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经鼻间歇正压通气联合猪肺磷脂注射液治疗新生儿呼吸窘迫综合征的临床疗效*

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摘要 目的:探讨经鼻间歇正压通气联合猪肺磷脂注射液治疗新生儿呼吸窘迫综合征临床疗效及安全性的影响。**方法:**前瞻性研究于我院进行治疗的呼吸窘迫综合征患儿 60 例,根据电脑生成的随机数字表将所有患儿随机分为实验组与对照组,每组各 30 例,对照组患儿使用经鼻间歇正压通气进行治疗,实验组患儿在对照组的基础上联合猪肺磷脂注射液进行治疗。治疗结束后比较两组患儿动脉血氧分压(PaO_2)、动脉血二氧化碳分压(PaCO_2)、氧合指数及血样饱和度(SaO_2)水平的变化,统计并记录两组患儿并发症的发病情况,并对两组患儿的临床疗效进行评价。**结果:**与治疗前相比,两组患儿 PaCO_2 水平均降低, PaO_2 、 SaO_2 水平及氧合指数均升高($P<0.05$);与对照组相比,实验组患儿 PaCO_2 水平较低, PaO_2 、 SaO_2 水平及氧合指数较高($P<0.05$);且与对照组相比,实验组的并发症发病率较低,临床总有效率较高($P<0.05$)。**结论:**经鼻间歇正压通气联合猪肺磷脂注射液治疗新生儿呼吸窘迫综合征安全有效,值得在临床上推广应用。

关键词:经鼻间歇正压通气;猪肺磷脂注射液;呼吸窘迫综合征;临床疗效

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Clinical Efficacy and Safety of Nasal Intermittent Positive Pressure Ventilation combined with Poractant Alfa Injection in the Treatment of Neonatal Respiratory Distress Syndrome*

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ABSTRACT Objective: To investigate the clinical efficacy and safety of nasal intermittent positive pressure ventilation combined with poractant alfa injection in the treatment of neonatal respiratory distress syndrome. **Methods:** 60 children with respiratory distress syndrome who were treated in our hospital were selected and randomly divided into experiment group and control group with 30 cases in each group. The patients in the control group were treated with nasal intermittent positive pressure ventilation treatment, and the patients in the experiment group were treated with poractant alfa injection on the basis of the control group. Then the levels of the arterial blood oxygen partial pressure(PaO_2), arterial blood CO_2 partial pressure (PaCO_2), oxygenation index and blood sample saturation (SaO_2) and the clinical efficacy and the incidence of the complications in the two groups were observed and compared before and after the treatment. **Results:** Compared with before treatment, the levels of PaCO_2 in the two groups decreased after treatment, while the levels of PaO_2 and SaO_2 and oxygenation index increased ($P<0.05$); Compared with the control group, the level of PaCO_2 in the experiment group was lower, while the levels of PaO_2 and SaO_2 and the oxygenation index were higher ($P<0.05$); Compared with the control group, the incidence of complications in the experiment was lower, and the clinical total effective rate was higher ($P<0.05$). **Conclusion:** Nasal intermittent positive pressure ventilation combine with poractant alfa injection in the treatment of neonatal respiratory distress syndrome is safe and effective, which is worth of clinical application.

Key words: Nasal intermittent positive pressure ventilation; Poractant alfa injection; Respiratory distress syndrome; Clinical efficacy

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新生儿呼吸窘迫综合征(NRDS)亦称新生儿肺透明膜病,是儿科疾病的一种,常见于早产儿,是一种因肺泡表面活性物质缺乏而导致肺泡进行性萎陷的疾病^[1]。轻型患儿起病较晚,可迟至产后 24-48 h,且呼吸困难、呻吟、发绀等症状较轻,经治疗,三天后即可好转^[2]。较为严重的患儿在刚出生时哭声正常,

但在 6~12 h 后,即会出现逐渐加重得呼吸困难,发绀、面色灰白或青灰,吸气时胸廓软组织凹陷,并伴有呻吟^[3]。若未能进行及时有效的治疗,婴儿可在三天内出现死亡,已有研究表明^[4],该病患儿在产后第二天的病死率最高,且体重越轻病死率越高。目前,临床上医者多采用经鼻间歇正压通气进行治疗,机械

