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重组人干扰素α-2b联合布地奈德雾化吸入对毛细支气管炎患儿炎性因子和康复进程的影响*

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摘要 目的:探讨重组人干扰素α-2b联合布地奈德雾化吸入对毛细支气管炎患儿炎性因子和康复进程的影响。**方法:**选取于2015年3月至2018年5月间徐州医科大学附属淮安医院收治的102例毛细支气管炎患儿，根据随机数字表法将患儿分为对照组(n=51)和研究组(n=51),对照组给予布地奈德雾化吸入治疗,研究组在对照组基础上联合重组人干扰素α-2b治疗。比较两组患儿临床疗效、临床指标情况,比较两组患儿治疗前、治疗6d后的炎症因子指标,观察两组患儿不良反应发生情况。**结果:**研究组患儿治疗6d后临床总有效率为92.16%,高于对照组患儿的76.47%(*P<0.05*)。研究组患儿喘息消失时间、肺部啰音消失时间、退热时间、咳嗽消失时间以及住院时间均短于对照组(*P<0.05*)。两组患儿治疗6d后白介素-4(IL-4)、白介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)均较治疗前降低,且研究组低于对照组(*P<0.05*),干扰素-γ(INF-γ)均较治疗前升高,且研究组高于对照组(*P<0.05*)。两组患儿治疗过程中不良反应发生率比较无统计学差异(*P>0.05*)。**结论:**毛细支气管炎患儿采用重组人干扰素α-2b联合布地奈德雾化吸入治疗,疗效显著,可有效改善患儿临床症状,加速康复进程,能有效改善炎性因子水平,不良反应较少,具有一定的临床应用价值。

关键词:重组人干扰素α-2b;布地奈德;雾化吸入;毛细支气管炎;炎性因子

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Effects of Inhalation of Recombinant Human Interferon α-2b Combined with Budesonide on Inflammatory Factors and Rehabilitation Process in Children with Bronchiolitis*

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ABSTRACT Objective: To investigate the effects of inhalation of recombinant human interferon α-2b combined with budesonide on inflammatory factors and rehabilitation process in children with bronchiolitis. **Methods:** 102 children with bronchiolitis who were admitted to Huaian Hospital Affiliated to Xuzhou Medical University from March 2015 to May 2018 were selected as the research subjects. According to the digital table method, the children were randomly divided into control group (n=51) and research group (n=51). The control group was given budesonide aerosol inhalation therapy, the research group was treated with recombinant human interferon α-2b on the basis of the control group. The clinical efficacy and clinical indicators of the two groups were compared. The inflammatory factors before and 6d after treatment were compared between the two groups, and adverse reactions of the two groups were observed. **Results:** The total effective rate in the research group was 92.16% at 6d after treatment, which was significantly higher than that in the control group 76.47% (*P<0.05*). The time of wheezing disappearance, fever abatement, lung rale disappearance, cough disappearance and hospitalization in the research group were shorter than those in the control group (*P<0.05*). 6d after treatment, the levels of interleukin-4 (IL-4), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in both groups were lower than those before treatment, and the research group was lower than the control group (*P<0.05*). The levels of interferon-γ (INF-γ) were higher than those before treatment, and the research group was higher than the control group (*P<0.05*). There was no significant difference in the incidence of adverse reactions between the two groups (*P>0.05*). **Conclusion:** Recombinant human interferon α-2b combined with budesonide aerosol inhalation in the treatment of children with bronchiolitis has a significant effect,it can effectively improve the clinical symptoms of children, accelerate the rehabilitation process, and can effectively improve the level of inflammatory factors, without increasing the incidence of adverse reactions, it has a certain clinical value.

