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胸腔注射糖皮质激素联合标准四联抗结疗法对结核性胸膜炎患者临床症状及肺功能的影响*

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摘要 目的:探讨胸腔注射糖皮质激素联合标准四联抗结疗法对结核性胸膜炎患者肺功能及临床症状的影响。方法:选取 2013 年 1 月到 2020 年 5 月期间来我院进行诊治的结核性胸膜炎患者 756 例,入选的患者按照随机数字表法分为对照组和实验组,各 378 例。对照组予以标准四联抗结疗法治疗,实验组予以胸腔注射糖皮质激素联合标准四联抗结疗法治疗。对比两组疗效、肺功能[第 1s 用力呼气容积占预计值百分比(FEV₁%pred)、每分钟最大通气量占预计值百分比(MVV%pred)、用力肺活量占预计值百分比(FVC%pred)],记录两组胸水吸收时间、胸膜厚度、临床症状缓解时间、住院时间、并发症及胸膜肥厚粘连发生情况。结果:实验组的临床总有效率较对照组高($P<0.05$)。治疗后,两组 FEV₁%pred、MVV%pred、FVC%pred 均升高,且实验组高于对照组($P<0.05$)。实验组临床症状缓解时间、胸水吸收时间、住院时间较对照组短($P<0.05$),胸膜厚度大于对照组($P<0.05$)。实验组的胸膜肥厚粘连、并发症总发生率低于对照组($P<0.05$)。结论:胸腔注射糖皮质激素联合标准四联抗结疗法治疗结核性胸膜炎,疗效可靠,可改善患者肺功能,促进症状改善。

关键词:糖皮质激素;标准四联抗结疗法;结核性胸膜炎;肺功能;临床症状

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Effect of Intrapleural Injection of Glucocorticoid Combined with Standard Quadruple Anti Tuberculous Therapy on Clinical Symptoms and Pulmonary Function of Patients with Tuberculous Pleurisy*

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ABSTRACT Objective: To investigate the effect of intrapleural injection of glucocorticoid combined with standard quadruple anti tuberculous therapy on pulmonary function and clinical symptoms of patients with tuberculous pleurisy. **Methods:** 756 patients with tuberculous pleurisy from January 2013 to May 2020 were selected, the enrolled patients were randomly divided into control group and experimental group according to random number table method, 378 cases in each group. The control group was treated with standard quadruple anti tuberculous therapy, and the experimental group was treated with intrapleural injection of glucocorticoid combined with standard quadruple anti tuberculous therapy. The curative effect, pulmonary function [percentage of forced expiratory volume in predicted value in 1s (FEV₁%pred), maximum ventilation volume per minute as a percentage of predicted value (MVV%pred), forced vital capacity as a percentage of predicted value (FVC%pred)] were compared between the two groups. Pleural fluid absorption time, pleural thickness, clinical symptom remission time, hospitalization time, complications and pleural hypertrophy adhesion were recorded between the two groups. **Results:** The total effective rate of the experimental group was higher than that of the control group ($P<0.05$). After treatment, FEV₁%pred, MVV%pred and FVC%pred of the two groups were increased, and the experimental group was higher than the control group ($P<0.05$). The clinical symptom remission time, pleural fluid absorption time and hospitalization time of the experimental group were shorter than those of the control group($P<0.05$), and the pleural thickness of the experimental group was greater than that of the control group ($P<0.05$). The total incidence rate of pleural hypertrophy adhesion and complications of the experimental group were lower than those of the control group ($P<0.05$). **Conclusion:** The intrapleural injection of glucocorticoid combined with standard quadruple anti tuberculous therapy in the treatment of tuberculous pleurisy has a reliable effect, which can improve the pulmonary function and promote the improvement of symptoms.

