonin combined with IL-6 and C-reactive protein in diagnosis of intrauterine bacterial infection in neonates. **Methods:** The clinical date of 121 neonates who were suspected cases of intrauterine bacterial infection were analyzed retrospectively. The level of PCT, IL-6 and CRP were detected and the intrauterine bacterial infection was proved by imaging and bacteriology. **Results:** In 121 neoates, 41 children were confirmed as intrauterine bacterial infection. The sensitivity value of IL-6 (>100ng/L) combined with CRP detection in diagnosis of NBI was 90.1% , the specificity was 76.9%,and the negative predictive rate was 91.7%, the positive predictive rate was 71.9%. When IL-6 and CRP combined with PCT was used in diagnosis of NBI, the sensitivity value was 98.3%, the specificity was 67.8%, the negative predictive rate was 99.2%, the positive predictive rate was 57.0% respectively. **Conclusion:** PCT can be used as the auxiliary diagnosis of intrauterine bacterial infection, and can enhance the negative predictive value and sensitivity of IL-6 combined with CRP in diagnosis of NBI.

Key words: Procalcitonin; C-reactive protein; IL-6; Intrauterine bacterial infection

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前言

细菌感染性疾病在我国新生儿重症监护中占有相当的比例，其早期无特异怀症状，但发病迅速隐匿，临床及时诊断及合理用药对降低新生儿感染病死率有重要意义[1,2]。宫内细菌感染就由于病原微生物经过某种渠道进入羊膜腔导致胎膜、绒毛膜、羊水、胎盘等的感染。新生儿宫内感染是导致新生儿死亡的存活率。IL-6 及 CPR 的检测对感染的诊断都有着较高的敏感性及特异性，已被广泛应用于新生儿宫内细菌感染的协助诊断，但由于新生儿的生理特点，IL-6 和 CPR 的检测应用有一定的局限性[3-5]。近年来，研究发现，PCT 在血清中的含量与细菌感染密切相关，且被认定为诊断细菌感染性疾病的重要标志物[6,7]。本研究采用回顾性分析法探讨 PCT 联合 IL-6 及 CRP 对新生儿宫内细菌感染的诊断水平。

1 资料与方法

1.1 一般资料

将 2013 年 2 月至 2013 年 12 月于我院行胎盘病理检查、分娩的 121 例新生儿做为研究对象，研究前与患儿家属签署知情同意书，所有操作均符合伦理学要求。被收录患儿均有体温异常（肛温低于 36.5℃或高于 38℃）、心血管功能异常（持续性心动过速或心率小于 8 次 /min）、喂养不耐受（胃残留量多于喂养总量的 20%或有呕吐症状）和呼吸功能障碍等症状。

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1.2 研究方法

1.2.1 检测内容 本院产科对有孕母有感染、胎膜早破和早产等病理状况的新生儿进行病理检查。镜检胎盘标本观察是否有淋巴细胞、中性粒细胞或浆细胞浸润等症状,判断是否存在羊膜炎、绒毛膜炎、绒毛膜羊膜炎或胎膜炎。密切观察患儿的临床症状,提取脐血液标本,对血清中的 PCT、CRP 及 IL-6 水平进行检测并进行细菌培养。对脑脊液、血液、尿液进行细菌培养并对患儿进行影像学检查以确诊新生儿是否有细菌感染。

1.2.2 IL-6、CRP 和 PCT 的检测 采用 ELISA 法对 IL-6 进行检测,试剂盒由加拿大 YES 生物技术有限公司的购得。运用全自动生化分析仪,通过颗粒增强免疫透射比浊法对 CRP 进行定量检测。PCT 则采用酶联免疫法进行定量检测,定量试剂盒购自德国 BRAHMS 公司。计算 IL-6、CRP 及 PCT 和联合检测时的敏感性、特异性、阴性预测率和阳性预测率,根据受者工作特征曲线计算 PCT 临界值。

1.3 统计学处理

数据采用 SPSS18.0 统计学软件进行分析,IL-6、CRP 及 PCT 采用中位数表示,运用秩和检验对组间差异比较。

2 结果

2.1 患儿血液指标检测

对 121 例患儿进行脐血血清水平检测并进行影像学检查,41 例新生儿被确诊为宫内细菌感染。血液中各指标水平检测结果显示细菌感染患儿与非感染者相比 IL-6、CRP 和 PCT 水平明显较高,且差异有统计学意义(P<0.05),结果见表 1。

表 1 患儿血液指标检测

Table 1 Detection of blood indexes

指标 Indexes	非感染患儿(n=80) Non infected children	NBI 患儿(n=41) NBI children	P
白细胞(×10^9/L) White blood cells(×10^9/L)	14.1(7.1~20.3)	13.8(3.8~48.1)	0.471
血小板(×10^9/L) Blood platelet(×10^9/L)	352(79.0~765.1)	191(23.6~533.9)	0.000
IL-6(ng/L)	22.5(22.7~63.5)	367(58.7~623.5)	0.000
CRP(mg/L)	2.1(2.1~39.5)	21.7(5.8~98.3)	0.000
PCT(μg/L)	0.5(0.2~1.8)	1.8(0.5~34.9)	0.000

