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A 型肉毒毒素不同注射方式治疗单纯性咬肌肥大患者的疗效及对咬肌厚度的影响 *

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摘要 目的: 探讨 A 型肉毒毒素不同注射方式治疗单纯性咬肌肥大患者的疗效及对咬肌厚度的影响。**方法:** 选择 2014 年 6 月-2016 年 6 月在我院接受治疗的单纯性咬肌肥大患者 84 例, 根据随机数字表法将患者均分为研究组和对照组, 两组各 42 例, 其中对照组进行单次注射 A 型肉毒毒素, 研究组给予连续注射 A 型肉毒毒素。所有患者在治疗前、治疗后 1 个月、治疗后 3 个月、治疗后 6 个月、治疗后 9 个月、治疗后 12 个月, 采用超声对咬肌厚度进行检测; 在治疗后 12 个月调查两组患者对治疗效果的主观评价, 同时邀请两名专家对患者的治疗效果进行评价。记录患者在治疗后出现的不良反应。**结果:** 研究组在治疗后 9 个月、治疗后 12 个月的咬肌厚度显著低于对照组, 差异有统计学意义 ($P < 0.05$), 对照组患者的咬肌厚度在治疗后 1 个月至治疗后 6 个月逐渐降低, 治疗后 6 个月达到最低值, 在治疗后 9 个月和治疗后 12 个月开始回升。研究组患者的咬肌厚度在治疗后一直呈下降的趋势, 并在治疗后 12 个月达到最低值。两组治疗后的各个时间点的咬肌厚度均低于治疗前, 差异有统计学意义 ($P < 0.05$)。研究组患者本人的主观评价和专家评价为 A、B、C 的比例均显著低于对照组, D、E 的比例均显著高于对照组, 差异有统计学意义 ($P < 0.05$)。两组患者不良反应发生情况无统计学差异 ($P > 0.05$)。**结论:** 与单次注射相比, A 型肉毒毒素连续注射能更好的降低咬肌厚度, 同时患者对治疗效果的主观评价和专家的评价较好, 且不良反应少, 临床上治疗咬肌肥大时可选用连续注射 A 型肉毒毒素的方式。

关键词: 咬肌肥大; 注射方式; A 型肉毒毒素; 疗效; 咬肌厚度

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Curative Effect of Different Botulinum Toxin Type A Injection Methods on Patients with Simple Masseter Muscle Hypertrophy and Their Effects on Masseter Muscle Thickness*

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ABSTRACT Objective: To investigate the efficacy of different botulinum toxin type A injection methods in the treatment of simple masseter muscle hypertrophy and their influence on the masseter muscle thickness. **Methods:** 84 cases of simple masseteric hypertrophy patients who were treatment in our hospital from June 2014 to June 2016 were selected and were divided into study group and control group according to the random table method, with 42 cases in each group. The control group was given single time injection of botulinum toxin type A, while the study group was given continuous injection of botulinum A toxin. Before treatment and 1 month after treatment, 3 months after treatment, 6 months after treatment, 9 months after treatment, 12 months after treatment, ultrasound was used to detect the masseter muscle thickness of all the patients. 12 months after treatment, the subjective evaluation on curative effect of patients in the two groups were investigated, and two experts were invited to evaluate the curative effect at the same time. The adverse reactions of the patients after treatment were recorded. **Results:** The masseter muscle thickness of the patients in study group 9 months and 12 months after treatment were significantly lower than the control group, the differences were statistically significant ($P < 0.05$). The masseter muscle thickness in the control group decreased gradually from 1 months after treatment to 6 months after treatment, and reached the minimum at 6 months after treatment, and began to rise from 9 months to 12 months after treatment. The masseter muscle thickness of the patients in the study group decreased after treatment and reached a minimum at 12 months after treatment. The masseter muscle thickness at each time point after treatment in the two groups was lower than before treatment, the difference was statistically significant ($P < 0.05$). The

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proportion of A, B, C of the subjective evaluation and expert evaluation of the patients in the study group were significantly lower than those of the control group, while the proportion of D and E of those were significantly higher than those of the control group, the differences were statistically significant ($P<0.05$). There was no significant difference in adverse reactions between the two groups ($P>0.05$).