Key words: Intrapleural injection of glucocorticoid; Standard quadruple anti tuberculous therapy; Tuberculous pleurisy; Pulmonary function; Clinical symptoms

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前言

结核性胸膜炎是指机体感染结核杆菌后,导致结膜出现渗出、充血、坏死、纤维化等炎症性病变,并伴有胸腔积液,若未能得到及时的治疗,可产生乏力、向心性肥胖、骨质疏松等一系列并发症^[1,2]。相关流行病学数据显示^[3],我国每年新发肺结核病例数约在 113 万以上,其中结核性胸膜炎约占 17.6%。现临床针对结核性胸膜炎的治疗通常采用标准四联抗结核法^[4],但不少患者由于胸腔内存在持续的渗出液,导致药物吸收缓慢,药物作用下降,同时不少患者还存在胸膜肥厚粘连等现象,治疗效果并不理想^[5]。糖皮质激素具有减轻炎症因子早期渗出、促进毛细血管扩张的作用,同时还可抑制炎症晚期结缔组织、肉芽组织形成,从而减少胸膜肥厚粘连的发生^[6,7]。本研究拟探讨标准四联抗结核法联合胸腔注射糖皮质激素对结核性胸膜炎患者的临床效果,以期为指导临床治疗提供参考。

1 资料与方法

1.1 临床资料

选取 2013 年 1 月到 2020 年 5 月期间来我院进行诊治的 756 例结核性胸膜炎患者。纳入标准:(1)参考《临床诊疗指南·结核病分册》^[8],均经医学影像学检查、结核菌素试验、细菌培养及胸膜活检等确诊;(2)患者及其家属知情本研究,并签署了同意书;(3)初治患者,年龄 >18 岁;(4)对本研究所用药物无禁忌症者。排除标准:(1)合并凝血功能障碍者;(2)入院时已发生胸膜肥厚粘连者、干性结核性胸膜炎者;(3)合并精神异常者;(4)妊娠或哺乳期妇女;(5)合并心肝肾等脏器功能障碍者;(6)合并免疫缺陷者。入选的患者按照随机数字表法分为对照组(378 例)和实验组(378 例)。实验组女性 149 例,男性 229 例,病变部位:左侧 201 例,右侧 177 例;病程 2~11 年,平均(5.71±0.87)年;年龄 23~54 岁,平均(38.62±4.35)岁;胸水:大量(>1000 mL)74 例,中量(500~1000 mL)189 例,少量(<500 mL)115 例。对照组女性 157 例,男性 221 例,病变部位:左侧 196 例,右侧 182 例;病程 2~10 年,平均(5.72±0.98)年;年龄 22~52 岁,平均(38.49±3.97)岁;胸水:大量 69 例,中量 182 例,少量 127 例。两组一般资料组间比较,无统计学差异($P>0.05$),均衡可比。研究方案通过我院伦理学委员会批准。

1.2 方法

对照组给予标准四联抗结核法治疗,具体如下:异烟肼(国药准字 H41023846,开封明仁药业有限公司,规格:0.1 g),口服,0.3 g/次,1 次/d;乙胺丁醇(国药准字 H31021140,上海上药信谊药厂有限公司,规格:0.25 g),口服,0.75 g/次,1 次/d;利福平(国药准字 H51020281,佑华制药(乐山)有限公司,规格:0.15 g),口服,0.6 g/次,1 次/d;吡嗪酰胺(国药准字 H31021753,上海上药信谊药厂有限公司,规格:0.5 g),口服,1.25 g/次,1 次/d。疗程为 6 周。实验组在对照组的基础上联合胸腔注射地塞米松(国药准字 H44024618,广东南国药业有限公司,规格:0.75 mg)治疗,每 3 天进行 1 次胸腔积液引流,于每次引流完毕后经引流管注入地塞米松 3 mg,当 B 超检查显示胸腔积液完全消退则停止地塞米松治疗。

1.3 疗效

考察两组治疗后的临床总有效率。总有效率参考《临床诊疗指南·结核病分册》^[8]的标准,具体如下:症状及异常体征完全消失,X 线检查胸腔积液少量残留或完全吸收为治愈。X 线检查胸腔积液少量残留或明显吸收,症状及异常体征基本消失为好转。未能达到上述标准者为无效。总有效率=治愈率+好转率。