2.2 各指标检测 NBI 的特异性、敏感性、阳性预测值及阴性预测值

计算 IL-6、CRP 及 PCT 和联合检测时的敏感性、特异性、阴性预测率和阳性预测率,结果显示单独进行 PCT 检测的敏感性高于单独 IL-6 和 CRP 检测,但特异性偏低。IL-6 与 CRP 联合检测时敏感性为 90.1%,特异性为 76.9%,阴性预测值为 91.7%,阳性预测值为 71.9%;与 PCT 结合后,诊断新生儿宫内细菌感染的敏感性升高至 98.3%,特异性为 67.8%,阴性预测值为 99.2%,阳性预测值为 57.0%,结果见表 2。

表 2 三种标记物单独及联用检测 NBI 的情况(%)

Table 2 Three kinds of markers alone and combined in detection of NBI

指标 Indexes	敏感性 Sensitivity	特异性 Specificity	阳性预测率 Positive predictive rate	阴性预测率 Negative predictive rate
IL-6(>100 ng/L)	94(77.7)	104(86.0)	91(75.2)	104(86.0)
CRP(>10 mg/L)	83(68.6)	101(83.5)	83(68.6)	101(83.5)
PCT(>0.7 μg/L)	99(81.8)	91(75.2)	76(62.8)	108(89.3)
CRP+IL-6	109(90.1)	93(76.9)	87(71.9)	111(91.7)
CRP+IL-6+PCT	119(98.3)	82(67.8)	69(57.0)	120(99.2)

2.3 PCT 检测的接受者工作特征曲线分析

ROC 曲线即受试者工作特征曲线,是将特异性和敏感性相结合来评价试验准确程度的方法。此曲线通过构图法将两个采用指标的特异性和敏感性通过曲线形式相结合,连续地反应指标不同临界值的特异度和灵敏度的变化。本研究根据 ROC 显示,PCT 达到最高特异性和敏感性时,临界值为 0.83 μg/L,由此可得出敏感性为 97.4%,特异性为 67.9%,PPV 为 62.1%,NPV 为 99.1%。

3 讨论

宫内感染指孕妇在妊娠期间受到感染而引起胎儿的宫内感染,因此又被称先天性感染或母婴传播疾病,主要包括羊水、胎膜、胎盘及胎儿的感染。宫内感染的病原菌主要是细菌,多数病原菌来源于阴道,提示下生殖道感染与上行性的羊膜腔感染有关,主要病原菌为大肠埃希菌、葡萄球菌、无乳链球菌等,病毒感染少见。在进行新生儿宫内细菌感染诊断时,心动过缓和呼吸暂停是临床诊断中两个重要指标,但有些非感染患儿也

会出现类似的临床症状,因此能否及时并准确的判断及确诊对患儿的预后非常重要[8-12]。但目前国内临床上对新生儿宫内细菌感染的早期诊断缺乏可靠快速的检测手段,常用的检测方法均有一定的局限性。

PCT 在近年来的国外的临床诊断中被广泛运用于重症感染的早期诊断的新型指标,是由 116 个氨基酸构成的无激素活性的糖蛋白,属于降钙素的前肽。在正常生理条件下,极少量的 PCT 可由甲状腺 C 细胞生产, 在健康者的血清中,PCT 的水平通常低于 0.1ng/mL,但在机体受到细菌感染时,甲状腺、肝脏细胞、内分泌细胞等都可分泌 PCT,血清中的 PCT 水平会显著增高,且会随着病情的发展进行升高,在感染得到控制后显示下降由于其较高的特异性和敏感性[13-16]。

CRP 与 IL-6 已被广泛应用于临床, 是用来诊断细菌感染的常用指标[17-20]。本研究的目的是探讨在对新生儿宫内细菌感染的检测中,除了 IL-6 和 CRP 之外,额外的 PCT 检测能否进一步提高感染诊断的准确性。研究结果发现,IL-6 与 CRP 联合检测时敏感性为 90.1%, 特异性为 76.9%, 阳性预测值为 91.7%,阳性预测值为 71.9%。而与 PCT 结合后,诊断新生儿宫内细菌感染的敏感性升高至 98.3%,特异性为 67.8%,阴性预测值为 99.2%,阳性预测值为 57.0%,三者进行联合后,对新生儿宫内细菌感染检测的敏感性和阴性预测率几乎接近 100%。新生儿,特别是早产儿,细菌感染的发生较高,高敏感性的诊断方法对及时有效的控制感染有重要意义。IL-6、CRP 与 PCT 联合后,阴性预测率升高,有利于及时停止进行中的抗生素治疗,从而大大减小了患儿患坏死性小肠结肠炎的风险。PCT 的临界值是诊断新生儿宫内细菌感染的另一个重要指标,其值可直接影响检测的特异性、敏感性,阴性预测率及阳性预测率。

综上所述,对新生儿进行宫内细菌感染检测时,在进行常规 CRP 与 IL-6 的检测基础上, 对血清中 PCT 的含量进行检测,可提高诊断的敏感性。对避免假阴性高危新生儿的诊断有重要意义。且其较高的阴性预测率也可为临床合理用药,及时停止使用抗生素确保患儿预后有重要参考作用。

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