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· 论著 ·

嗅觉训练治疗嗅觉障碍的临床观察

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摘要: **目的** 初步探讨复杂香味进行嗅觉训练对外伤或上呼吸道感染引起的嗅觉障碍的疗效。**方法** 2016年12月~2018年3月于中国医科大学附属第一医院门诊收治的外伤及上呼吸道感染后嗅觉障碍患者36例, 其中男12例, 女24例; 年龄20~80岁, 平均年龄(47.61±16.68)岁, 病程3~60个月, 平均病程(13.58±13.51)个月。分别按病因分为上呼吸道感染组(19例)和外伤组(17例), 按嗅觉下降程度分为嗅觉下降组(18例)和嗅觉丧失组(18例)。均采用患者自行购买的4种味道明显不同的香水进行嗅觉训练, 治疗前后进行嗅觉综合VAS评分, 并分别对香味、臭味进行嗅觉评分。用Fisher确切概率法进行统计学分析。**结果** 所有患者均完成治疗方案, 总有效率为55.56%(20/36)。嗅觉下降组有效率77.78%(14/18), 嗅觉丧失组有效率33.33%(6/18), 经比较差异具有统计学意义($P < 0.05$)。上呼吸道感染后嗅觉障碍组有效率73.68%(14/19), 外伤后嗅觉障碍组有效率35.29%(6/17), 经比较差异具有统计学意义($P < 0.05$)。治疗有效患者中50.00%(10/20)对香味感知的恢复明显优于臭味, 经比较差异具有统计学意义($P < 0.05$)。**结论** 本研究所采用的嗅觉训练方案具有简便易行、灵活度高、患者负担轻、患者依从度高的特点, 对嗅觉障碍患者有一定的疗效, 其中对有残余嗅觉的患者疗效更显著, 上呼吸道感染引起的嗅觉障碍比外伤后的嗅觉障碍更易于恢复。另外, 嗅觉训练通常采用香味嗅剂, 因而有重要警示作用的臭味嗅觉恢复明显落后于香味, 应该受到重视。

关键词: 嗅觉训练; 嗅觉障碍

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The clinical observation of olfactory training in the treatment of olfactory disorders

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Abstract: **Objective** This study was to explore the effects of olfactory training via complex perfume patterns on patients with olfactory dysfunction due to head trauma or upper respiratory tract infection. **Methods** From December 2016 to March 2018, 36 patients with olfactory dysfunction due to head trauma or upper respiratory tract infection were treated in First Affiliated Hospital of China Medical University, including 12 males and 24 females, aged from 20 to 80 years, with an average age of 47.61 ± 16.68 years old; course of 3 months to 60 months, the mean course of 13.58 ± 13.51 months. The patients were divided into "upper respiratory tract infection group" (19 cases) and "trauma group" (17 cases) according to the etiology, and "olfactory decline group" (18 cases) and "olfactory loss group" (18 cases) according to the degree of olfactory decline. Four kinds of perfumes with obviously different flavors purchased by the patients themselves were used for olfactory training. Comprehensive olfactory VAS scores were evaluated before and after olfactory training, which was performed for all the patients. Olfactory comprehensive VAS score was performed before and after treatment, and olfactory score was performed for aroma and odor respectively. Fisher exact probability method was used for statistical analysis ($P = 0.05$). **Results** Thirty-six patients completed the whole regimen. The total effective rate was 55.56% (20/36) and the cure rate was 13.89% (5/36). The effective rate of the olfactory loss group was 33.33% (6/18); The

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effective rate of the olfactory decline group was 77.78% (14/18), and the difference was statistically significant ($P < 0.05$). The effective rate of the olfactory dysfunction group due to upper respiratory tract infection was 73.68% (14/19); the effective rate of the olfactory dysfunction group due to head trauma was 35.29% (6/17), and the difference was statistically significant between them ($P < 0.05$). Among the patients with effective treatment, 50.00% (10/20) was significantly superior to the recovery of odor perception, and the difference was statistically significant ($P < 0.05$).

Conclusions The therapeutic regime of the olfactory training adopted in this study is characterized by the simple and convenient operation, high flexibility, low cost on patients, and high compliance of patients. Certain therapeutic effects were observed for patients with residual smell and patients with upper respiratory tract infection induced olfactory dysfunctions. Scent is commonly used as an odorant in olfactory training. However, odor has an important warning effect and it deserves more attention that the odor recovery lags significantly behind the scent.

