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鼓室内注射地塞米松联合盐酸氨溴索对分泌性中耳炎患者听力水平及免疫功能的影响*

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摘要 目的：探讨鼓室内注射地塞米松联合盐酸氨溴索对分泌性中耳炎（SOM）患者听力水平及免疫功能的影响。**方法**：选取2017年5月-2017年11月期间我院收治的SOM患者240例为研究对象。根据随机数字表法将患者分为对照组（n=120）与研究组（n=120），对照组给予鼓室内注入地塞米松治疗，研究组在此基础上联合盐酸氨溴索治疗。比较两组患者临床疗效，比较两组患者治疗前后0.5KHz、1.0KHz、2.0KHz频率下的气导听力水平、鼓室压及$CD4^+$、$CD8^+$、$CD4^+/CD8^+$水平，同时观察两组不良反应发生情况。**结果**：治疗后研究组患者总有效率为86.67%（104/120），高于对照组的70.83%（85/120）（P<0.05）。两组患者治疗后0.5KHz、1.0KHz、2.0KHz的气导听力水平以及鼓室压均较治疗前升高，且研究组高于对照组（P<0.05）。两组患者治疗后$CD4^+$、$CD4^+/CD8^+$均较治疗前升高，且研究组高于对照组（P<0.05）；两组患者治疗后$CD8^+$较治疗前降低（P<0.05），但研究组与对照组比较无差异（P>0.05）。两组患者在治疗期间均未发生严重的不良反应。**结论**：地塞米松联合盐酸氨溴索治疗SOM患者疗效确切，对患者的免疫功能及听力水平均有一定的改善作用，安全性好，具有一定的临床应用价值。

关键词：地塞米松；盐酸氨溴索；分泌性中耳炎；听力水平；免疫功能；疗效

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Effect of Intratincular Injection Dexamethasone Combined with Ambroxol Hydrochloride on Hearing Level and Immune Function in Patients with Secretory Otitis Media*

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ABSTRACT Objective: To investigate the effect of Intratincular injection dexamethasone combined with ambroxol hydrochloride on hearing level and immune function in patients with secretory otitis media(SOM). **Methods:** 240 cases of SOM patients who were treated in our hospital from May 2017 to November 2017 were selected as the research object. The patients were divided into control group (n=120) and study group (n=120 group) according to the number table method. The control group was treated with intratincular injection dexamethasone, the study group was treated with ambroxol hydrochloride on this basis. The clinical efficacy of the two groups was cimpared, The level of air conduction at 0.5 KHz, 1.0 KHz and 2.0 KHz frequencies, tympanum pressure and $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ levels were compared between the two groups before and after treatment, at the same time, the two groups of adverse reactions were observed. **Results:** The total effective rate of the patients in the study group was 86.67% (104/120), which was significantly higher than 70.83% (85/120) of the control group(P<0.05). The level of air conduction at 0.5 KHz, 1.0 KHz and 2.0 KHz frequencies and tympanum pressure in the two groups after treatment were higher than before treatment, and the study group was higher than that of the control group (P<0.05). The $CD4^+$ and $CD4^+/CD8^+$ in the two groups after treatment were higher than before treatment, and the study group was higher than that of the control group (P<0.05); the $CD8^+$ in the two groups after treatment was lower than before treatment (P<0.05); but there was no difference between the study group and the control group (P>0.05). There was no adverse reaction in the two groups during the treatment. **Conclusion:** Intratincular injection dexamethasone combined with ambroxol hydrochloride is effective and safe in the treatment of patients with SOM, and it can improve the immune function and hearing level of patients, which has certain clinical application value.