Conclusion: Compared with single injection, continuous injection of botulinum toxin type A can better reduce masseter muscle thickness, and the subjective evaluation and expert evaluation of the therapeutic effect are better, and the side effects are less. The botulinum toxin type A can be used continuously in the treatment of hypertrophy of masseter muscle.

Key words: Masseter hypertrophy; Injection method; Botulinum toxin type A; Efficacy; Masseter muscle thickness

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前言

咬肌肥大又称咬肌良性肥大,患者脸型多为方形或圆形,虽然咬肌肥大对患者咀嚼能力无负面影响,但患者的脸型与当今主流的审美存在一定的冲突,影响美观,许多咬肌肥大患者均愿意通过现代医疗手段对自身的脸型进行修正,因此如何快速有效的治疗咬肌肥大成为目前整形行业的研究热点^[1,2]。咬肌是产生咬合动作及维持下颌形态的重要肌肉,其大小、形态、功能与面部轮廓紧密相关。咬肌肥大主要是长时间或频繁咀嚼食物,尤其是较为坚硬的食物,会充分刺激咬肌,导致其过度增长,最终导致咬肌肥大出现^[3,4]。手术切除是临床治疗咬肌肥大的常用方法,但是其操作较为繁杂、治疗周期长、恢复时间久,且手术可能会导致患者出现较为严重的不良反应^[5,6]。A型肉毒毒素是一种用于治疗眼睑痉挛、面肌痉挛等疾病的药物,能够抑制周围运动神经末梢突触前膜乙酰胆碱释放,引起肌肉出现松弛性麻痹^[7,8]。多项研究发现^[9-11],A型肉毒毒素治疗单纯性咬肌肥大较好的疗效,且其操作简便、创伤小、见效快,现已在临床广泛应用。虽然A型肉毒毒素治疗单纯性咬肌肥大的疗效已得到证实,但对于不同注射方式的疗效对比报道较少。本研究旨在探讨A型肉毒毒素不同注射方式治疗单纯性咬肌肥大患者的疗效及对咬肌厚度的影响,以为临床治疗选择合适的注射方式提供参考,现将研究结果整理如下。

1 资料与方法

1.1 一般资料

选择2014年6月-2016年6月在我院接受治疗的单纯性咬肌肥大患者84例,纳入标准:①所有患者均有单纯性咬肌肥大的临床症状,即脸型为方形或圆形,且在收缩咬肌时可明显感觉到咬肌范围较大和咬肌明显增厚;②符合咬肌肥大的影像学特征;③所有患者临床治疗完整;④患者均为首次接受A型肉毒毒素治疗;⑤患者及其家属对本次研究知情同意。排除标准:①合并有其他脸部疾病者;②急性传染病者;③合并有严重器质性疾病者;④近期使用过氨基糖苷类抗菌素者;⑤妊娠期和哺乳期妇女;⑥未能按时前来复查或随访失联者。采用随机数字表法将患者均分为研究组和对照组,两组各42例。研究组男12例,女30例,年龄21-49岁,平均年龄 (28.8 ± 5.6) 岁;对照组男13例,女29例,年龄21-51岁,平均年龄 (28.1 ± 5.8) 岁。两组患者的一般资料差异无统计学意义($P>0.05$),可以进行组间对比。

1.2 治疗方法

对照组患者给予单次注射A型肉毒毒素治疗(兰州生物制品研究所有限责任公司,国药准字:S10970037),注射前加入生理盐水2mL,患者取仰卧位,咬肌处注射50U/侧,选择咬肌膨隆最显著的地方作为第一注射点,注射剂量控制在15~30U,选择下颌角处作为第二注射点,分2~3个点围成扇形进行注射,每点的注射量在10U以下。研究组给予连续注射A型肉毒毒素治疗,第一次注射方式与对照组一致,首次注射6个月后进行再次注射。注射A型肉毒毒素时的具体剂量需根据患者的具体病情而做出一定的调整,如患者两侧咬肌大小不一,则需对注射剂量做出调整。在注射A型肉毒毒素时应备有1:1000肾上腺素,注射结束后对患者进行常规的护理,并且患者留院内短期观察。