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通气虽然可以挽救患儿的生命,减轻临床症状,但治标不治本,治疗效果一般,故应寻找更好的治疗方案,给予猪肺磷脂注射液属于表面活性物质替代治疗的一种^[9]。猪肺磷脂是一种天然提取物,磷脂占干重的90%,大部分为磷脂酰胆碱,具有表面活性的磷脂酰胆碱为二棕榈酸磷脂酰胆碱,其余的磷脂还包括磷脂酰丝氨酸、磷脂酰乙醇胺、鞘磷脂及磷脂酰肌醇^[9]。因此,本研究通过对经鼻间歇正压通气联合猪肺磷脂注射液治疗新生儿呼吸窘迫综合征临床疗效及安全性的研究,以期为新生儿呼吸窘迫综合征的治疗提供可能的依据。

1 资料与方法

1.1 临床资料

选取2014年12月~2016年6月于我院儿科病房进行治疗的呼吸窘迫综合征患儿60例,男性患儿40例,女性患儿20例,胎龄35~40周,平均胎龄(37.58±4.52)周。根据其X线可将患儿分为3级,其中45例为I级毛玻璃样病变的患儿,12例为II级支气管充气征患儿,3例为III级白肺的患儿。应用随机数字表对所有患儿进行1~60号编号,实验组为单号,对照组为双号。经统计学分析,两组患儿在胎龄、性别、体重、疾病分级、发病至治疗时间及分娩方式等一般情况相当,差异不具有统计学意义($P>0.05$)。患儿均符合第五版《西医儿科学》中关于新生儿呼吸窘迫综合征的诊断标准;胎龄在35~40周之间,且属于自然分娩者;发病24小时内进行治疗的患儿;对研究中使用的药物不发生过敏反应。排除不符合新生儿呼吸窘迫综合征的诊断标准;合并先天性心脏病、先天性膈疝或先天性呼吸道畸形的患儿;合并严重呼吸道感染或败血症患儿;不符合经鼻间歇正压通气临床应用指征。本实验经我院伦理协会批准,患儿家属签署知情同意书。

1.2 方法

患儿确诊为呼吸窘迫综合征后立即进行气管插管处理,并使患儿采取仰卧位,立刻清理呼吸道内的分泌物。实验组:在患

儿家属同意的基础上予以猪肺磷脂注射液(进口药品 意大利 Chiesi Farmaceutici S.p.A., 注册证号:H20080428, 2008-08-04),用法用量:先按照50 mg/kg的量取出本品后,将其逐渐升温至37℃后轻轻摇晃,调为均匀液体后后沿气管插管快速注入,随后连接经鼻间歇正压通气装置,给予通气治疗。对照组:不给予猪肺磷脂注射液,仅使用经鼻间歇正压通气装置给予通气治疗。

1.3 观察指标

比较治疗前及治疗结束后24小时两组患儿 PaO_2 、 PaCO_2 、 SaO_2 水平及氧合指数变化情况,并对两组患儿发生的并发症(腹胀、气漏、鼻部损伤、肺出血)进行统计,计算并发症发病率。并发症发病率=(腹胀+气漏+鼻部损伤+肺出血)/总例数×100%。

1.4 疗效判断

显效:患儿口唇发绀、呼吸困难或呻吟等临床表现明显减轻;有效:患儿口唇发绀、呼吸困难或呻吟等临床表现有所减轻;无效:患儿临床症状及体征未见减轻,甚至加重。总有效率=(显效+有效)/总例数×100%。

1.5 统计学分析

所有计量数据录入SPSS19.0软件进行统计学分析,并发症发病情况及临床疗效采用卡方检验, PaO_2 、 PaCO_2 、 SaO_2 水平及氧合指数采用t检验,若检验后 $P<0.05$,则认为有统计学意义。