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前言

毛细支气管炎是一种常见的下呼吸道感染性疾病,好发于婴幼儿[1,2],轻者可导致肺气肿、心肌损伤,严重者可诱发哮喘或心力衰竭,给患儿性命带来严重威胁[3,4]。毛细支气管炎发病机制复杂,近年来免疫学认为该病是由于病毒感染,从而诱发与哮喘免疫发病机制相似的炎症反应,包括炎症细胞浸润、炎症介质释放,进而引发气道黏膜上皮受损、水肿[5,6]。现临床针对该病的主要治疗思路为抗感染及氧疗,然而疗效一般。布地奈德是一种高效的局部抗炎糖皮质激素类药物,其在治疗毛细支气管炎中的疗效已得到证实[7,8]。重组人干扰素 α-2b 是可对病毒进一步复制进行有效干扰,同时还具有保护未感染的细胞的作用,抗病毒效果良好[9,10]。本研究对我院收治的毛细支气管炎患儿给予重组人干扰素 α-2b 联合布地奈德雾化吸入治疗,疗效确切,现报道如下。

1 资料与方法

1.1 一般资料

选取 2015 年 3 月 ~2018 年 5 月间徐州医科大学附属淮安医院接收的 102 例毛细支气管炎患儿,纳入标准:(1)所有患儿均符合《诸福棠实用儿科学》[11]中的相关诊断标准;(2)均有喘息咳嗽、呼气性哮鸣音以及气促等临床症状;(3) 均为首次发病,且入院前未接受过其他治疗;(4)患儿监护人知情本次研究并签署同意书。排除标准:(1)合并严重并发症患儿,如心力衰竭、哮喘等;(2)合并先天性支气管发育不全患儿;(3)合并自身免疫功能缺陷患儿;(4)合并心肺等功能障碍患儿;(5)对本次研究使用药物过敏患儿。根据随机数字表法将患儿分为对照组(n=51)和研究组(n=51),其中对照组男 27 例,女 24 例,年龄 3~30 个月,平均(21.62± 2.80)个月;病程 4~15d,平均(9.34± 1.15)d。研究组男 25 例, 女 26 例, 年龄 3~29 个月, 平均(22.08± 3.40)个月;病程 4~15d,平均(9.42± 1.26)d。两组患儿一般资料比较无差异(*P>0.05*),组间可比。

1.2 治疗方法

入院后给予抗感染、吸痰、镇静、止咳等常规治疗,在此基础上,对照组给予布地奈德吸入气雾剂(上海上药信谊药厂有限公司, 国药准字 H20010552)0.5~1.0 mg 雾化吸入治疗,布地奈德溶于生理盐水 2 mL 中,2 次 /d。研究组在对照组基础上联合重组人干扰素 α-2b (海南通用同盟药业有限公司,国药准字 S20040028)治疗,取 8 万 ~10 万 U/(kg·d)重组人干扰素溶于 2 mL 生理盐水中,行雾化吸入,2 次 /d。两组患儿均连续治疗 6d。

1.3 观察指标

(1)比较两组患儿治疗 6d 后的临床疗效,疗效判定标准为[12]:显效:治疗 6d 后患儿临床症状改善,呼吸平稳;有效:治疗 6d 后患儿临床症状有所好转;无效:治疗 6d 后患儿临床症状未见明显改善或加重。总有效率 = 显效率 + 有效率。(2)比较两组患儿临床各项指标情况,包括喘息消失时间、肺部啰音消失时间、退热时间、咳嗽消失时间以及住院时间。(3)于治疗前、治疗 6d 后采集患儿清晨空腹静脉血 4 mL,以 2600 r/min 速率离心 8 min,离心半径为 12 cm,取上清液,置于 -30℃冰箱中待测。采用酶联免疫吸附法检测患儿白介素 -4(Interleukin-4,IL-4)、白介素 -6(Interleukin-6,IL-6)、肿瘤坏死因子 -α(Tumor necrosis factor-α,TNF-α)以及干扰素 -γ(Interferon-γ,INF-γ)水平,试剂盒购自深圳晶美生物科技有限公司,严格遵守试剂盒说明书进行检测。(4)观察两组患儿治疗期间不良反应。