1.3 观察指标

所有患者在治疗前、治疗后1个月、治疗后3个月、治疗后6个月、治疗后9个月、治疗后12个月,采用超声对进行咬肌厚度进行检测,统一采用IU22型号超声机(荷兰PHIUPS公司),L17-5探头。探头与下颌缘平行的状态下,确保在口角与耳垂连线的安全平面以下范围内进行平行移动。叮嘱患者紧咬后牙根使咬肌处于收缩状态,找出最厚位置并记录厚度;每侧分别至少测量3次并取平均值。两组患者在治疗后12个月,联系患者了解其治疗效果的自我评价,同时邀请两名专家对患者的治疗前后的症状进行对比,患者可以给予A、B、C、D、E的评分,其中A表示无效果,B表示效果较差,C表示效果一般,D表示虽然有效果,但和预期结果还有差距,E表示效果满意,并达到预期结果。同时在患者每次上门复查时了解其治疗后出现的不良反应,并作比较。

1.4 统计学方法

选用SPSS19.0对所有数据进行统计分析,计数资料以率(%)表示,进行卡方检验,计量资料以均值 $\pm$ 标准差($\bar{x}\pm s$)表示,进行t检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者在各个时间点的咬肌厚度比较

与治疗前比较,两组患者治疗后的咬肌厚度均明显下降($P<0.05$)。两组患者在治疗前治疗后1个月、治疗后3个月、治疗后6个月的咬肌厚度比较无统计学差异($P>0.05$),研究组在治疗后9个月、治疗后12个月的咬肌厚度显著低于对照组,差异有统计学意义($P<0.05$),对照组患者的咬肌厚度在治疗后1个月至治疗后6个月逐渐降低,治疗后6个月达到最低值,在治疗后9个月和治疗后12个月开始回升。研究组患者的咬肌

厚度在治疗后一直呈下降的趋势,并在治疗后 12 个月达到最低值。两组治疗后的各个时间点的咬肌厚度均低于治疗前,差异有统计学意义($P<0.05$)。具体见下表。

表 1 两组患者在各个时间点的咬肌厚度比较

Table 1 Comparison of masseter muscle thickness at different time points in two groups

Groups	n	Before treatment	1 months after treatment	3 months after treatment	6 months after treatment	9 months after treatment	12 months after treatment
Control group	42	14.36± 0.19	11.23± 0.16*	10.67± 0.17*	9.87± 0.15*	10.21± 0.15*	12.03± 0.18*
Study group	42	14.38± 0.20	11.26± 0.17*	10.71± 0.16*	9.91± 0.16*	9.63± 0.18*	9.31± 0.16*
t		0.470	0.833	1.110	1.182	16.043	73.195
P		0.640	0.407	0.270	0.241	0.000	0.000

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

2.2 两组患者对治疗效果的主观评价以及专家评价的对比 均显著低于对照组,D、E 的比例均显著高于对照组,差异有统计学意义($P<0.05$),具体见下表。

表 2 患者和专家对治疗效果主观评价的对比

Table 2 Comparison of subjective evaluation of treatment effectiveness between patients and specialists

Group	n	Appraiser	A	B	C	D	E
Control group	42	Patient himself	12(28.57)	16(38.10)	10(23.81)	3(7.14)	1(2.38)
		Expert	8(19.05)	14(33.33)	12(28.57)	6(14.29)	2(4.76)
Study group	42	Patient himself	2(4.76)*	4(9.52)*	2(4.76)*	18(42.86)*	16(38.10)*
		Expert	1(2.38)*	2(4.76)*	2(4.76)*	19(45.24)*	18(42.86)*

Note: Compared with control group, * $P<0.05$.

