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甲泼尼龙联合普米克令舒治疗小儿急性喉炎的疗效及对血清 IFN-γ、SAA、IL-6 水平的影响 *

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摘要 目的:探讨甲泼尼龙联合普米克令舒治疗小儿急性喉炎的疗效及对血清干扰素 -γ(IFN-γ)、淀粉样蛋白(SAA)、白介素 -6(IL-6)水平的影响。**方法:**选择 2015 年 6 月至 2018 年 6 月我院接诊的急性喉炎患儿 76 例,通过随机数表法将其分为观察组 40 例和对照组 36 例。在常规治疗上,对照组以地塞米松联合普米克令舒治疗,观察组以甲泼尼龙联合普米克令舒治疗,两组均连续治疗 3~5d。比较两组的临床疗效、临床症状缓解时间、治疗前后血清 IFN-γ、SAA、IL-6 水平的变化及不良反应的发生情况。**结果:**治疗后,观察组临床疗效总有效率明显高于对照组[92.50%(37/40) vs. 75.00%(27/36)](*P<0.05*);观察组咳嗽、声嘶、呼吸困难、哮鸣音、发热缓解时间均明显短于对照组[(3.19± 0.51)d vs. (4.01± 0.64)d,(1.76± 0.21)d vs. (2.48± 0.30)d,(1.02± 0.14)d vs. (1.76± 0.19)d,(2.74± 0.42)d vs. (3.39± 0.53)d,(1.45± 0.20)d vs. (2.04± 0.27)d](*P<0.05*);观察组血清 IFN-γ、SAA、IL-6 均明显低于对照组[(43.03± 3.47)ng/L vs. (52.81± 4.60)ng/L,(37.40± 4.12)mg/L vs. (49.83± 5.47)mg/L,(11.02± 1.42)ng/L vs. (15.73± 1.70)ng/L](*P<0.05*);两组不良反应总发生率比较差异无统计学意义(*P>0.05*)。**结论:**甲泼尼龙联合普米克令舒治疗急性喉炎患儿的临床效果显著优于地塞米松治疗,其可更有效促进疾病恢复,其内在机制可能和显著降低血清 IFN-γ、SAA、IL-6 水平,抑制机体过度炎症反应相关。

关键词:急性喉炎;普米克令舒;甲泼尼龙;干扰素 -γ;淀粉样蛋白;白介素 -6

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Curative Efficacy of Methylprednisolone Combined with Pulmicort in the Treatment of Acute Laryngitis and Its Effects on the Serum IFN-γ, SAA and IL-6 Levels*

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ABSTRACT Objective: To study the curative efficacy of methylprednisolone combined with pulmicort in the treatment of acute laryngitis and its effect on the serum interferon-γ (IFN-γ), amyloid protein (SAA) and interleukin-6 (IL-6) levels. **Methods:** 76 cases of patients with acute laryngitis who were treated from June 2015 to June 2018 in our hospital were selected as the research objects, they were divided into the observation group (40 cases) and the control group (36 cases) by the random number table method. On the basis of routine treatment, the control group was treated by dexamethasone combined with Pulmicort, the observation group was treated by methylprednisolone combined with Pulmicort, they were continuously treated for 3~5d. The clinical efficacy, remission time of clinical symptoms, changes of serum IFN-γ, SAA, IL-6 levels before and after treatment and the incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of the control group [92.50%(37/40) vs. 75.00%(27/36)](*P<0.05*); the cough, hoarseness, dyspnea, wheezing and fever remission time in the observation group were significantly shorter than those in the control group[(3.19± 0.51)d vs. (4.01± 0.64)d, (1.76± 0.21)d vs. (2.48± 0.30)d, (1.02± 0.14)d vs. (1.76± 0.19)d, (2.74± 0.42)d vs. (3.39± 0.53)d, (1.45± 0.20)d vs. (2.04± 0.27)d](*P<0.05*); the serum IFN-γ, SAA, IL-6 in the observation group were significantly lower than those in the control group[(43.03± 3.47)ng/L vs. (52.81± 4.60)ng/L, (37.40± 4.12)mg/L vs. (49.83± 5.47)mg/L, (11.02± 1.42)ng/L vs. (15.73± 1.70)ng/L](*P<0.05*); there was no significant difference in the incidence of adverse reactions between the two groups (*P>0.05*). **Conclusion:** The clinical effect of methylprednisolone combined with Pulmicort resuscitation in the treatment of acute laryngitis is significantly better than that of dexamethasone alone, its internal mechanism may be related to the significant reduce of serum IFN-γ, SAA, IL-6 levels and inhibition of the excessive inflammatory response.