Key words: Dexamethasone; Ambroxol hydrochloride; Secretory otitis media; Hearing level; Immune function; Curative effect

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前言

分泌性中耳炎(Secretory otitis media,SOM)是一种以听力下降以及中耳积液为主要特征的中耳非化脓性炎性病变,其发病原因通常与细菌性感染、T 细胞亚群失调以及咽鼓管功能出现异常等情况有关[1-3]。若 SOM 病情未得到有效控制,可引发中耳黏连、硬化等病变情况,甚至导致患者语言障碍,严重影响患者工作及生活[4,5]。因此,临床应针对 SOM 患者采取积极有效的治疗,以提高患者听力水平。地塞米松是临床常用的治疗 SOM 药物,具有强效的抗过敏、抗炎作用,同时还可抑制结缔组织增生[6,7]。盐酸氨溴索的功能主要有促进粘液排出、促进分泌物溶解,已有多项研究指出其在呼吸系统相关疾病的治疗中可获得确切的疗效[8,9]。近年来相关报道指出盐酸氨溴索可用于辅助治疗 SOM 患者[10],但其作用机制尚不十分明确。因此,本研究针对 SOM 患者采用鼓室内注射地塞米松联合盐酸氨溴索治疗,探讨对其听力水平及免疫功能的影响,旨在为 SOM 患者临床治疗提供数据支持,现作如下报道。

1 资料与方法

1.1 一般资料

选取 2017 年 5 月 -2017 年 11 月期间我院收治的 SOM 患者 240 例为研究对象。纳入标准[11]:(1)所有患者均符合 SOM 相关诊断标准;(2)临床表现为耳朵阻塞感、听力衰退、耳镜检查鼓膜内陷、鼓膜穿刺积液量 >0.1 mL;(3)入院前一周内未接受过相关治疗者;(4)精神状态正常,意识清醒者;(5)患者及其家属知情本研究并签署知情同意书。排除标准:(1)有耳毒性药物使用史或者耳聋家族史者;(2)化脓性中耳炎;(3)合并鼻咽部肿瘤者;(4) 伴有重症高血压及其他脏器疾病障碍者;(5)伴有噪声性听力损伤或者鼓膜穿孔者;(6) 对本研究使用药物存在禁忌症者。根据随机数字表法将患者分为对照组(n=120)与研究组(n=120),其中对照组男 64 例,女 56 例,年龄 16-44 岁,平均(27.35± 3.57)岁;病程 2-14 周,平均(7.19± 2.35)周;单耳发病 97 例,双耳发病 23 例。研究组男 62 例,女 58 例,年龄 18-43 岁,平均(28.37± 4.01)岁;病程 3-16 周,平均(7.83± 2.67)周;单耳发病 91 例,双耳发病 29 例。两组患者一般资料比较无差异(P>0.05),本研究经医院伦理委员会批准同意。

1.2 治疗方法

所有患者取坐立位,患处耳朵正对医师,头微向前倾。采用碘伏对患者外耳道行常规消毒处理,使用带有鼓膜穿刺针头的注射器(10 mL),选取鼓膜前下象处距离鼓膜边缘 1-2 mm 处为穿刺点,将所有可能存在的积液抽出,若存在注射器难以吸出的黏稠状分泌物,则使用 9 号长针头或者负压吸引器将其吸出,之后给予中耳腔药物常规治疗。对照组在中耳腔内注入地塞米松(浙江仙琚制药股份有限公司,国药准字 H20045100)5 mg,研究组则在中耳腔内注入 5 mg 地塞米松以及 15 mg 盐酸氨溴索(山东罗欣药业集团股份有限公司,国药准字 H20153115),注药完毕后,将患者头部微微偏向另一侧,同时轻压患者耳屏部位,当患者咽部出现药液流出时即停止,将消毒干棉球置于患者外耳道口处,留置 30 min。7 d 后复查,若患者仍未治愈可重复治疗,重复次数≤ 4 次。在治疗期间,两组患者均使用 1%麻黄素滴鼻液进行滴鼻,同时给予抗生素治疗。