1.4 统计学方法

通过 SPSS26.0 软件处理统计数据。计数资料用率表示,实施 x^2 检验。计量资料用($\bar{x}\pm s$)表示,实施 t 检验。*P<0.05* 为差异有统计学意义。

2 结果

2.1 临床疗效比较

研究组患儿治疗 6d 后临床总有效率为 92.16%(47/51),高于对照组患儿的 76.47%(39/51)(*P<0.05*),详见表 1。

表 1 两组患儿临床疗效比较 例(%)

Table 1 Comparison of clinical efficacy of two groups of children n(%)

Groups	Excellence	Good	Invalid	Total effective rate
Control group(n=51)	23(45.10)	16(31.37)	12(23.53)	39(76.47)
Research Group(n=51)	33(64.71)	14(27.45)	4(7.84)	47(92.16)
x^2				4.744
P				0.029

2.2 两组患儿临床各项指标情况比较

研究组患儿喘息消失时间、肺部啰音消失时间、退热时间、咳嗽消失时间以及住院时间均短于对照组(*P<0.05*),详见表 2。

2.3 两组患儿炎症因子指标比较

两组患儿治疗前 IL-4、IL-6、TNF-α 以及 INF-γ 比较无统计学差异(*P>0.05*),两组患儿治疗 6d 后 IL-4、IL-6、TNF-α 均较治疗前降低, 且研究组低于对照组 (*P<0.05*),INF-γ 较治疗前升高,且研究组高于对照组(*P<0.05*),详见表 3。

2.4 两组患儿不良反应发生情况比较

对照组治疗期间发生 1 例腹泻,1 例发热, 不良反应发生

表 2 两组患儿临床各项指标情况比较($\bar{x}\pm s$,d)

Table 2 Comparison of clinical indicators between two groups($\bar{x}\pm s$, d)

Groups	Time of wheezing disappearance	Time of fever abatement	Time of lung rale disappearance	Time of cough disappearance	Hospitalization time
Control group(n=51)	4.25± 0.89	2.23± 0.73	6.11± 1.03	7.20± 1.17	8.97± 1.31
Research Group(n=51)	2.92± 0.91	1.54± 0.62	4.85± 0.98	5.69± 1.03	6.62± 1.20
t	7.462	5.145	6.329	6.918	9.447
P	0.000	0.000	0.000	0.000	0.000

表 3 两组患儿炎症因子指标比较($\bar{x}\pm s$)

Table 3 Comparison of inflammatory factor indicators between two groups of children($\bar{x}\pm s$)

Groups	IL-4(ng/L)		IL-6(ng/L)		TNF-α(ng/L)		INF-γ(IU/mL)	
	Before treatment	6d after treatment	Before treatment	6d after treatment	Before treatment	6d after treatment	Before treatment	6d after treatment
Control group (n=51)	102.78± 22.52	83.54± 14.48*	254.16± 26.47	211.83± 24.66*	184.12± 18.64	171.67± 20.18*	6.74± 1.63	10.45± 1.82*
Research Group(n=51)	103.02± 21.48	62.63± 14.58*	255.22± 30.18	173.11± 23.59*	185.56± 16.50	158.57± 22.21*	6.75± 1.12	14.93± 2.04*
t	0.055	7.267	0.189	8.103	0.413	3.118	0.036	11.703
P	0.956	0.000	0.851	0.000	0.680	0.002	0.971	0.000

Note: Compared with before treatment,*$P<0.05$

率为 3.92%(2/51)，研究组治疗期间发生 2 例腹泻,1 例发热，不良反应发生率为 5.88%(3/51)，两组患儿治疗过程中不良反应发生率比较无统计学差异(x^2=0.210,P=0.647)。

