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Changes of Maternal and Neonatal Plasma Prolactin Levels in Neonatal Asphyxia

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Abstract: Objective Some research has shown that prolactin (PRL) is closely related to severity of hypoxic-ischemic encephalopathy (HIE). However, the role of maternal and neonatal plasma PRL levels in neonatal asphyxia has not been reported so far. This paper aims at studying the changes of PRL levels in the cord blood, maternal blood and plasma of newborns in neonatal asphyxia. **Methods** The maternal blood, cord blood and neonatal plasma PRL levels in 25 neonates with asphyxia (asphyxia group) and 20 normal ones (control group) were detected by radioimmunoassay. **Results** The maternal blood, cord blood and neonatal plasma PRL levels [(362.5 ±127.1), (984.6 ±262.3) and (386.3 ±216.2) μg/L, respectively] in the asphyxia group were significantly higher than those in the control group [(96.4 ±26.2), (92.3 ±18.4) and (68.7 ±7.27) μg/L, respectively] ($P < 0.01$). The maternal blood, cord blood and neonatal plasma PRL levels [(445 ±216), (996 ±284) and (412 ±221) μg/L, respectively] in the severe asphyxia group were higher than those in the mild asphyxia group [(298 ±102), (612 ±221) and (309 ±19.2) μg/L, respectively] ($P < 0.01$ or 0.05). The cord blood and neonatal plasma PRL levels had a positive correlation both in the mild and the severe asphyxia group ($r = 0.54$, $r = 0.63$, both $P < 0.05$). The plasma PRL level right after resuscitation was higher than that of the control group ($P < 0.01$). It gradually reduced from the 2nd day after birth, but was higher than that of the control group ($P < 0.01$). The PRL level on the 10th day after birth was not different from that of the control group. **Conclusions** The PRL levels of neonatal plasma, cord blood and maternal blood increase in the perinatal asphyxial newborns. The plasma PRL level may be a good marker to evaluate the degree of asphyxia.

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Key words: Asphyxia; Prolactin; Newborn

新生儿窒息母儿血浆催乳素水平变化的研究

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[**摘 要**] **目的** 目前发现催乳素(PRL)与缺氧缺血性脑病(HIE)的严重程度密切相关,PRL 与新生儿窒息的关系较少报道,该文探讨窒息新生儿母儿血浆催乳素(PRL)水平变化与相关性及其意义。**方法** 采用放射免疫分析法对 25 例围产期窒息新生儿(窒息组,其中轻度窒息 14 例,重度窒息 11 例)及 20 例正常新生儿(对照组)母血、脐血及新生儿血浆 PRL 水平进行测定并进行动态观察。**结果** 窒息组母血、脐血及新生儿血浆 PRL 水平[(362.5 ±127.1),(984.6 ±262.3),(386.3 ±216.2) μg/L]均显著高于对照组[(96.4 ±26.2), (92.3 ±18.4), (68.7 ±7.27) μg/L](P均 < 0.01);重度窒息组母血、脐血及新生儿血浆 PRL 水平[(445 ±216),(996 ±284),(412 ±221) μg/L]均高于轻度窒息组[(298 ±102), (612 ±221), (309 ±19.2) μg/L]($P < 0.01$或0.05)。轻、重度窒息组中脐血与新生儿血浆 PRL 水平具有显著的正相关关系($r = 0.54, 0.63$, $P < 0.05$)。窒息新生儿复苏后血浆 PRL 水平高于对照组($P < 0.01$);生后第 2 天 PRL 水平逐渐下降,但仍高于对照组($P < 0.05$);生后第 10 天血浆 PRL 水平与对照组差异无显著性($P > 0.05$)。**结论** 围产期窒息时新生儿血浆、脐血及母血 PRL 水平显著增高,血浆 PRL 水平可作为判断新生儿窒息程度的一项参考指标。 [**中国当代儿科杂志,2003, 5(6): 505 - 508**]

[**关 键 词**] 窒息;催乳素;新生儿

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Neonatal asphyxia is an important cause of neonatal brain damage and it may result in hypoxic-ischemic encephalopathy (HIE). Studies have shown that prolactin (PRL) released by the anterior pituritary has a positive correlation with the degree of HIE. However, few reports about the relationship between maternal and neonatal plasma PRL levels in neonatal asphyxia are found. This study aims at exploring the role of PRL in development of neonatal asphyxia by measuring maternal and neonatal plasma PRL levels in neonates with asphyxia.

