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胎盘组织学绒毛膜羊膜炎与未足月胎膜早破后早产儿脑损伤关系*

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摘要 目的:研究胎盘组织学绒毛膜羊膜炎与未足月胎膜早破后早产儿出现脑损伤的相关性。**方法:**选取我院妇产科 2017 年 1 月至 2019 年 12 月收治的因胎膜早破生产的未足月早产儿 80 例,根据是否存在绒毛膜羊膜炎分为观察组(绒毛膜羊膜炎)和对照组(无绒毛膜羊膜炎),每组 40 例,患儿于胎龄 40 w 时行颅脑核磁共振检查(Magnetic Resonance Examination, MRI),对比两组脑室周围白质软化(periventricular leukomalacia, PVL)阳性率,且采用新生儿 20 项行为神经评分量表(neonatal behavior neurological assessment, NBNA)评价两组患儿神经行为,然后在纠正胎龄 3、6 个月时对两组患儿进行智能发育指数(mental developmental index, MDI)及心理运动发育指数(psychomotor development index, PDI)测定并对比。**结果:**观察组 PVL 阳性率为 27.5%,高于对照组的 10.0% ($P<0.05$);观察组纠正胎龄 40 w NBNA 得分为 (31.02 ± 3.51) 分,对照组为 (35.21 ± 4.02) 分,差异具有统计学意义 ($P<0.05$);胎龄 3 个月,MDI 得分在观察组与对照组间差异无统计学意义 ($P>0.05$),但其 PDI 得分低于对照组 ($P<0.05$);胎龄 6 个月,观察组 MDI 及 PDI 得分均低于对照组 ($P<0.05$)。**结论:**绒毛膜羊膜炎与未足月胎膜早破后早产儿的脑部损伤情况具有一定相关性,可以作为预测早产儿脑损伤程度的一项指标。

关键词:绒毛膜羊膜炎;早产儿;脑损伤

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The Relationship between Placental Histology Chorioamnionitis and Brain Damage in Preterm Infants after Preterm Rupture of Membranes*

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ABSTRACT Objective: To study the correlation between placental histology, chorioamnionitis, and brain damage in preterm infants after preterm rupture of membranes. **Methods:** 80 cases of preterm infants born due to premature rupture of membranes treated in our obstetrics and gynecology department from January 2017 to December 2019 were selected and divided into observation group (chorioamnionitis) and chorioamnionitis based on the presence or absence of chorioamnionitis and In the control group (non chorioamnionitis), 40 patients in each group received craniocerebral MRI at 40 weeks of gestational age, compared the PVL positive rate between the two groups, and evaluated the neurobehavior of the two groups with 20 NBNA of newborns Then at the correct gestational age of 3 and 6 months, MDI and PDI were measured and compared between the two groups of children. **Results:** The positive rate of PVL in the observation group was 27.5 %, which was higher than 10.0 % in the control group, and the difference was statistically significant ($P<0.05$). The corrected NBNA score of the observation group at 40 weeks was (31.02 ± 3.51) points, and the control group was (35.21 ± 4.02) points. The difference was statistically significant ($P<0.05$). At 3 months of gestational age, there was no significant difference in MDI score between the observation group and the control group ($P>0.05$), but its PDI score was lower than Control group ($P<0.05$). MDI and PDI scores in observation group were lower than those in control group ($P<0.05$). **Conclusion:** Chorioamnionitis and brain damage in preterm infants with preterm premature rupture of membranes have a certain correlation, which can be used as an index to predict the degree of brain damage in preterm infants.

Key words: Chorioamnionitis; Premature infants; Brain injury

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前言

未足月胎膜早破是指孕妇妊娠已满 28 w,但尚未达到 37 w 时这个时间段内出现的胎膜破裂^[1],该现象不仅会使孕妇再次

妊娠时发生胎膜破裂的几率增加,同时还会直接引发早产的发生,威胁胎儿生命健康^[2,3]。研究发现引发胎膜早破的原因主要有胎膜病变、下生殖道感染、微量元素缺乏以及宫内感染等,其中宫内感染是引发胎膜早破的重要原因^[4,5]。既往研究显示,代

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谢性酸中毒、胎膜破裂、缺血缺氧等都是胎儿脑损伤的影响因素,但近些年的研究指出,围产期感染也会引发未足月胎膜破裂现象的出现^[6,7]。胎毛膜羊膜炎是胎膜炎症的一种,研究指出该症与胎膜破裂存在较为密切的联系,同时该症还会引发胎儿败血症、呼吸窘迫等现象,影响胎儿脑组织正产发育^[8]。目前临床上还没有找到预测未足月胎膜早破后早产儿的脑部损伤满意的指标,国外对绒毛膜羊膜炎对新生儿的预后存在一定的争议。本文研究发现绒毛膜羊膜炎与未足月胎膜早破后早产儿的脑部损伤情况具有一定相关性,可以作为预测早产儿脑损伤程度的一项指标,现报道如下。