Key words: Acute laryngitis; Pulmicort; Methylprednisolone; Interferon-γ; Amyloid protein; Interleukin -6

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前言

小儿急性喉炎是一种以声门区为主的喉粘膜急性炎症，由于小儿喉腔小，喉部粘膜松弛，喉部肿胀时可致使声门堵塞，加之小儿咳嗽反射差，喉部和气管的分泌物不易排出，极易引发严重喉梗阻，严重的甚至危及生命[1,2]。大量炎症因子的释放是导致急性喉炎发生、发展的重要机制。其中，血清干扰素 -γ(IFN-γ)、淀粉样蛋白(SAA)、白介素 -6(IL-6)在此过程中发挥着关键作用，抑制此类因子的表达在改善患者预后和转归中具有积极意义[3,4]。

地塞米松是目前治疗急性喉炎患儿的常用治疗药物，但起效较慢，部分患儿症状改善不明显。普米克令舒属强效糖皮质激素，具有较高的脂溶性，局部用药药物可达到较高的浓度，近年来也逐渐用于急性喉炎的治疗[5,6]。甲泼尼龙属合成糖皮质激素，具有免疫抑制、抗过敏、抗炎等作用，近年来有学者发现其对急性喉炎的疗效优于常规地塞米松，但目前相关报道仍较少[7,8]。因此，本研究通过检测患者血清 IFN-γ、SAA、IL-6 水平的变化，探讨了甲泼尼龙联合普米克令舒治疗急性喉炎患儿的疗效及可能作用机制。

1 资料与方法

1.1 病例资料

选择 2015 年 6 月至 2018 年 6 月我院接诊的 76 例急性喉炎患儿作为本研究对象。纳入标准：① 符合急性喉炎诊断标准[9]，经电子喉镜、实验室检查确诊；② 发病至入院时间＜48h；③ 患儿家属签署本研究知情同意书。排除标准：① 近 2 周内服用过糖皮质激素、抗菌类药物；② 合并重度营养不良、免疫缺陷者；③ 合并肝肾心等重要脏器功能障碍；④ 合并先天性喉部疾病、支气管肺炎、支气管异物疾病、扁桃体炎、扁桃体脓肿等疾病；⑤ 对研究药物过敏。通过随机数表法将所有患者分为观察组 40 例和对照组 36 例，两组一般资料比较差异无统计学意义($P>0.05$)，具有可比性。本研究已通过我院伦理委员会批准。

表 1 两组一般资料的比较[$\bar{x}\pm s$，n(%)]

Table 1 Comparison of the general data between two groups[$\bar{x}\pm s$, n(%)]

Groups	n	Sex(male)	Age(years)	Course of disease (h)	Severity of illness		
					I	II	III
Observation group	40	24(60.00)	7.32± 1.54	24.59± 4.38	20(50.00)	14(35.00)	6(15.00)
Control group	36	20(55.56)	7.24± 1.57	24.83± 4.20	19(52.78)	12(33.33)	5(13.89)
x^2/t		0.154	0.224	0.243		0.060	
P		0.695	0.823	0.809		0.970	