1.4 观察指标

(1)记录两组胸水吸收时间、胸膜厚度、临床症状缓解时间、住院时间。(2)记录两组治疗期间胸膜肥厚粘连及并发症发生情况,并发症包括向心性肥胖、骨质疏松、乏力多汗。(3)治疗前后采用 6200 型肺功能仪(美国 SensorMedics 公司生产)检测患者肺功能指标,包括第 1s 用力呼气容积占预计值百分比(FEV₁%pred)、每分钟最大通气量占预计值百分比(MVV%pred)、用力肺活量占预计值百分比(FVC%pred)。

1.5 统计学方法

数据采用 SPSS25.0 软件进行分析。计数资料以率的形式表示,行卡方检验。计量资料以均值±标准差的形式表示,组间比较进行成组 t 检验,组内前后比较进行配对 t 检验。检验标准设为 $\alpha=0.05$ 。

2 结果

2.1 两组疗效对比

实验组的临床总有效率较对照组高($P<0.05$),详见表 1。

表 1 两组疗效对比 [例(%)]

Table 1 Comparison of curative effect between the two groups [n(%)]

Groups	Cure	Become better	Invalid	Total effective rate
Control group(n=378)	86(22.75)	205(54.23)	87(23.02)	291(76.98)
Experimental group (n=378)	112(29.63)	230(60.85)	36(9.52)	342(90.78)
χ^2				25.255
P				0.000

2.2 两组肺功能指标对比

治疗前, 两组 FEV₁%pred、MVV%pred、FVC%pred 组间对比差异无统计学意义 ($P>0.05$); 治疗后, 两组 FEV₁%pred、

MVV%pred、FVC%pred 均升高, 且实验组高于对照组 ($P<0.05$), 详见表 2。

表 2 两组肺功能指标对比($\bar{x} \pm s, \%$)

Table 2 Comparison of pulmonary function indexes between the two groups($\bar{x} \pm s, \%$)

Groups	FEV ₁ %pred		MVV%pred		FVC%pred	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=378)	62.90± 5.02	69.62± 4.90*	50.76± 4.39	57.61± 5.42*	71.04± 5.43	78.27± 4.51*
Experimental group (n=378)	63.16± 4.30	75.66± 4.54*	50.69± 6.72	64.19± 4.94*	71.12± 6.39	85.63± 4.57*
t	0.765	17.580	0.170	17.445	0.185	22.827
P	0.446	0.000	0.865	0.000	0.853	0.000

Note: compared with before treatment, * $P<0.05$.

2.3 两组临床症状指标对比

实验组胸水吸收时间、临床症状缓解时间、住院时间短于

对照组 ($P<0.05$), 胸膜厚度大于对照组 ($P<0.05$), 详见表 3。

表 3 两组临床症状指标对比($\bar{x} \pm s$)

Table 3 Comparison of clinical symptoms between the two groups($\bar{x} \pm s$)

Groups	Pleural fluid absorption time (d)	Pleural thickness (mm)	Clinical symptom remission time(d)	Hospitalization time(d)
Control group(n=378)	18.36± 2.26	1.32± 0.26	13.16± 2.15	29.53± 2.54
Experimental group (n=378)	13.64± 2.87	1.65± 0.31	8.93± 1.36	24.13± 2.27
t	25.121	15.858	32.327	30.820
P	0.000	0.000	0.000	0.000

2.4 两组胸膜肥厚粘连及并发症发生情况对比

实验组的胸膜肥厚粘连、并发症总发生率低于对照组

($P<0.05$), 详见表 4。

表 4 两组胸膜肥厚粘连及并发症发生情况 [例(%)]

Table 4 Incidence of pleural hypertrophy adhesion and complications in the two groups [n(%)]