1 资料与方法

1.1 一般资料

选取我院妇产科 2017 年 1 月至 2019 年 12 月收治的因胎膜早破生产的未足月早产儿 80 例,根据是否存在绒毛膜羊膜炎分为观察组(绒毛膜羊膜炎)和对照组(无绒毛膜羊膜炎),每组 40 例。观察组:男 21 例,女 19 例,胎龄(32.06 ± 2.56)w,体重(1536.25 ± 450.63)g,顺产 22 例,剖宫产 18 例;对照组:男 23 例,女 17 例,胎龄(31.96 ± 3.01)w,体重(1486.39 ± 462.35)g,顺产 21 例,剖宫产 19 例,两组一般资料差异不具有统计学意义($P>0.05$),具有可比性。

纳入标准:①符合组织学绒毛膜羊膜炎诊断标准;②母亲意识清晰,能够协助患儿配合调研;③孕妇及家属知情同意,研究符合伦理道德。排除标准:①孕妇精神疾病及意识障碍;②孕妇合并妊娠并发症;③分娩过程中出现缺血缺氧者;④合并遗传性疾病如神经系统畸形者。

1.2 研究方法

出现胎膜早破的孕妇分娩后,医院指定专人对其胎盘胎膜进行采样分析,具体方法如下:以胎膜破口为中心,取 $10\text{ cm} \times 10\text{ cm}$ 大小的胎膜制作为胎膜卷,而后于胎盘中心、边缘等进行多处采样,样品中要包含羊膜、绒毛膜板、绒毛和底蜕膜,采样要指定专人负责,取得的样本使用 10%甲醛进行处理,而后石蜡包埋,制成切片,使用 HE 进行染色,而后请病理科经验丰富、中级职称以上医生进行阅片,确定孕产妇是否存在绒毛膜

羊膜炎。

早产儿头颅 MRI 检查:早产儿均于纠正胎龄 40 w 时,使用飞利浦 1.5 T 核磁共振仪对其进行头颅 B 超检查,根据检测结果将早产儿病情进行分级。

早产儿 NBNA、MDI 及 PDI 测定:于纠正胎龄 40 w 时,使用 NBNA 所有新生儿神经行为进行测定评分,于纠正胎龄 3 个月和 6 个月时,使用 MDI 和 PDI 量表对所有新生儿智能发育情况和心理发育情况进行测定。

1.3 研究指标

1.3.1 早产儿脑室周围白质软化(PVL)情况测定 根据早产儿 MRI 检测结果可将 PVL 病变程度分级^[9]:①轻度:侧脑室三角区旁边白质出现减少,附近脑沟突出,但脑室未出现显著异常;②中度:半卵圆中心出现白质减少情况,同时侧脑室四周白质出现显著减少,侧脑室出现扩张;③重度:白质基本消失,现空囊腔,脑室呈现显著扩大, $\text{PVL 阳性率} = (\text{轻度} + \text{中度} + \text{重度}) / \text{总例数} \times 100\%$ 。

1.3.2 早产儿新生儿 20 项行为神经评分法(NBNA)评分 NBNA 量表能够对新生儿的神经活动能力进行测定^[10],同时能够尽早的发现新生儿脑损伤情况,对早期发现病情,尽早实施干预具有重要意义,该量表共分为 5 个维度,合计 20 项测评,总分为 40 分,得分越高代表神经行为能力越强。

1.3.3 早产儿智能发育指数(MDI)及心理运动发育指数(PDI)评分 患儿均于纠正胎龄 3、6 个月时用婴幼儿智能运动发育检测量表(CDCC)对其 MDI 及 PDI 进行测定,该量表能够对 0-3 岁儿童的智力发育及运动协调能力进行测定^[11]。

1.4 统计学方法

采用 SPSS 25.0 对数据整理分析,计数资料以率(%)的形式表示,采用卡方检验(χ^2)或 Fisher 检验,计量资料以($\bar{x} \pm s$)的形式表示,采用 t 检验,取 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患儿 PVL 阳性率比较

观察组 PVL 阳性率为 27.5%,高于对照组的 10.0%,差异具有统计学意义($P<0.05$),见表 1。

表 1 两组 PVL 阳性率对比[例(%)]

Table 1 Comparison of PVL positive rates between the two groups[n(%)]

Groups	n	Mild	Moderate	Severe	Positive rate
Observation group	40	4 (10.0)	4 (10.0)	3 (7.5)	11 (27.5)*
Control group	40	2 (5.0)	2 (5.0)	0 (0.0)	4 (10.0)

Note: Compared with the control group, * $P<0.05$.