Materials and methods

Clinical materials

Forty-five term neonates, who were born in the Second Hospital of Xi'an Jiaotong University between December, 2000 and December, 2001, were enrolled in this study. Of them there were 25 cases of asphyxia (14 males and 11 females - asphyxia group) and 20 normal neonates (11 males and 9 females - control group). According to the classic scoring method[1], the asphyxia group was further divided into the severe asphyxia group (n = 11) whose one minute Apgar score was 0 - 3 and the mild asphyxia group (n = 14) whose one minute Apgar score was 4 - 7. The gestational ages of the asphyxia group ranged from 38 to 42 weeks (with the mean of 40 weeks) and the birth weight were (3 200 ±300) g. The gestational ages of the control group ranged from 38 to 41 weeks [(39 ± 1.8) weeks] and the birth weight were (3 180 ± 298) g. There were 17 cases of natural birth and 8 cases of caesarean birth in the asphyxia group and there were 6 cases of caesarean birth and 14 cases of natural birth in the control group. There were no significant differences in gestational age, birth weight and age among these groups.

Methods

The samples of cord vein blood and maternal blood (2 ml each) were taken immediately after the infants were born. The neonatal vein blood samples (2 ml) were taken in neonates with asphyxia right after asphyxia resuscitation and after a further 2 and 10 days of life, respectively, and those of the control group were taken within 24 hours of birth. The supernates of the samples were separated by centrifugation at 4 ℃ with 3 000 rpm/min for 10 minutes and were preserved in the refrigerator at - 20 ℃. The PRL levels were measured by radioimmunoassay. The kit was provided by Jiuding Medical Biological Engineering Corp (Tianjin, China).

Statistical analysis

All data were expressed as $\bar{x} \pm s$. Analysis of variance (ANOVA), linear correlation analysis and *t* test were used.

Results

Comparison of the maternal blood, cord blood and neonatal plasma PRL levels between the asphyxia group and the control group

The PRL levels of the maternal blood, cord blood and neonatal plasma (right after resuscitation) in the asphyxia group were significantly higher than those in the control group ($P < 0.01$). See Table 1.

Table 1 PRL levels in the asphyxia group and the control group ($\bar{x} \pm s$, μg/L)

Group	n	Maternal blood	Cord blood	Neonatal plasma
Control	20	96.4 ±26.2	92.3 ±18.4	68.7 ±7.2
Asphyxia	25	362.5 ±127.1[a]	984.6 ±262.3[a]	386.3 ±216.2[a]

Note: a vs the control group $P < 0.01$

Comparison of the maternal blood, cord blood and neonatal plasma PRL levels (right after resuscitation) between the mild asphyxia group and the severe asphyxia group

The PRL levels of the maternal blood, cord blood and neonatal plasma (right after resuscitation) in the severe asphyxia group were significantly higher than those in the mild asphyxia group ($P < 0.01$ or 0.05). See Table 2. The cord blood and neonatal plasma PRL levels had a positive correlation in the mild asphyxia group and the severe asphyxia group, respectively ($r = 0.54$ and $r = 0.63$, $P < 0.05$).

Table 2 PRL levels in the two asphyxia groups ($\bar{x} \pm s$, μg/L)

Groups	n	Maternal blood	Cord blood	Neonatal plasma
Mild asphyxia	14	298 ±102	612 ±221	309 ±19.2
Severe asphyxia	11	445 ±216[a]	996 ±284[b]	412 ±221[a]

Note: a vs the mild asphyxia group $P < 0.01$; b vs the mild asphyxia group $P < 0.05$

Changes of the plasma PRL levels of asphyxia neonates in different day ages

The PRL level right after resuscitation was significantly higher than that of the control group ($P < 0.01$) and then reduced gradually from the 2nd day after birth. The PRL level on the 2nd day after birth was lower than that right after resuscitation and higher than that of the control group ($P < 0.01$). The differences of the PRL levels on the 10th day after birth in the asphyxia group and the control group were not significant ($P > 0.05$). See Table 3.

Table 3 Changes of plasma PRL levels of asphyxia neonates in different day ages

	n	PRL (μg/L)
Control group	20	68.7 ±7.2
Asphyxia group		
right after resuscitation	25	386.30 ±216.20[a]
2 days of life	24	138.10 ±52.80[a]
10 days of life	21	60.24 ±12.22

Note: a vs the control group $P < 0.01$

Discussion

PRL is a kind of polypeptide hormone secreted by the anterior pituitary. It was named after the function of stimulating milk secretion. Studies showed that the plasma and cerebral PRL levels after acute brain ischemia and reperfusion 30 min after ischemia were obviously higher than those in the control group[2]. Recent studies have shown that the release of excitatory amino acid (EAA) caused an increase of PRL in neonates with brain damage[3,4] and that there was a relationship between the plasma PRL level and the degree of brain damage[5]. However, it has not reported whether the neonatal plasma PRL levels are associated with the PRL levels of cord blood and maternal blood in the newborns with asphyxia.

This study showed that the maternal blood, cord blood and neonatal plasma PRL levels in the asphyxia group were higher than those in the normal control group. It indicated that hypoxia and ischemia of the brain might lead to an increase of EAA level. This caused the anterior pituitary to release PRL and thus the PRL levels in the fetal plasma rose. The cord blood PRL levels also rose through the fetal circulation system. The reason for the increase of the maternal blood PRL levels needs further investigation.