Groups	Pleural hypertrophy adhesion	Centripetal obesity	Osteoporosis	Fatigue and sweating	Total incidence rate
Control group(n=378)	93(24.60)	21(5.56)	18(4.76)	36(9.52)	75(19.84)
Experimental group(n=378)	36(9.52)	12(3.17)	7(1.85)	19(5.03)	38(10.05)
χ^2	30.368				14.244
P	0.000				0.000

3 讨论

结核性胸膜炎除了胸痛、呼吸困难等常见症状外, 还会引起胸膜肥厚甚至胸膜纤维化, 导致机体限制性的肺功能下降^[9-11]。此外, 结核性胸膜炎患者普遍处于免疫力低下状态, 并伴有炎症范围扩大、胸膜广泛充血、迟发性超敏反应高、水肿、大量炎性产物渗出等症状, 进而导致的不同程度的胸腔积液^[12]。由于标准四联抗结核治疗方案的普遍应用, 有效控制患者结核病变和消除急性期的胸腔积液已不是难题。然而随着急性期的胸腔

积液消退, 部分患者会出现胸膜肥厚粘连或纤维胸, 严重者甚至出现患侧胸廓塌陷, 导致患者肺功能下降, 不利于患者后续恢复^[13]。糖皮质激素也是结核性胸膜炎治疗的常用药物, 但临床中对其效果一直存在争议。糖皮质激素具有抗炎、抗免疫、抗过敏及抗病毒等多重作用, 在抵抗各种早期炎症性疾病方面具有独特优势^[14,15]。

本次研究以标准四联抗结核治疗方案为对照, 在此基础上结合糖皮质激素治疗, 结果显示, 实验组的临床症状改善优于对照组, 临床总有效率高于对照组。标准四联抗结核治疗可杀灭胸

腔中分布的结核杆菌,加快坏死病灶吸收。在此基础上,经胸腔注射糖皮质激素可显著提高胸腔积液中药峰浓度,其进入机体后与血浆蛋白结合可发挥以下作用:降低毛细血管壁及细胞膜的通透性,减少胸膜毛细血管扩张,减少胸膜渗出,促进胸水吸收^[16,17]。其中地塞米松可减轻标准四联抗结核治疗引起的变态反应,促进症状改善^[18]。同时本研究还显示,联合治疗者的肺功能改善效果更为显著,可能与联合治疗可迅速控制病情,减少对肺部脏器的损害有关。

不少研究发现^[19,20],结核菌活化可引起炎症细胞因子大量产生,而炎症因子在结核性胸膜炎发生、发展中发挥着重要作用。使用糖皮质激素后,机体血管通透性下降,白细胞渗出及充血缓解,溶酶体酶的释放减少、吞噬作用以及炎症化学中介物的合成与释放被抑制^[21-23];糖皮质激素还可全面抑制肉芽组织形成和成纤维细胞增生,从而减轻炎症反应^[24-26];此外,地塞米松还能抑制结缔组织增生,促进胸腔积液中蛋白质降解,促进机体炎症修复^[27]。另外,本研究还发现实验组的胸膜肥厚粘连、并发症总发生率低于对照组,胸膜肥厚粘连形成主要由胸水中大量纤维蛋白沉积于脏、壁层胸膜上所致^[28]。而向心性肥胖、骨质疏松、乏力多汗则是病情控制不佳者极易出现的并发症^[29]。在糖皮质激素的治疗下,细胞新陈代谢降低,可以抑制纤维组织过度增生及粘连,从而有效减少胸膜肥厚粘连发生^[30,31]。同时联合治疗者的各项临床症状指标改善均更为显著,有利于促进机体恢复,降低并发症的发生风险。本研究不足之处在于样本量较小、观察时间较短,未能追踪远期疗效,同时未能考察有关糖皮质激素对结核性胸膜炎免疫状态的影响,有待进一步深入研究。

综上所述,胸腔注射糖皮质激素联合标准四联抗结核疗法治疗结核性胸膜炎,疗效可靠,可改善患者肺功能,促进症状改善。

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(上接第 2871 页)

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