2.2 两组 NBNA 得分比较

观察组纠正胎龄 40 w NBNA 得分为(31.02 ± 3.51)分,对照组为(35.21 ± 4.02)分,差异具有统计学意义($P<0.05$)。

2.3 两组 MDI 及 PDI 得分对比

胎龄 3 个月,MDI 得分在观察组与对照组间差异无具有统计学意义($P>0.05$),但其 PDI 得分低于对照组,差异具有统计学意义($P<0.05$);胎龄 6 个月,观察组 MDI 及 PDI 得分均低于对照组,差异均具有统计学意义($P<0.05$),见表 2。

3 讨论

未足月胎膜破裂约占全部早产儿中的 30%,且近些年随着居民生活方式和饮食结构的改变,该比例有逐年增多趋势^[12,13]。随着医疗技术的发展与进步,早产儿的存活率不断提升,但早产会对胎儿的脑组织发育造成较大伤害,存活率的提升意味着早产儿脑损伤率也相应增高^[14,15],因而我们可以推断为:胎膜早破引发早产发生,而早产的出现意味着新生儿脑损伤几率增加

表 2 两组 MDI 及 PDI 得分对比

Table 2 Comparison of MDI and PDI scores between the two groups

Groups	n	Gestational age 3 months		Gestational age 6 months	
		MDI	PDI	MDI	PDI
Observation group	40	98.21± 10.26	102.12± 14.62*	102.69± 15.21*	86.52± 8.41*
Control group	40	102.31± 9.56	113.26± 15.02	108.21± 9.85	103.25± 7.56

[16]。有学者的研究指出,脑损伤在早产儿中的发生率高达 25.5%,即使新生儿平安度过危险期,存活的早产儿中的 10%会出现脑瘫,严重影响其生活及社会经济的发展[17],依据现有的治疗手段尚无法彻底治疗早产儿的脑损伤,故现阶段对早产儿脑损伤的预防成为医务工作者研究的重点方向[18,19]。未足月胎膜破裂是引发早产发生、导致新生儿脑损伤的重要原因,而有学者的研究指出,产妇发生胎膜破裂的原因主要为宫内感染[20,21]。

绒毛膜羊膜炎是孕产妇常见炎症之一,发病原因主要为各类微生物感染,该病发生后常导致产程延长或胎膜早破,增加了新生儿败血症、呼吸窘迫的发生率,以致也提高了胎儿的死亡率,对于该病与胎膜早破之间的关联[22,23],多名学者进行了研究,有学者通过对 80 例合并绒毛膜羊膜炎未足月胎膜早破患儿的的研究,发现孕产妇体内绒毛膜羊膜炎发生率与其破膜时间之间存在正相关联系,提示绒毛膜羊膜炎是引发未足月胎膜早破的原因之一[24];同样有研究按照胎膜早破时间将 60 例胎膜早破产妇分为 A、B、C 三组,结果发现绒毛膜羊膜炎发生率与胎膜早破时间存在正相关联系[25]。

本文作者通过设立病例组和对照组的方式,对胎盘组织学绒毛膜羊膜炎和未足月胎膜早破后早产儿脑损伤之间的关联进行了研究,结果发现,相比于未出现绒毛膜羊膜炎的对照组患儿,病例组患儿 PVL 程度更高、NBNA、MDI 及 PDI 得分更低,提示病例组患儿脑组织损伤更为严重,分析其机理为绒毛膜羊膜炎为宫内感染的一种,炎症引发各类细胞因子的大量分泌,是胎膜脆性增加,最终引发胎膜破裂,而胎膜破裂引发早产,早产儿会因为发育不全或缺血缺氧而引发脑组织损伤,形成链条反应,故而对孕产妇胎盘组织学绒毛膜羊膜炎的监测是预防早产儿出现脑损伤的重要途径之一。对于绒毛膜羊膜炎是否与未足月胎膜早破后早产儿脑损伤之间存在关联,多名学者也进行了研究,有研究通过对因绒毛膜羊膜炎引发胎膜破裂的早产儿的研究发现[26,27],与无绒毛膜羊膜炎早产儿相比,出现病变的早产儿其脑部白质软化情况更为严重,脑室周围出血情况发生率也较高[27],该学者认为绒毛膜羊膜炎与早产儿脑损伤之间存在一定关联,该病能够增加早产儿白质软化的严重程度[28];研究发现,绒毛膜羊膜炎早产儿脑损伤出现率远高于无绒毛膜羊膜炎早产儿,其白质损伤程度更高,提示绒毛膜羊膜炎与早产儿脑损伤间存在一定关联,通过上述研究我们可以发现,胎盘组织学绒毛膜羊膜炎能够诱发胎膜早破,而胎膜早破导致的早产则是导致新生儿脑损伤的重要原因[29,30]。目前临床上还没有找到预测未足月胎膜早破后早产儿的脑部损伤满意的指标,国外对绒毛膜羊膜炎对新生儿的预后存在一定的争议,因此,本文通过研究发现绒毛膜羊膜炎与未足月胎膜早破后早产儿的脑部损伤情况具有一定相关性,可以作为预测早产儿脑损伤

程度的一项指标,为后期胎盘组织学绒毛膜羊膜炎与未足月胎膜早破后早产儿脑组织损伤的研究提供了研究的方向和基础。

综上所述,胎盘组织学绒毛膜羊膜炎与未足月胎膜早破后早产儿脑组织损伤之间存在一定关联,可以作为评估及预防新生儿脑组织损伤的指标,值得临床推广。本研究也存在一定的不足,样品量少,来源单一,且没研究患儿 PVL、NBNA、MDI 及 PDI 与新生儿脑组织损伤的相关性,后续研究需要深入探究。

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