1.3 观察指标

(1)临床疗效 于治疗后观察两组患者临床疗效。疗效判定标准[12]:鼓室导抗图可见明显好转,自觉症状基本消失,各频率下气导听力水平接近健耳水平则显示痊愈;鼓室导抗图基本好转,自觉症状基本好转,各频率下气导听力水平提高幅度 >20dB,尚未接近健耳水平则显示显效;鼓室导抗图无明显变化,自觉症状有所好转,各频率下气导听力水平提高幅度处于 15-20 dB 则显示有效;自觉症状、鼓室导抗图均无变化,且各频率下气导听力水平提高幅度 <15 dB 则显示无效。总有效率 = 痊愈率 + 显效率 + 有效率。(2)听力水平 所有患者均采用丹麦 MADSEN-OB922 型听力计检测不同频率下(0.5 KHz、1.0 KHz、2.0 KHz)的气导听力水平,同时采用 AT-22 声导抗仪检测所有患者鼓室压。(3)免疫功能 分别于治疗前后采集所有患者清晨空腹外周静脉血 5 mL,置于 EDTA 抗凝管中,10 min 内送检,应用 IMK2-Lymphocyte 细胞分离试剂盒分离血液中的免疫细胞,然后应用流式细胞仪测定 $CD4^+$、$CD8^+$ 细胞比例,计算 $CD4^+/CD8^+$。(4)不良反应 观察所有患者治疗期间不良反应发生情况。

1.4 统计学方法

研究数据录入 SPSS25.0 软件处理,计量资料用($\bar{x}\pm s$)表示,采用 t 检验,计数资料以率(%)表示,采用 x^2 检验,α=0.05 被设置为检验标准。

2 结果

2.1 两组患者临床疗效比较

治疗后研究组总有效率为 86.67%(104/120),高于对照组的 70.83%(85/120)(P<0.05)。详见表 1。

表 1 两组治疗后临床疗效比较[n(%)]

Table 1 Comparison of clinical efficacy after treatment between the two groups[n(%)]

Groups	Recovery	Effective	Good	Invalid	Total effective rate
Control group(n=120)	12(10.00)	26(21.67)	47(39.16)	35(29.17)	85(70.83)
Study group(n=120)	21(17.50)	35(29.17)	48(40.00)	16(13.33)	104(86.67)
x^2					8.988
P					0.003

2.2 两组患者治疗前后听力水平及鼓室压比较

两组患者治疗前 0.5 KHz、1.0 KHz、2.0 KHz 的气导听力水平以及鼓室压比较无差异(P>0.05);两组患者治疗后 0.5 KHz、1.0 KHz、2.0 KHz 的气导听力水平以及鼓室压均较治疗前升

高，且研究组高于对照组（P<0.05）。详见表 2。

表 2 两组患者治疗前后听力水平及鼓室压比较（$\bar{x}\pm s$）

Table 2 Comparison of hearing levels and tympanum pressure before and after treatment between the two groups（$\bar{x}\pm s$）

Groups	Time	Hearing level			Tympanum pressure (daPa)
		0.5KHz(dB)	1.0KHz(dB)	2.0KHz(dB)	
Control group(n=120)	Before treatment	25.68± 5.25	34.56± 5.08	44.31± 6.25	-136.23± 13.04
	After treatment	36.61± 7.04*	43.53± 6.15*	54.07± 7.17*	-102.69± 12.57*
Study group(n=120)	Before treatment	27.23± 5.65	35.36± 4.52	45.37± 5.65	-138.04± 14.29
	After treatment	48.88± 6.67*#	53.98± 5.47*#	63.34± 6.67*#	-79.69± 13.26*#

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

2.3 两组患者治疗前后免疫功能比较

两组患者治疗前 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$ 比较无差异（P>0.05）；两组患者治疗后 $CD4^+$、$CD4^+/CD8^+$ 均较治疗前升高，且研究组高于对照组（P<0.05）；两组患者治疗后 $CD8^+$ 较治疗前降低（P<0.05），但研究组与对照组比较无差异（P>0.05）。详见表 3。

表 3 两组患者治疗前后免疫功能比较（$\bar{x}\pm s$）

Table 3 Comparison of immune function before and after treatment between the two groups（$\bar{x}\pm s$）

Groups	Time	$CD4^+$(%)	$CD8^+$(%)	$CD4^+/CD8^+$
Control group(n=120)	Before treatment	34.68± 2.25	34.56± 3.08	1.21± 0.05
	After treatment	41.61± 2.04*	25.53± 3.15*	1.47± 0.10*
Study group(n=120)	Before treatment	34.23± 2.65	33.96± 2.52	1.18± 0.08
	After treatment	44.88± 2.67*#	26.98± 2.47*	1.93± 0.04*#