1.2 治疗方法

两组均给予常规止咳、平喘、预防感染、解除支气管痉挛等处理，对照组给予地塞米松(规格 1 mL : 5 mg，厂家：国药集团容生制药有限公司，国药准字 H41020036)0.3~0.5 mg/kg/d 加入 50 mL 生理盐水中静脉滴注，1 次 /d，普米克令舒(规格 2 mL : 1 mg，厂家：AstraZeneca Pty Ltd，国药准字 H20140475)1 mg 加入 1 mL 生理盐水中雾化吸入，10 分钟 / 次，2 次 /d；观察组给予普米克令舒 1 mg 加入 1 mL 生理盐水中雾化吸入，10 分钟 / 次，2 次 /d，甲泼尼龙(规格 40 mg，厂家：辉瑞制药有限公司，国药准字 H20170197) 剂量 1 mg/kg 加入 50 mL 生理盐水中静脉滴注，2 次 /d。根据病情改善情况连续治疗 3~5d。

1.3 观察指标

记录和比较两组患儿咳嗽、声嘶、呼吸困难、哮鸣音、发热症状的缓解时间；采集治疗前、后 3 mL 空腹静脉血，置于不含抗凝剂的食管中，待其凝固后使用 3500 r/min 的速度离心 10 min，提取血清待检，血清 IFN-γ、SAA、IL-6 的检测均使用酶联免疫吸附法，试剂盒均由美国 R&D 公司提供；记录相关不良反应的发生情况。

1.4 疗效评价标准

参照相关文献评价临床疗效[9]。治愈：治疗 48h 内，主要临床症状完全消失，可正常进食和睡觉；好转：治疗 72h 内，主要临床症状大部分缓解，可正常进食和睡觉；无效：上述临床症状无明显改善，甚至加重。总有效率 =(治愈例数 + 好转例数)/ 总例数× 100%。

1.5 统计学分析

以 spss18.0 软件包处理实验数据，正态分布计量资料用均数± 标准差($\bar{x}\pm s$)表示，组间比较使用独立样本 t 检验，组内比较使用配对样本 t 检验，计数资料以率表示，组间比较采用 x^2 检验，以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后，观察组临床疗效总有效率为 92%，明显高于对照组(75%，$P<0.05$)，见表 2。

2.2 两组临床症状缓解时间的比较

观察组咳嗽、声嘶、呼吸困难、哮鸣音、发热缓解时间均明显比对照组显著缩短($P<0.05$)，见表 3。

2.3 两组治疗前后血清 IFN-γ、SAA、IL-6 水平的比较

两组经治疗后血清 IFN-γ、SAA、IL-6 水平较治疗前均明显降低($P<0.05$)，且观察组血清 IFN-γ、SAA、IL-6 水平均明显低于对照组($P<0.05$)，见表 4。

2.4 两组不良反应发生情况的比较

两组治疗期间均未发生免疫异常、全身反应等不良反应，观察组有支气管痉挛 1 例、恶心呕吐 2 例，对照组有支气管痉挛 1 例、咽喉刺激 1 例，停药后自行缓解，两组不良反应总发生率分别为 7.50%(3/40)、5.56%(2/36)，组间比较差异无统计

学意义(*P>0.05*)。

表 2 两组临床疗效比较[例(%)]

Table 2 Comparison of the clinical efficacy between two groups[n(%)]

Groups	n	Cure	Improve	Invalid	Total effective rate
Observation group	40	22(55.00)	15(37.50)	3(7.50)	37(92.50)
Control group	36	15(41.67)	12(33.33)	9(25.00)	27(75.00)
x^2					4.364
P					0.037

表 3 两组临床症状缓解时间的比较($\bar{x}\pm s$,d)

Table 3 Comparison of the relief time of clinical symptom between two groups($\bar{x}\pm s$,d)

Groups	n	Cough	Hoarseness	Dyspnea	Wheezing sound	Fever
Observation group	40	3.19± 0.51	1.76± 0.21	1.02± 0.14	2.74± 0.42	1.45± 0.20
Control group	36	4.01± 0.64	2.48± 0.30	1.76± 0.19	3.39± 0.53	2.04± 0.27
t		6.206	12.217	19.458	5.954	10.895
P		0.000	0.000	0.000	0.000	0.000

表 4 两组治疗前后血清 IFN-γ、SAA、IL-6 水平的比较($\bar{x}\pm s$)

