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帕拉米韦氯化钠注射液对流感病毒 A 型肺炎患儿的成本 - 效益分析 *

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摘要 目的：探讨帕拉米韦氯化钠注射液对流感病毒 A 型肺炎患儿的成本 - 效益。**方法：**选择我院 2015 年 1 月至 2018 年 12 月收治的 96 例流感病毒 A 型肺炎患儿，根据随机数字表法，将 96 例患儿分为 A 组及 B 组，每组 48 例，A 组患儿给予磷酸奥司他韦颗粒，B 组患儿给予帕拉米韦氯化钠注射液，对比两组患儿的治疗效果、临床症状消失时间、住院时间、用药成本、成本 - 效益，对比两组患儿治疗前及治疗后的血常规及肝肾功能，对比两组患儿的不良反应发生率。**结果：**B 组患儿的治疗有效率明显较 A 组高（$P<0.05$）。观察组患儿的临床症状消失时间及住院时间明显较对照组低（$P<0.05$）。A 组患儿的平均用药成本明显低于 B 组（$P<0.05$），A 组的成本 - 效益较 B 组低。与治疗前相比，治疗后两组患儿的中性粒细胞总数明显升高，白细胞总数、淋巴细胞总数明显降低（$P<0.05$）；而治疗前后，两组患儿的血常规指标对比无统计学意义（$P>0.05$）。治疗前后，两组患儿的肝肾功能对比均无统计学意义（$P>0.05$）。B 组患儿的不良反应发生率较 A 组高，但组间对比无统计学意义（$P>0.05$）。**结论：**与磷酸奥司他韦相比，帕拉米韦氯化钠注射液对流感病毒 A 型肺炎患儿的疗效更佳，但其成本 - 效益较低，临床上可根据患儿实际情况选择用药。

关键词：帕拉米韦氯化钠注射液；磷酸奥司他韦；流感病毒 A 型肺炎；成本 - 效益；不良反应

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The Cost-benefit Analysis of Peramivir Sodium Chloride Injection in Children with Influenza Virus Type A Pneumonia*

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ABSTRACT Objective: To investigate the cost-benefit analysis of peramivir sodium chloride injection in children with influenza virus type A pneumonia. **Methods:** 96 children with influenza virus A pneumonia admitted to our hospital from January 2015 to December 2018 were selected, who were divided into two groups according to the random number table method, each group had 48 cases, group A were given Oseltamivir phosphate granules, group B were given Peramivir sodium chloride injection, the treatment effect, clinical symptoms disappearance time, stay length , medication cost, cost-benefit in two groups were compared, the blood routine and liver and kidney function before and after treatment were compared in two groups, and the incidence of adverse reactions was compared between the two groups. **Results:** The effective rate of treatment in group B was significantly higher than that in group A ($P<0.05$). The average drug cost of group A was significantly lower than that of group B ($P<0.05$), and the cost-benefit of group A was lower than that of group B ($P<0.05$). Compared with before treatment, the total number of neutrophils was significantly increased, and the total number of white blood cells and lymphocytes were significantly decreased in two groups after treatment ($P<0.05$). Before and after treatment, there were no statistical significance in blood routine indexes of two groups ($P>0.05$). Before and after treatment, there was no statistical significance in liver and kidney function of two groups ($P>0.05$). The incidence of adverse reactions in group B was higher than that in group A, but the comparison between groups was not statistically significant ($P>0.05$). **Conclusion:** Compared with Oseltamivir phosphate, Peramivir sodium chloride injection has better efficacy in the treatment of children with influenza virus type A pneumonia, while the cost-benefit was low, and medication could be selected according to the actual situation of children.

Key words: Peramivir sodium chloride injection; Oseltamivir phosphate; Influenza virus A pneumonia; Cost-effectiveness; Adverse reactions

