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经鼓膜穿刺与肌肉注射鼠神经生长因子对突发性耳聋的治疗效果对比*

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摘要 目的: 对比分析经鼓膜穿刺与肌肉注射鼠神经生长因子对突发性耳聋的治疗效果。**方法:** 选择 2014 年 1 月~2016 年 12 月在西安体育学院健康科学系进行诊治的 75 例突发性耳聋患者, 将所有患者随机分为鼓膜穿刺组 (n=37 例) 和肌肉注射组 (n=38 例)。肌肉注射组患者采用肌肉注射的方法给予鼠神经生长因子治疗, 每次 20 μg, 每天 1 次; 鼓膜穿刺组患者采用经鼓膜穿刺方法给予治疗鼠神经生长因子治疗, 每次 20 μg, 每天 1 次。两组均治疗 14 d。比较两组的临床治疗效果、治疗前后纯音听阈的变化及不良反应的发生情况。**结果:** 治疗后, 鼓膜穿刺组痊愈 9 例, 显效 14 例, 有效 22 例, 无效 3 例, 有效率为 91.89% (34/37), 明显高于肌肉注射组 [73.68% (28/38)] ($P<0.05$); 两组纯音听阈均与治疗前相比均明显降低 ($P<0.05$), 且鼓膜穿刺组明显低于肌肉注射组 ($P<0.05$)。两组突发性耳聋患者治疗过程中均未出现明显的不良反应。**结论:** 经鼓膜穿刺鼠神经生长因子治疗突发性耳聋的临床效果明显优于肌肉注射, 且安全性较高。

关键词: 鼓膜穿刺; 肌肉注射; 鼠神经生长因子; 突发性耳聋

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Comparison of the Effect of Tympanic Membrane Puncture and Intramuscular Injection of Rat Nerve Growth Factor in the Treatment of Sudden Deafness*

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ABSTRACT Objective: To compare the clinical effect of tympanic membrane puncture and intramuscular injection of rat nerve growth factor in the treatment of sudden deafness. **Methods:** 75 cases of patients with sudden deafness who were treated in Xi'an Physical Education University from January 2011 to December 2016 were selected and randomly divided into the tympanic membrane puncture group (n=37 case) and the intramuscular injection group (n=38 case). The intramuscular injection group was treated with intramuscular injection rat nerve growth factor, while the tympanic membrane puncture group was treated with tympanum puncture, 20 μg each time, 1 times a day. The clinical therapeutic effects, changes of pure tone threshold before and after treatment, and the incidence of adverse reactions were compared between the two groups. **Results:** After treatment, the effective rate of observation group was 91.89% (34/37), which was significantly higher than that of the control group [73.68%(28/38)] ($P<0.05$); the pure tone hearing thresholds of both groups were significantly improved compared with those before treatment ($P<0.05$), which was significantly better in the tympanic membrane puncture group than that of the intramuscular injection group ($P<0.05$). There was no obvious adverse reactions in the two groups during the treatment. **Conclusion:** The clinical effect of mural puncture and mouse nerve growth factor on the sudden deafness is superior to that of the intramuscular injection, and the safety is high.

Key words: Tympanic membrane puncture; Intramuscular injection; Rat nerve growth factor; Sudden deafness

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前言

突发性耳聋作为临床上常见的突发性神经性耳聋, 通常在数分钟、数小时内, 患者的听力降低至最低点, 听力下降幅度超

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过 20 dB,最少会累及邻近 2 个听力的检测频率^[1,2]。突发性耳聋发病原因不明,有外界刺激和内部微循环的影响,目前认为与循环障碍、病毒感染、血管阻塞性疾病、血浆纤维蛋白含量升高、自身免疫性疾病以及膜迷路破裂等密切相关^[3,4]。临床上常用的治疗方法是注射鼠神经生长因子,鼠神经生长因子与人类神经因子同源性极高,具有维持神经细胞存活,促进神经细胞分化和成熟等功能^[5-7]。