The maternal blood, cord blood and neonatal plasma PRL levels in the severe asphyxia group were remarkably higher than those in the mild asphyxia group. This indicated that the increase of PRL was associated with perinatal asphyxia. The plasma PRL level may be regarded as a marker for evaluating the degree of asphyxia.

Studies have shown that the plasma PRL levels increased markedly during the acute period of HIE and had a positive correlation with the degree of asphyxia[6]. This study showed that plasma PRL levels rose remarkably after resuscitation and steadily decreased 2 days after birth. The plasma PRL level 10 days after birth was no different from that of the control group. The possible mechanism was that hypoxia and ischemia resulted in an increase of EAA and then caused the anterior pituitary to release PRL. When hypoxia and ischemia ameliorated, the stimulation to the anterior pituitary steadily decreased and the plasma PRL levels reduced.

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病例报告 ·

流感嗜血杆菌性脑膜炎致听力减退 1 例

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[中图分类号] R378.4+1 [文献标识码] E

患儿,4 $\frac{1}{2}$ 岁,白族,因发热、咳嗽 2 d 入院。患儿 2 d 前因受凉后出现发热,体温 39.6 ℃,干咳,入院当天呕吐 4 次胃内容物,量少,非喷射性,无头痛,抽搐等。入院第 2 天及第 3 天两次出现畏寒、寒颤、面色苍白、皮肤发花、气促、口唇发绀、肢端凉,测体温 39.2 ℃~40.5 ℃。

入院查体:T 37.7 ℃,P 120 次/min,R 28 次/min,神清、精神差,咽充血,双肺呼吸音粗,无罗音,心腹正常,神经系统检查阴性。入院第 3 天查体:意识不清,反应迟钝,不能对答,双瞳孔等大等圆,对光反射存在,四肢肌力,肌张力正常,生理反射正常,椎体束征阴性,颈抵抗,左克氏征(+)。

辅助检查:血常规 WBC 18.3 ×10^9/L,N 0.85,L 0.09,M 0.06,Hb 115 g/L,PLT 251 ×10^9/L,脑电图:异常脑电图:①弥漫性δ为主慢波异常;②双侧额、枕区多灶性棘波放电。头颅 CT:颅内未见异常。脑脊液常规检查:混浊,乳白色,潘氏试验强阳性,白细胞 6.2 ×10^9/L,N 94 %,L 6 %,涂片检出革兰阴性杆菌 + +;生化:氯化物 116 mmol/L,糖 0.02 mmol/L,蛋白 714 mg/L,脑脊液 LDH 163 U/L,脑脊液培养结果:流感嗜血杆菌,对青霉素、磷霉素,庆大霉素、氨苄青霉素、头孢呋新、头孢噻甲羧肟、克林霉素、环丙沙星,优立新耐药,对头孢三嗪、先锋必中敏,对氯霉素、利福平敏感。

诊断及治疗:诊断为流感嗜血杆菌性脑膜炎,给氯霉素、利福平、甘露醇、脑细胞活化剂等治疗,住院第 6 天神志清楚,第 8 天发现听力下降(病程第 10 天),行脑干听觉诱发电位(ABR)检查:左耳 ABR 重度异常,短声听阈 70 dB,右耳 ABR 中度异常,短声听阈 60 dB。诊断流感嗜血杆菌性脑膜炎并发中枢性听力减退,又加用神经生长因子、维生素 B_1、维生素 B_{12} 治疗,治疗半个月复查脑脊液常规:清晰,无色,潘氏试验阳性,白细胞 242 ×10^6/L,N 18 %,L 82 %,涂片未检出细菌;生化:糖 3.2 mmol/L,氯化物 118 mmol/L,LDH 37 U/L,培养无菌生长,复查头颅 CT:颅内未见异常。住院治疗 22 d 体温正常,治疗 30 d 复查脑脊液常规:清晰,无色,潘氏试验弱阳性,白细胞数 78 ×10^6/L,N 5 %,L 95 %,涂片未检出细菌;生化:糖2.69 mmol/L,氯化物 121 mmol/L,LDH 19 U/L,培养无菌生长,住院 35 d 出院,出院后口服利福平疗程 3 个月。随诊 8 个月,患儿听力仍未恢复。

讨论:B 型流感嗜血杆菌是细菌性脑膜炎的主要病原菌之一,所致听力障碍占 2.7 %,但各种文献均未报道听力障碍发生的时间,原因是多方面的。本例小儿初次到医院怕见生人,对诊疗存在惧怕心理,民族语言交流困难,最主要是患儿入院第 3 天出现意识不清,故不易发现听力障碍。脑脊液培养出流感嗜血杆菌对多种抗生素耐药,致病力较强,有一定嗜神经性,特别是对耳蜗神经损害,是细菌内毒素还是耳蜗神经微动脉血栓导致的听力障碍,有待进一步证实。

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