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前言

流感病毒的流行病学特点为迅速扩散、突然爆发，会导致不同程度的流行，其属于正粘病毒科，包括 A、B、C 三种类型[1,3]。有研究发现，在 1977 年以来，每年全球流感发生的病毒类型包括 A、B、C 三种类型，目前全球流行的主要是 A 型及 B 型，其具有高度传染性，多通过接触病毒污染物体表面、呼吸道飞沫近距离传播、空气传播等方式进行传播，其可发生于各年龄的人群中，儿童是流感易感人群[4-6]。有研究发现[7]，儿童感染流行病毒 A 型后的肺炎发病率较高，流感病毒 A 型肺炎多发生于冬春寒冷季节，且在 3 岁以下患儿的发病率较高，与 3 岁以下婴幼儿的支气管肺发育尚不完善及婴幼儿免疫系统较低有关。儿童感染 A 型流感病毒肺炎后，疾病进展较快，若不及时治疗，甚至会导致患儿死亡，因此需要给予积极治疗，而临床上选择经济有效的一种治疗方法或药物非常重要。帕拉米韦氯化钠注射液是一种新型的新型流感病毒神经氨酸酶抑制剂，而奥司他韦也是儿童流感的有效治疗药物，目前关于二者对儿童流感病毒的疗效研究较多[8-10]，而二者在流感病毒 A 型肺炎患儿中的成本 - 效益研究较少，因此本文分析了帕拉米韦氯化钠注射液对流感病毒 A 型肺炎患儿的成本 - 效益，以为流感病毒 A 型肺炎患儿选择经济有效的药物提供依据。

1 资料与方法

1.1 一般资料

选择我院 2015 年 1 月至 2018 年 12 月收治的 96 例流感病毒 A 型肺炎患儿，所有患儿均经采用直接免疫荧光法检测鼻咽分泌物，确定为流感病毒 A 型患儿，同时符合《诸福棠实用儿科学》中关于肺炎的诊断标准[11]；排除抽搐者、脑病者、血液疾病者、意识障碍者、免疫治疗者、激素治疗者、机械通气者、有明确其他病毒感染者、严重心肝肾功能不全者、恶性肿瘤者、对本研究使用药物过敏者、近 1 个月内使用过抗病毒药物者等。96 例患儿中男 56 例，女 40 例，年龄范围为 6 个月 ~5 岁，平均年龄为 2.15± 0.45 岁。根据随机数字表法，将 96 例患儿分为 A 组及 B 组，每组 48 例，A 组患儿中男 29 例，女 19 例，年龄范围为 7 个月 ~5 岁，平均年龄为 2.08± 0.39 岁，B 组患儿中男 27 例，女 21 例，年龄范围为 6 个月 ~5 岁，平均年龄为 2.15± 0.45 岁。两组患儿的性别、年龄等资料对比无统计学意义（P>0.05）。本研究所有患儿家长知情同意，且经医院伦理委员会批准同意。

1.2 检查方法

患儿入院后 48 h 内，取其鼻咽部分泌物，采用无菌的吸痰管将分泌物吸至含 2 mL 0.9 %氯化钠溶液中，之后在检验科采用直接免疫荧光标记过的流感病毒 A 单克隆抗体（购自美国 Chemicon 公司）对流感病毒 A 型抗原进行检测，阳性为结果中发现≥ 2 个完整细胞内出现明亮黄绿色荧光[12]。

1.3 治疗方法

本研究 96 例患儿均给予吸氧、静脉输注、清理上呼吸道分泌物、保持呼吸道畅通等对症治疗。A 组患儿给予磷酸奥司他韦颗粒，购自宜昌东阳光长江药业股份有限公司，批准文号：国药准字：H20080763，规格：15 mg/ 袋，根据患儿体重给药，>40 kg 患儿每次 75 mg，23~40 kg 患儿每次 60 mg，15~23 kg 患儿每次 45 mg，≤ 15 kg 患儿每次 30 mg。

B 组患儿给予帕拉米韦氯化钠注射液，药物购自广州南新药业股份有限公司，批准文号：国药准字：H20130029，规格为 100 mL：0.3 g，给予静脉滴注，药物剂量为 10 mg/kg，每天 1 次，且单次的最大剂量≤ 300 mg。

两组患儿治疗疗程均为 5 d，若病情蔓延时，可延长疗程。

1.4 成本计算

成本 - 效益分析中的成本不包括护理、其他检查、辅助药物费用，本研究只计算药物成本，磷酸奥司他韦颗粒每盒为 10 袋，每盒 45.98 元，每袋 15 mg，帕拉米韦氯化钠注射液每瓶 100 mL，每瓶 233 元。