2 结果

2.1 治疗前后两组 PaO_2 、 PaCO_2 、 SaO_2 水平及氧合指数比较

与治疗前相比,两组患儿 PaCO_2 水平均降低, PaO_2 、 SaO_2 水平及氧合指数均升高($P<0.05$);与对照组比较,实验组患儿 PaCO_2 水平较低, PaO_2 、 SaO_2 水平及氧合指数较高,差异具有统计学意义($P<0.05$)。见表1。

表1 治疗前后两组 PaO_2 、 PaCO_2 、 SaO_2 水平及氧合指数比较($\bar{x}\pm s$)

Table 1 Comparison of the levels of PaO_2 , PaCO_2 and SaO_2 and oxygenation indexes between two groups before and after treatment($\bar{x}\pm s$)

Groups		PaO_2 (mmHg)	PaCO_2 (mmHg)	SaO_2 (%)	oxygenation index(mmHg)
Experiment group (n=30)	Before treatment	46.49±4.88	57.87±8.03	77.46±7.85	113.56±13.64
	After treatment	76.87±9.64* [#]	39.87±4.05* [#]	95.86±13.05* [#]	277.26±33.53* [#]
Control group(n=30)	Before treatment	46.33±4.79	57.91±8.08	77.53±7.88	116.43±13.75
	After treatment	62.76±7.75*	49.45±5.98*	88.45±10.74*	210.54±26.44*

Note: Compared with before treatment, * $P<0.05$. Compared with the control group, [#] $P<0.05$.

2.2 两组患儿并发症发病情况比较

与对照组相比,实验组患儿的并发症发病率明显较低,差异有统计学意义($P<0.05$)。见表2。

2.3 治疗后两组患儿临床疗效比较

与对照组相比,实验组临床总有效率较高,差异有统计学意义($P<0.05$)。见表3。

3 讨论

新生儿窘迫呼吸综合征是指出生不久的新生儿发生呼吸困难,性质为进行性,进而发生呼吸衰竭等症状,因病理上显示有肺透明膜,又叫做新生儿肺透明膜病^[7]。本病多见于早产儿,由于其机体各种生理功能尤其是呼吸系统功能尚未发育完善,先天有所欠缺,造成患儿的肺表面活性物质(ps)含量降低,导致肺不张进而使机体与外界的气体交换受阻,诱发呼吸衰竭,是新生儿致死的主要原因之一^[8,9]。患儿出生时哭声可为正常,在出生后的六至十二小时内发生进行性呼吸困难,症状逐渐加

表 2 两组并发症情况比较[例(%)]

Table 2 Comparison of the incidence of complications between two groups [n(%)]

Groups	Abdominal distention	frequent hemorrhoid	Nose injury	Pulmonary hemorrhage	Complication incidence rate
Experiment group (n=30)	1(3.33)	2(6.67)	1(3.33)	2(6.67)	6(20.00)*
Control group(n=30)	4(13.33)	4(13.33)	3(10.00)	5(16.67)	16(53.33)

Note: compared with the control group after treatment, *P<0.05.

表 3 两组患儿疗效比较[例(%)]

Table 3 Comparison of the clinical curative effect between two groups [n(%)]

Groups	Excellence	Effective	Invalid	Clinical rate
Experiment group(n=30)	12(40.00)	14(46.67)	4(13.33)	26(86.67)*
Control group(n=30)	7(23.33)	10(33.33)	13(43.33)	17(56.67)