Key words: Olfactory training; Olfactory disorders

据统计,约有超过200多种疾病或120种物质可导致嗅觉障碍^[1],除了年龄相关性嗅觉减退外,临床最常见引起嗅觉障碍的原因为:头部外伤、上呼吸道感染、鼻-鼻窦疾病^[2],上述3种原因占临床嗅觉障碍的2/3^[3]。2009年Hummel等^[4]发现嗅觉训练可增加嗅觉敏感度,从而提出嗅觉训练可用于治疗嗅觉障碍,改善患者生存质量。嗅觉感觉神经元的可再生性表明某些干预措施可能会唤醒神经元或其前体细胞。嗅觉训练是通过频繁的吸嗅和/或暴露于强烈的气味来刺激或诱导嗅觉感觉神经通路的重建,起到改善嗅觉的作用^[5]。嗅觉训练还处在初始阶段,尚无统一干预标准,不同研究也得出不同的结论,如Poletti等^[6]认为高分子量嗅剂的效果较好,而Oleszkiewicz等^[7]则认为嗅剂的复杂性或使用的先后顺序对疗效没有影响。Pekala等^[5]的研究中不限制香味的浓度、品牌,以达到降低治疗成本、简化治疗过程的目的。本研究应用嗅觉训练治疗头部外伤和上呼吸道感染引起的嗅觉障碍,观察临床疗效,初步摸索简便易行、灵活度高、成本低、患者依从度高的嗅觉训练方案。

1 资料与方法

1.1 一般资料

选取2016年12月~2018年3月于我院耳鼻喉科门诊临床诊断为头部外伤或上呼吸道感染引起的嗅觉障碍患者36例,其中男12例,女24例;年龄20~80岁,平均(47.61±16.68)岁;病程3~60个月,平均病程(13.58±13.51)个月。按嗅觉下降的程度分为完全丧失察觉嗅素能力的嗅觉丧失组^[8](男6例,年龄35~69岁;女12例,年龄24~79岁)和察觉嗅素能力下降的嗅觉下降组^[8](男7例,年龄36~80岁;女11例,年龄23~79岁)。按病因分为

上呼吸道感染后嗅觉障碍组^[8](男4例,20~80岁;女15例,年龄31~79岁)和外伤后嗅觉障碍组(男8例,35~70岁;女9例,年龄23~71岁)。纳入标准:①有明确的嗅觉障碍病史;②耳鼻咽喉专科鼻镜检查或CT或MRI示双鼻腔及嗅裂通畅,影像学无明显嗅球、嗅束及嗅中枢病变;③无颅脑及鼻腔手术史;④未采用其他治疗手段。本研究经我院伦理学委员会审查通过,所有纳入患者均签订知情同意书。

1.2 方法

指导患者自行购买4种味道明显不同的香水,每种香水吸嗅20 s/次,相继闻过4种香水为一轮,休息5 min后再闻一轮,共30 min,每日早晚各一次^[9]。

1.3 疗效评定

于治疗前和治疗后12周进行嗅觉综合VAS评分^[10]。治疗后评分提高>1分为有效,治疗前后评分无差别或下降或提高<1分为无效。

1.4 统计学方法

应用SPSS 25.0进行统计学数据分析。计量资料以 $\bar{x} \pm s$ 表示,计数资料以率(%)表示。按 $\alpha = 0.05$ 水准, $P < 0.05$ 表示差异具有统计学意义。资料中 $n < 40$,选用四格表资料的Fisher确切概率法。另分布不知是否正态的小样本资料,应选用秩转换的非参数检验。

2 结果

36例完成治疗,嗅觉训练后总有效率为55.56% (20/36)。治疗前VAS评分为(1.64±2.24)分,治疗后(3.89±3.63)分,经配对样本比较的Wilcoxon符号秩检验后差异具有统计学意义($P < 0.05$)。

按照嗅觉损伤的程度分为有残余嗅觉的嗅觉下

降组(18例)和完全没有嗅觉的嗅觉丧失组(18例)。Fisher确切概率法两组结果差异具有统计学意义($P < 0.05$)。其中嗅觉下降组的治疗有效率为77.78%(14/18);嗅觉丧失组的有效率为33.33%(6/18),具体数据见表1。