鼠神经生长因子不仅可以对正常神经细胞发挥营养因子功效,还可以修复以及保护受到损伤的神经细胞,因此被广泛应用于临床治疗神经系统疾病的研究中^[8,9]。目前许多研究表明鼠神经生长因子在内耳的发育和成熟过程中都有不同程度的表达,促进耳蜗神经轴突的再生,保护并且修复。但其注射方式存在很大的区别,常规的注射是肌肉注射,但是由于发挥作用的周期长,最后作用于内耳的剂量几乎很少,治疗效果不佳,无法达到预期的效果。目前,临床上也采用鼓室内注射。本研究主要比较了经鼓膜穿刺与肌肉注射鼠神经生长因子对突发性耳聋的治疗效果,结果报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 1 月~2016 年 12 月在西安体育学院健康科学系进行诊治的 75 例突发性耳聋患者,均符合相关的诊断标准^[4],排除伴有高血压、糖尿病、血液病和冠心病等基础代谢疾病者,患有内听道、颅脑和中耳疾病者,随机分为两组。鼓膜穿刺组 37 例,男 20 例,女 17 例;年龄 22~69 岁,平均(40.35±11.24)岁;病程 1~39 天,平均(14.39±6.45)天;单侧发病 26 例,双侧发病 11 例;合并症:眩晕 13 例,耳鸣 20 例。肌肉注射组 38 例,男 22 例,女 16 例;年龄 23~70 岁,平均(41.37±10.93)

岁;病程 1~38 天,平均(15.19±7.38)天;单侧发病 26 例,双侧发病 12 例;合并症:眩晕 14 例,耳鸣 20 例。两组的基线资料对比无显著性差异($P>0.05$),具有可比性。

1.2 治疗方法

肌肉注射组采用肌肉注射的方法给予鼠神经生长因子(批号:国药准字 S20100005,生产厂家:丽珠集团丽珠制药厂,规格:30 μg)治疗,每次 20 μg,每天 1 次;鼓膜穿刺组采用经鼓膜穿刺方法给予治疗鼠神经生长因子治疗,给药方法如下:患者取仰卧位,头部偏向健侧,使患耳朝上,首先对外耳道的耵聍进行仔细的清理,并且使用 75%的酒精对外耳道的皮肤进行消毒,然后对鼓膜采取表面麻醉,行鼓膜穿刺后,把 20 μg 鼠神经生长因子缓慢注入患耳的鼓室中,每天 1 次。疗程 14 d。

1.3 观察指标

临床治疗效果:①痊愈:患者在 0.25~4 kHz 各频率听阈恢复正常听力水平;②显效:在 0.25~4 kHz 中听力平均提高>30 dB;③有效:在 0.25~4 kHz 中听力平均提高幅度为 15~30 dB;④无效:在 0.25~4 kHz 中听力平均改善<15 dB。有效率=(痊愈+显效+有效)/总耳数×100%。检测治疗前后的纯音听阈,并观察不良反应发生率。

1.4 统计学分析

采用 SPSS15.00 软件进行数据分析,计量资料以($\bar{x}\pm s$)表示,组间比较采用 t 检验,计数资料以%表示,组间比较行 χ^2 检验,以 $P<0.05$ 差异有统计学意义。

2 结果

2.1 两组临床疗效对比

治疗后,鼓膜穿刺组的有效率为 91.89%(34/37),明显高于肌肉注射组[73.68%(28/38)]($P<0.05$),见表 1。

表 1 两组临床疗效对比[例(%)]

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

Groups	n	Recovery	Obviously effective	Effective	Invalid	Effective rate
Intramuscular injection group	38	5(13.16)	13(34.21)	10(26.32)	10(26.32)	73.68
Tympanic membrane puncture group	37	9(24.32)	14(37.84)	11(29.73)	3(8.11)	91.89*

Note: Compared with the intramuscular injection group, * $P<0.05$.