3 讨论

毛细支气管炎好发于 2.5 岁以下婴幼儿,多由呼吸道合胞病毒、腺病毒以及副流感病毒等感染引起[13-15]。由于婴幼儿支气管管腔较为狭窄,通气功能相对较差,同时病毒感染可促进炎症因子分泌,炎症分泌物、肌收缩以及水肿等易引起肺气肿和肺不张,因此毛细支气管炎患儿易出现支气管平滑肌痉挛等一系列症状[16-18]。据以往相关研究表明[19],约有 20%~40%的毛细支气管炎患儿可发展成为哮喘,因此,毛细支气管炎的早期干预治疗对预防哮喘的发生具有重要的作用。目前国内外针对毛细支气管炎多采用综合治疗,如氧疗、抗感染、糖皮质激素局部抗炎、扩张支气管剂以及支持治疗等,但治疗效果均不令人满意[20,21]。布地奈德是可发挥高效的局部抗炎作用,其益处在重症患儿中体现较为明显,但在轻症患儿中显效较慢[22]。重组人干扰素 α-2b 可通过结合细胞表面受体抑制病毒复制，从而发挥抗病毒效果[23-25]。

研究表明,研究组治疗后总有效率为 92.16%,高于对照组的 76.47%，提示本研究联合用药治疗毛细支气管炎患儿可进一步提高治疗效果。郭玉皎等人[26]认为布地奈德混悬液、重组人干扰素 α-2b 雾化吸入联合治疗小儿毛细支气管炎疗效较佳,可有效缩短病程,这与本次研究结果基本一致。布地奈德可减少呼吸道粘膜水肿以及黏液分泌,收缩气道血管,降低气道高反应性,可一定程度上缓解患儿临床症状;而重组人干扰素 α-2b 进入人体后可产生一系列抗病毒蛋白,对病毒核酸及蛋白质的复制过程产生干扰。因此两者联合使用可进一步提升治疗效果[27,28]。本研究结果显示,研究组患儿临床各项指标时间均短于对照组,表明上述联合治疗可有效加快患儿康复进程。这可能是由于重组人干扰素 α-2b 可从源头上干扰病毒复制，从而减缓了患儿病情进展;而布地奈德则可对患儿临床症状进行有效根治,使得患儿恢复进程加快[29]。本次研究结果还表明,两组患儿治疗后炎症因子水平均得到有效控制,且研究组控制效果更佳。IL-4 是肥大细胞生长因子,可刺激肥大细胞增殖,促进 Th2 细胞介导的免疫反应。IL-6 主要由巨噬细胞、T 细胞、内皮细胞共同产生,是促使患儿发热的主要发病机制之一。TNF-α 是由单核巨噬细胞产生的具有多种生物活性的多肽类调节因子,过量的 TNF-α 可加重机体炎性损伤。INF-γ 是有核细胞在对病毒刺激人体产生的免疫应答中所合成的宿主衍生蛋白,可发挥抗病毒、免疫调节等作用。本研究中研究组改善炎性因子水平更佳的原因可能是因为重组人干扰素 α-2b 进入人体,结合细胞表面受体,干扰病毒复制过程,抑制了炎症因子的分泌;同时重组人干扰素 α-2b 可杀伤 T 细胞、巨噬细胞、肥大细胞的活力,提高机体抗病毒能力,改善炎性因子分泌水平。另外,两组患儿治疗过程中不良反应发生率比较无统计学差异,表明重组人干扰素 α-2b 联合布地奈德雾化吸入治疗安全性较好。王翠等学者[30]研究亦认为,毛细支气管炎患者采用重组人干扰素 α-2b 与布地奈德联合治疗,无严重不良反应,疗效较好。

综上所述，毛细支气管炎患儿给予重组人干扰素 α-2b 联合布地奈德雾化吸入治疗,疗效显著,安全性较好,患儿临床症状、炎性因子水平均得到改善,康复进程加快,两药联合使用在临床上具有一定的应用价值。

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