1.5 观察指标

（1）对比两组患儿的治疗效果，治疗 7 d 内患儿的各项体征、症状恢复至正常，治疗 3 d 内患儿的体温下降为痊愈；治疗 7 d 后患儿的各项体征、症状改善为好转，治疗 7 d 后患儿体征、症状无改善甚至加重为无效；（2）对比两组患儿的临床症状（发热、咳嗽、肺部啰音）消失时间及住院时间；（3）对比两组患儿的平均用药成本及成本 - 效益；（4）对比两组患儿治疗前及治疗后 6 d 的血常规及肝肾功能；（5）对比两组患儿的不良反应发生率。

1.6 统计学方法

应用 SPSS23.0 软件，计数资料或计量资料分别用百分比或 $\bar{x}\pm s$ 表示，用卡方检验或 t 检验对比分析，P<0.05 为差异有统计学意义。

2 结果

2.1 对比两组患儿的治疗效果

B 组患儿的治疗有效率为 97.92 %，A 组为 83.33 %，B 组患儿的治疗有效率明显较 A 组高（P<0.05），见表 1。

表 1 对比两组患儿的治疗效果[例（%）]

Table 1 The efficacy in two groups[n(%)]

Groups	n	Heal	Improvement	Invalid	Efficacy
Group A	48	30	10	8	40（83.33）*
Group B	48	37	10	1	47（97.92）

Note: Compare with the group B, *P<0.05.

2.2 对比两组患儿的临床症状消失时间及住院时间

观察组患儿的临床症状消失时间及住院时间明显较对照组低（P<0.05），见表 2。

2.3 对比两组患儿的用药成本及成本 - 效益

A 组患儿的平均用药成本明显低于 B 组（P<0.05），A 组的成本 - 效益较 B 组低，见表 3。

表 2 对比两组患儿的临床症状消失时间及住院时间($\bar{x}\pm s$,d)

Table 2 The clinical symptom disappearance time and hospital stay of the two groups were compared($\bar{x}\pm s$, d)

Groups	n	Temperature recovery time	Lung rales disappearance time	Cough resolution time	Length time
Group A	48	2.71± 0.45*	6.67± 0.89*	9.02± 1.31*	7.81± 1.21*
Group B	48	4.85± 0.89	10.86± 1.12	11.25± 1.79	12.85± 2.41

Note: Compare with the group B, *P<0.05.

表 3 对比两组患儿的平均用药成本及成本 - 效益

Table 3 The average drug cost and cost-benefit of the two groups were compared

Groups	n	Average drug cost(Yuan)	Cost-benefit
Group A	48	132.89± 28.79*	1.59
Group B	48	398.21± 35.78	4.07

Note: Compare with the group B, *P<0.05.

2.4 对比两组患儿治疗前及治疗后的血常规

与治疗前相比,治疗后两组患儿的中性粒细胞总数明显升高,白细胞总数、淋巴细胞总数明显降低(P<0.05);而治疗前后,两组患儿的血常规指标对比无统计学意义(P>0.05),见表 4。

表 4 对比两组患儿治疗前及治疗后的血常规($\bar{x}\pm s$)

Table 4 The blood routine before and after treatment was compared between the two groups($\bar{x}\pm s$)

Groups	n	Total neutrophils (× 10^9/L)		Leukocyte count (× 10^9/L)		Hemoglobin count (g/L)		Total lymphocyte (× 10^9/L)		Platelet count (× 10^9/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A	48	1.58± 0.31	1.98± 0.20*	7.63± 1.56	6.24± 0.97*	116.56± 18.15	117.15± 20.41	3.71± 0.75	2.84± 0.64*	232.21± 65.23	229.14± 45.12
Group B	48	1.57± 0.28	2.05± 0.32*	7.59± 1.63	6.30± 1.20*	116.87± 17.43	118.25± 24.13	3.73± 0.86	2.91± 0.72*	232.56± 66.12	230.57± 50.45

Note: Compared with the same group before treatment, *P<0.05.

2.5 对比两组患儿的肝肾功能

治疗前后,两组患儿的肝肾功能对比均无统计学意义(P>0.05),见表 5。

表 5 对比两组患儿的肝肾功能($\bar{x}\pm s$)

Table 5 The liver and kidney functions of the two groups were compared($\bar{x}\pm s$)

Groups	n	AST(U/L)		ALT(U/L)		BUN(mmol/L)		Cr(μmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A	48	28.61± 4.89	27.89± 3.81	28.87± 5.69	27.82± 6.12	3.62± 0.89	3.71± 0.95	61.78± 10.25	60.42± 9.13
Group B	48	28.72± 5.02	28.02± 4.02	28.69± 6.02	27.99± 5.78	3.65± 0.95	3.75± 1.02	61.89± 11.21	60.71± 10.56