2.2 两组治疗前后纯音听阈对比

两组治疗后的纯音听阈均较治疗前明显降低,且鼓膜穿

刺组纯音听阈明显低于肌肉注射组($P<0.05$),见表 2。

表 2 两组治疗前后纯音听阈对比($\bar{x}\pm s$, dB)

Table 2 Comparison of the pure tone threshold before and after treatment between two groups($\bar{x}\pm s$, dB)

Groups	n	Before treatment	After treatment
Intramuscular injection group	38	69.43±16.45	60.29±15.32 [#]
Tympanic membrane puncture group	37	70.12±18.37	49.58±13.74 ^{*#}

Note: Compared with the intramuscular injection group, * $P<0.05$, compared with before treatment, [#] $P<0.05$.

2.3 两组不良反应发生情况对比

两组在治疗过程中均未出现明显的不良反应,肌肉注射组 1 例发生眩晕,伴有恶心、呕吐,经过对症治疗后均缓解;鼓膜穿刺组 2 例患者于用药后发生恶心呕吐、眩晕和耳鸣,1 例发生短暂性耳痛,经过对症治疗后均缓解。

3 讨论

突发性耳聋指的是原因不明的感音神经性听力损失,按照患者的纯音听阈图,听力曲线可以分为平坦型、低频型、全聋型以及高频型四个类型。患者的听力大多会于 3 d 内迅速显著降

低,常为中度或重度,以单侧发病最为多见,会伴有耳鸣、耳闷、恶心呕吐以及眩晕等不良反应。如果未得到及时的治疗(一般2周内治疗即可有效),极易发展为永久性耳聋。突发性耳聋治疗方法很多,根据不同的发病情况采取治疗,而且治疗的效果也存在差别。多数研究学者认为突发性耳聋是一种综合而非孤立的疾病^[10,11]。目前,临床上常采用改善微循环、糖皮质激素、营养神经、抗病毒药物、高压氧和抗凝剂治疗,但尚未发现特别有效的治疗手段,临床治疗方法也尚未统一^[12-14]。听力主要依靠耳蜗螺旋神经元的传导和毛细胞的感受。神经生长因子具有促突起生长以及神经元营养双重生物学功能,对中枢及周围神经元的分化、发育、生长、再生以及功能特性的表达均发挥着重要的生物调控功能。由于其可以提高受损神经细胞的存活率,临床上主要用于治疗神经病变^[15-17]。研究表明鼠神经生长因子的治疗效果很可能是通过神经免疫网络间接对耳蜗神经以及耳蜗细胞发挥作用^[18,19]。

肌肉注射鼠神经生长因子在临床上广泛应用于外伤后神经修复以及糖尿病外周神经病变等外周神经病变的治疗,并取得了较好的治疗效果^[20-22]。但是采取肌肉注射鼠神经生长因子的治疗效果不佳,由于多次的臀位肌注,导致注射部位出现强烈的疼痛,而且患者也无法忍受,会中断治疗,拒绝注射^[23-25]。而经鼓膜穿刺注射鼠神经生长因子可以通过蜗窗膜的主动吸收或短距离渗透作用进入内耳中,使螺旋神经节细胞、内耳毛细胞以及支持细胞的内源性神经生长因子得到补充,恢复内耳功能,从而发挥治疗突发性耳聋的目的^[26,27]。

本研究结果显示鼓膜穿刺组的有效率明显高于肌肉注射组,治疗后的纯音听阈值显著高于肌肉注射组,表明与肌肉注射的给药方式相比,经鼓膜穿刺鼠神经生长因子可以显著提高突发性耳聋的临床治疗效果。分析其原因可能鼓膜穿刺注射法目的性强,直接作用于损伤的部位,能保持药物的浓度,达到治疗的效果。而且鼓膜穿刺治疗期间出现的不良反应少,安全性高。鼠神经生长因子进而可以与内耳相应的受体发生特异性结合,发挥营养神经、促进内耳功能的迅速恢复的临床治疗效果^[28-30]。

综上所述,经鼓膜穿刺鼠神经生长因子治疗突发性耳聋的临床效果明显优于肌肉注射方式,且安全性较高。

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