按照病因不同将患者分为上呼吸道感染组(19例)和外伤组(17例)。Fisher确切概率法两组结果差异具有统计学意义($P < 0.05$)。其中上呼吸道感染组中73.68%(14/19)经嗅觉训练治疗有效;外伤组中有效率为35.29%(6/17),具体数据见表2。

嗅觉训练有效的20例患者中,50.00%(10/20)的香味嗅觉恢复好于臭味。分别以视觉量表法评估香味和臭味的嗅觉水平,发现治疗后香味嗅觉水平提高(4.05 ± 2.65)分,臭味嗅觉水平提高(2.70 ± 2.77)分,经配对样本比较的Wilcoxon符号秩检验后两组差异具有统计学意义($P < 0.05$)。

表1 嗅觉下降组与嗅觉丧失组嗅觉训练有效率的比较(例,%)

组别	有效	无效	合计	有效率
嗅觉下降组	14	4	18	77.78
嗅觉丧失组	6	12	18	33.33
合计	20	16	36	55.56

注:Fisher确切概率法, $P < 0.05$

表2 上呼吸道感染后与外伤后患者出现嗅觉障碍的有效率比较(例,%)

组别	有效	无效	合计	有效率
上呼吸道感染组	14	5	19	73.68
外伤组	6	11	17	35.29
合计	20	16	36	55.56

注:Fisher确切概率法, $P < 0.05$

3 讨论

嗅觉障碍的治疗目前并无统一的标准化方案。糖皮质激素是治疗嗅觉障碍较为常用药物,其作用机制尚不完全清楚^[11],可能通过减轻嗅黏膜的炎症反应,减少嗅感觉神经元的凋亡或减少对其再生的抑制,对炎症如慢性鼻窦炎、变应性鼻炎等引起的嗅觉障碍的治疗效果较好^[12]。此外维生素E和维生素C通过抗氧化起到保护细胞的作用,在治疗神经损伤相关的嗅觉障碍有辅助作用,硫辛酸起到抗自由基和保护组织的作用,在治疗上呼吸道感染性嗅觉障碍中有一定疗效^[13]。中医疗法针刺^[14],配合

穴位注射对外伤、病毒感染后引起的嗅觉障碍有一定的改善^[15]。

嗅觉训练是一种较新的疗法,Hummel等^[4]在2009年提出嗅觉训练可增加嗅觉敏感度,之后不同的国内外学者进行临床观察认为嗅觉训练对感染、外伤^[16]、慢性鼻窦炎^[17]等导致的嗅觉障碍有一定的改善,高浓度的嗅素^[18]、更长的训练时间^[19]、增加嗅素种类^[20]可以提高嗅觉训练的有效率。在临床实践过程中,现有的大部分嗅觉训练方案的可行性有待提高,传统嗅剂选择的局限性、低性价比、疗效评价体系的复杂性都制约着嗅觉训练的临床应用^[21]。

本研究选择的4种味道明显不同的香水为患者自行购买,在降低治疗成本和门槛的同时,尽量全面地覆盖不同香味刺激,为患者提供了可行性高的治疗方案。同时,在评价指标的选择上,我们采用了较简单的VAS评分,VAS评分对嗅剂的选择更灵活,操作也更简便,比较适合快速筛查,如果在后期结合T&T嗅剂计、Sniffin'sticks嗅觉测试、嗅觉功能核磁共振检查等其他主客观检测,在更严格的条件下采用多种评价方式,将会有助于摸索到更加可行、更加可靠的嗅觉训练方案。

在治疗过程中,我们发现患者对香味感知能力的恢复好于臭味,考虑嗅感觉神经元向主嗅球投射时遵循区对区投射原则,嗅觉信息传导至嗅上皮带,而后定位于嗅球中特定的突触球带^[22]。不同的气味作用下,气味受体有不同的激活形式。常用的嗅觉训练均使用香味剂,有利于提高患者的顺应性,但可能忽略了对臭味相关受体的刺激和训练。煤气、沼气或焦糊味等警示性气味对患者的安全至关重要,针对臭味的嗅觉训练可能需要受到更多关注,本研究组正在针对臭味的嗅觉训练进行进一步的研究。

本研究作为探索简便易行、患者依从度高、治疗效果良好、成本低的初步试验,还存在病例数偏少,患者病因分类不细致等不足,但是基于结果的可比性及较高的疗效,本研究将为进一步的深入探索提供依据,并为临床上开展通过嗅觉训练治疗嗅觉障碍提供从嗅剂选择到疗效筛查的新思路。

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