Table 4 Comparison of the serum IFN-γ, SAA and IL-6 levels between two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Time	IFN-γ(ng/L)	SAA(mg/L)	IL-6(ng/L)
Observation group	40	Before treatment	74.34± 8.05	89.45± 9.40	20.38± 2.41
		After treatment	43.03± 3.47*#	37.40± 4.12*#	11.02± 1.42*#
Control group	36	Before treatment	74.65± 7.86	88.97± 9.79	20.17± 2.54
		After treatment	52.81± 4.60*	49.83± 5.47*	15.73± 1.70*

Note: Compared with before treatment, **P<0.05*; Compared with control group, #*P<0.05*.

3 讨论

急性喉炎患儿在受到细菌、病毒等感染后，声道粘膜受损，使粘膜通透性增加和疏松结缔组织充血水肿等，继而增加声道高反应性[10,11]。此外，由于儿童的喉部神经较为敏感，在遭受到急性刺激后，容易出现痉挛，继而出现呼吸困难、喘憋等症状，严重者甚至发生窒息[12,13]。大量研究显示急性喉炎主要是受中性粒细胞所介导，细菌、病毒的刺激可下调支气管上皮细胞 Toll 样受体 4，对中性粒细胞产生激活作用，使机体大量分泌 IFN-γ、SAA、IL-6 等炎症因子，加重气道炎症反应，促使疾病进展[14,15]。

早期应用糖皮质激素是急性喉炎的主要治疗手段，地塞米松是该病治疗的常用药物，其可降低毛细血管通透性、缓解充血及血浆渗出等症状，达到改善喉部水肿的目的，但该药物需在肝脏转化后方可产生效果，单独用药起效较慢[16,17]。普米克令舒是一种具有高效局部抗炎作用的糖皮质激素，近年来已有较多报道证实，给予静脉滴注地塞米松联合普米克令舒雾化吸入的疗效明显优于单独局部或全身使用地塞米松，且雾化吸入的的方式药物作用持续时间短，可减少长时间应用糖皮质激素所致的不良反应[18,19]。但上述研究多是以地塞米松作为基础治疗方案，但由于地塞米松起效较慢，且长期用药不良反应较多，仍部分患儿疗效欠佳[20,21]。因此，积极寻找一种更有效、安全的方案也是目前临床医师们重点关注的问题[22]。

甲泼尼龙属人工合成的中效糖皮质激素，具有起效快、半衰期短、易渗透组织等作用，且对肾上腺皮质激素无活性，具有较高的用药安全性[23,24]。有研究指出甲泼尼龙在用药 30 分钟后即可达到血药浓度高峰，半衰期仅为 2.5 小时，可迅速在体内清除，用于小儿治疗是安全性有效的[25,26]。此外，研究显示和地塞米松相比，甲泼尼龙具有更强的抗炎效果，可更有效的缓解急性喉炎合并喉梗阻患儿的临床症状，缩短治疗时间[27,28]。

本研究结果显示使用甲泼尼龙联合普米克令舒治疗的患儿血清 IFN-γ、SAA、IL-6 水平降低得更明显，分析原因可能是由于甲泼尼松和地塞米松相比起效更快，可更快的达到血药浓度高峰，早期发挥强效抗炎作用，且甲泼尼龙的局部抗炎效果是地塞米松的 5 倍，再加上雾化吸入普米克令舒可抑制上皮细胞增殖及炎症细胞活性[29,30]，两药联合发挥相互协同作用，因此血清 IFN-γ、SAA、IL-6 的降低程度更明显。此外，本研究中，甲泼尼龙联合普米克令舒治疗的患儿临床症状缓解时间和临床疗效也更具有优势，也进一步显示该方案在提高抗炎效果的同时，更利于患儿临床症状的早期恢复。

综上所述，甲泼尼龙联合普米克令舒治疗急性喉炎患儿的临床效果显著优于地塞米松治疗，其可更有效促进疾病恢复，

其内在机制可能和显著降低血清 IFN-γ、SAA、IL-6 水平，抑制机体过度炎症反应相关。

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