2.3 两组患者在治疗后出现的不良反应对比 一个月内出现,经过对症治疗后症状均明显改善,两组患者在治疗后出现的不良反应均无统计学意义($P>0.05$),详细见下表。

表 3 两组患者在治疗后出现的不良反应对比

Table 3 Comparison of adverse reactions in the two groups after treatment

Group	n	Local swelling	Masticatory weakness	Nausea	Infected
Control group	42	3(7.14)	2(4.76)	3(7.14)	1(2.38)
Study group	42	4(9.52)	4(9.52)	3(7.14)	2(4.76)
χ^2		0.156	0.718	0.000	0.346
P		0.693	0.397	1.000	0.557

3 讨论

由于咬肌肥大患者脸型与现代审美不符,再加上当今社会人们对美的不断追求和整形风气的蔓延,导致要求治疗咬肌肥大的患者与日俱增,目前咬肌肥大已成为面部整形方向最为常见的疾病之一^[12-14]。咬肌处于下颌角的下颌升支外侧,腮腺前方,部分咬肌被腮腺覆盖,咬肌的大小、形态、功能与面部轮廓紧密相关^[15,16]。咬肌肥大与日常饮食习惯息息相关,目前部分青少年喜欢咀嚼口香糖或频繁吃零食,会频繁刺激咬肌,且青少年的下颌骨可塑性强,肌肉也正处于发育期,两侧咬肌过度发育,导致下颌角肥大外翻,成年后便出现咬肌肥大^[17,18]。肉毒毒素有 A、B、C、D、E、F、G 七个亚型,其中 A 型肉毒毒素具有毒力强,性质稳定,便于生产等特点,因此应用最广^[19,20]。A 型肉毒毒素在自然状态下是一种与非毒性蛋白结合的复合物,该毒素

本身的分子量为 150 ku,而复合体的分子量却增加为 900 ku,能够致使肌肉出现不同程度的松弛性麻痹。A 型肉毒毒素早期常用于神经肌肉性疾病的治疗,现如今广泛应用于祛除动态皱纹及治疗咬肌肥大等整形美容领域^[21,22]。

在本次研究中,研究组在治疗后 9 个月、治疗后 12 个月的咬肌厚度显著低于对照组,差异有统计学意义($P<0.05$),对照组患者的咬肌厚度在治疗后 1 个月至治疗后 6 个月逐渐降低,治疗后 6 个月达到最低值,在治疗后 9 个月和治疗后 12 个月开始回升。研究组患者的咬肌厚度在治疗后一直呈下降的趋势,并在治疗后 12 个月达到最低值。这说明两种注射 A 型肉毒毒素的方式均能在一定时间内降低咬肌厚度,但连续注射的方式能够更加持久的将咬肌厚度控制在较低的状态,治疗效果更加明显。分析其中原因,A 型肉毒毒素在经过非共价键与毒素结合后使后者在酸性环境中得到稳定,该复合物在进入血流

后分离,抑制周围运动神经末梢突触前膜乙酰胆碱释放,致使肌肉出现松弛性麻痹,进而导致肌肉萎缩,降低咬肌厚度,在视觉上形成“瘦脸”效果^[23-25]。由于A型肉毒毒素对神经肌肉接头传递的抑制作用不是永久的,随着时间推移会有新的神经末梢形成,称之周围性发芽,这种发芽始见于用药后一个月左右,而神经肌肉复合体的功能需要经历3个月左右才能恢复,因此注射A型肉毒毒素后咬肌厚度会逐渐恢复,通过连续性注射可以进一步抑制神经肌肉接头传递,致使咬肌厚度持续降低^[26,27]。同时本研究结果还显示,研究组患者本人的主观评价和专家评价的A、B、C均显著低于对照组,D、E均显著高于对照组,差异有统计学意义($P<0.05$),这说明无论是患者本人的主观评价还是专家的评价均认为连续性注射有更好的治疗效果,主要是因为连续性注射能更有效的降低咬肌厚度,防止复发,并且可以直接在患者的脸部形态上得到体现,因此连续性注射的评价会更高,这与相关研究结果一致^[28]。同时研究还发现,两组患者在治疗后出现的不良反应较少,且均无统计学意义($P>0.05$),这说明两种注射方式均有较好的安全性,虽然A型肉毒毒素具有一定的毒性作用,但在临床上使用的剂量较低,且注射前均排除有A型肉毒毒素禁忌的患者,因此可以有效减少治疗过程中的不良反应^[29,30]。

综上所述,连续注射A型肉毒毒素能更好的降低咬肌厚度,并且维持时间较长,患者对治疗效果的主观评价和专家的评价较好,且不良反应少,值得临床推广应用。

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