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

重,伴有呻吟;患儿呼吸无规律,间或有呼吸暂停现象,面色呈现灰白或青灰,缺氧严重者四肢的肌张力明显降低^[10];体征主要有鼻翼扇动,起初胸廓隆起,之后随肺不张加重而逐渐塌陷,其中腋下表现最为明显,吸气时,胸廓软组织发生以胸骨下端、肋缘下处为明显的凹陷,肺呼吸音减弱,肺部听诊可以闻及吸气时细湿罗音^[11]。经鼻间歇通气(NIPPV)是一种无创伤的通气方式,通过使咽部压力间歇升高而使上呼吸道的压力升高,使喉部间歇性膨胀来实现激发呼吸运动的目的,增加肺泡的充盈度;NIPPV可使患儿的呼吸暂停发作次数减少,使气道压的平均值升高、呼吸功减少,支持肺泡扩张,进而使气体交换增加^[12-14]。猪肺磷脂注射液是一种提取猪肺肺泡有效成分而制成的天然表面活性物质,能够使肺泡表面张力降低,阻止肺泡发生萎缩;对肺泡表面的张力进行调节,使其内部压力稳定,保证小肺泡不易萎缩,大肺泡不易膨胀多度;维持肺的顺应性;使肺泡-毛细血管之间的液体平衡得以稳定,防止发生肺水肿;并且可以参与呼吸道的防御与免疫调节功能;对肺液的清除产生促进作用,使肺泡上皮细胞受到保护^[15-17]。

PaO₂即动脉血氧分压,指的是氧分子以物理形态在血浆中溶解所生成的张力,其主要受机体呼吸系统功能情况与吸入气体的氧分压高低应影响,同时与氧在细胞中的利用程度有关^[18]。PaO₂是影响血氧饱和度的关键因素,也是对机体氧合水平进行判断的一个良好指标,能够直观地反映出组织的缺氧程度。二氧化碳分压(PaCO₂)指的是二氧化碳分子以物理形态溶解在血液中所产生的压力,其中物理溶解的CO₂占血中总含量的5%,并多以碳酸形式存在,呼吸作用直接调节PaCO₂的大小,血液中的pH值受其数值大小影响,PaCO₂的水平能够反映肺泡的通气状况与呼吸系统对于酸碱平衡的调节能力情况^[19]。SaO₂即血氧饱和度,是指与氧结合的血红蛋白的数量在血红蛋白总量中所占的百分比,PaO₂与血红蛋白的质和量都能对其产生影响,尤其是PaO₂的轻度改变就能使SaO₂受到很大影响,SaO₂能够很好地反映血红蛋白与氧结合的能力,以及呼吸器官将氧传送到血中的能力,是对肺功能评价的可靠依据,能对组织的缺氧程度进行较准确的判断^[20]。氧合指数是指PaO₂/FiO₂的比值,其正常范围在400~500 mmHg内,临床呼吸救治的目的是使缺氧器官获得充足的氧气,用以完成氧合作用

来得到能量供给,但因为不能直接检测到细胞中的氧合情况,故而临床上常用氧合指数来间接了解机体的氧合情况。本实验结果显示,治疗后与对照组比较,实验组患者PaCO₂较低,PaO₂、SaO₂及氧合指数较高(P<0.05),证明经鼻间歇正压通气联合猪肺磷脂注射液能够有效改善患儿肺功能与缺氧症状。

在新生儿窘迫呼吸综合征的救治过程中,常见的并发症有腹胀、气漏、鼻部损伤、肺出血。由于新生儿机体娇弱,在应用设备进行经鼻间歇正压通气时可能会出现一些损伤,例如鼻部损伤,同时由于通气时呼气末气道仍保持一定压力,腹压可能异常增加,形成腹胀。气漏是由于肺泡壁受损,气体散入肺间质,或因为通气时MAP过高而导致间质性肺气肿发生,气体经由血管到达纵隔,造成纵隔气肿,当气漏发生时,患儿呼吸困难加重。新生儿的肺出血多为血性肺水肿,且其发生机率与新生儿体重成反比,肺出血的出现提示了患儿病情危重,死亡率高。本研究结果显示,治疗后与对照组相比,实验组患者的并发症发病率明显较低(P<0.05),证明了经鼻间歇正压通气联合猪肺磷脂注射液能够有效降低新生儿窘迫呼吸综合征并发症发病率。此外,治疗后与对照组相比,实验组临床总有效率较高(P<0.05),说明经鼻间歇正压通气联合猪肺磷脂注射液能够有效提高新生儿窘迫呼吸综合征的临床疗效。

综上所述,经鼻间歇正压通气联合猪肺磷脂注射液能够有效改善患儿肺功能与缺氧症状,降低并发症发生率,提高临床疗效。

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