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

2.4 两组患者不良反应发生情况比较

两组患者治疗期间均未发生严重的不良反应。

3 讨论

目前，SOM 的发病机制尚未完全明确，有相关研究报道，中耳感染、炎症反应增强以及免疫系统异常是 SOM 发生、发展的主要机制[13,14]。故该病的治疗可从抑制感染、减轻机体炎症反应以及抑制免疫系统异常等方面着手。地塞米松是治疗 SOM 的常用药物，经鼓室内注射后，可迅速到达病灶，直接作用于患处，达到消炎、抗感染的目的[15-17]。然而，地塞米松药效时间短，且易病情易反复发作，引发分泌物纤维黏连，同时因为注射次数过多，不良反应发生率较高。盐酸氨溴索是一种粘液溶解剂，可发挥润滑呼吸道、抗氧化等作用，经鼓室内注射后，可将鼓室内积液溶解并迅速排出，并恢复鼓膜表面正常分泌功能[18-20]。

本次研究结果表明，研究组患者治疗后总有效率为 86.67%（104/120），高于对照组的 70.83%（85/120）（P<0.05）。表明地塞米松联合盐酸氨溴索治疗，疗效确切。这主要是因为两种药物联合应用可发挥各自的特点，地塞米松发挥抗炎、抗过敏以及抗感染作用，盐酸氨溴索发挥杀菌、清洁分泌物的作用，二者起到协同治疗效果，最终提升 SOM 患者临床治疗效果[21,22]。另外，两组患者治疗后 0.5KHz、1.0KHz、2.0KHz 的气导听力水平以及鼓室压均较治疗前升高，且研究组高于对照组（P<0.05）。提示地塞米松联合盐酸氨溴索治疗 SOM，可显著改善患者听力水平。地塞米松作为临床治疗 SOM 的常用药物，其作用于 SOM 患者的药效机制已得到确切证实，联合盐酸氨溴索治疗可促进中耳通气，减少黏液量，促进排出中耳积液，同时有利于纤毛功能迅速恢复，提升清除率，从而改善患者临床症状，提高患者听力水平[23-25]。另一方面鼓膜内陷的原因主要是由于鼓膜内外气压不平衡造成，地塞米松联合盐酸氨溴索有助于降低黏膜表面张力和咽鼓管开放，进一步改善鼓室内生理功能[26]。本文还对 SOM 患者免疫功能进行了考察，由于 T 细胞的免疫调节作用主要由 $CD4^+$、$CD8^+$ 共同完成，$CD4^+$ 具有辅助细胞免疫和体液免疫的作用，$CD8^+$ 则抑制抗体合成分泌以及 T 细胞的增殖，两者的稳态维持着机体的正常免疫反应，另由于 $CD8^+$ 细胞具有杀伤作用，因此，$CD8^+$ 的增多对于机体的免疫应答可产生不利影响。本研究结果显示，两组患者治疗后 $CD4^+$、$CD4^+/CD8^+$ 均较治疗前升高，且研究组高于对照组（P<0.05），两组患者治疗后 $CD8^+$ 较治疗前降低（P<0.05）。提示地塞米松联合盐酸氨溴索治疗可促进 SOM 患者免疫功能恢复，改善患者免疫失调。这与胡全福等人研究结果基本一致[27]，分析其原因，地塞米松是一种人工合成的皮质类固醇激素，可发挥抑制机体延迟性过敏反应、免疫球蛋白与其受体的结合能力、T 淋巴细胞转化等免疫抑制疗效[28-30]。另外两组患者在治疗期间均未发生严重的不良反应，提示上述两种药物安全性好，无不良副作用。

综上所述，针对 SOM 患者采取鼓室内注射地塞米松联合盐酸氨溴索治疗，其效果显著优于地塞米松单药治疗，同时可改善患者听力水平以及促进患者免疫功能恢复，无严重不良反应发生，适于临床推广应用。

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