2.6 对比两组患儿的不良反应发生率

B 组患儿的不良反应发生率较 A 组高,但组间对比无统计学意义(P>0.05),见表 6。

表 6 对比两组患儿的不良反应发生率[例(%)]

Table 6 The adverse reactions of the two groups were compared[n(%)]

Groups	n	Nausea	Vomiting	Diarrhea	Total incidence
Group A	48	3	2	1	6(14.58)
Group B	48	2	0	0	2(4.17)

3 讨论

流感病毒是威胁人类健康的一类病原,其会累及各年龄人群,但其在儿童中发病率最高,且儿童感染流感病毒后容易合

并肺炎症状[13,14]。流感病毒 A 型肺炎是最为常见的流感病毒,容易引起肺炎。帕拉米韦氯化钠注射液是我国在 2013 年上市的唯一可经静脉注射给药的抗病毒神经氨酸酶抑制剂,可用于抗流感病毒治疗,用于各年龄段的人群[15]。有研究发现[16,17],2009 年美国 FDA 批准其可用于儿童中,其对儿童耐受性较好,而我国目前将其用于流感病毒 A 型肺炎患儿的研究较少,因此本文分析了其对感病毒 A 型肺炎患儿的疗效、安全性,并分析了其成本 - 效益,以为流感病毒 A 型肺炎患儿选择合适的用药提供依据。

本文结果表明,B 组患儿的治疗有效率明显较 A 组高,观察组患儿的临床症状消失时间及住院时间明显较对照组低,表明与磷酸奥司他韦相比,帕拉米韦氯化钠注射液为流感病毒 A 型肺炎患儿的疗效更好。主要是由于神经氨酸酶对宿主细胞释放子代病毒具有协助作用,而其对子代病毒在呼吸道粘膜扩散也具有协助作用[18,19],而帕拉米韦、奥司他韦均为神经氨酸酶抑制剂,其可对神经氨酸酶起到抑制作用,从而对流感病毒脱离宿主细胞产生抑制作用,进一步将病毒扩散链切断,阻止病毒在机体内的传播,产生治疗效果[20,21]。而磷酸奥司他韦的血浆达峰时间为 1~3.7 h,其血浆峰浓度仅为 0.25~2.7 mg/L,血浆半衰期仅为 6~10 h[22],帕拉米韦氯化钠注射液的疗效优于磷酸奥司他韦,主要是因为帕拉米韦是新型的小分子环戊烷类,而其氯化钠注射液不通过肠道给药,在静脉给药时其血浆峰浓度可达 200 mg/L,且半衰期较长,可维持 24 h[23],同时其具有胍基、羧基、乙酰氨基、异戊基极性不同的基团,可其在流感病毒神经氨酸酶结构的不同活性位点区域产生作用,可以更有效的将病毒杀死,同时因其半衰期较长,注射后可持续抑制病毒,从而降低了用药的次数,提高了治疗效果,缩短了患儿的临床症状改善时间[24,25]。

其次 A 组患儿的平均用药成本明显低于 B 组,A 组的成本 - 效益较 B 组低,表明帕拉米韦氯化钠注射液较磷酸奥司他韦的成本 - 效益较低,主要是因为帕拉米韦氯化钠注射液的成本较高。与治疗前相比,治疗后两组患儿的中性粒细胞总数明显升高,白细胞总数、淋巴细胞总数明显降低,而治疗前后,两组患儿的血常规指标对比无统计学意义,治疗前后,两组患儿的肝肾功能对比均无统计学意义,表明帕拉米韦氯化钠注射液与磷酸奥司他韦对流感病毒 A 型肺炎患儿应用安全,对肝肾功能影响较小[26-28],治疗后血常规指标均可恢复。A 组患儿的不良反应发生率较 A 组高,主要是由于帕拉米韦氯化钠注射液的半衰期较长,使得其用药次数较少,也降低了总用药量[29,30],从而降低了不良反应发生率,而本研究但组间对比无统计学意义,可能与本研究样本量较少有关,有待进一步扩大样本量,进行深入分析。

综上所述,与磷酸奥司他韦相比,帕拉米韦氯化钠注射液对流感病毒 A 型肺炎患儿的疗效更佳,但其成本 - 效益较低,临床上可根据患儿实际情况选择用药。

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(上接第 687 页)

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