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等离子射频消融术治疗儿童腺样体肥大的疗效观察 及对患儿通气功能和炎症反应的影响*

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摘要 目的:探讨等离子射频消融术治疗儿童腺样体肥大的临床疗效及对患儿通气功能和炎症反应的影响。**方法:**选取我院 2016 年 12 月至 2017 年 8 月治疗的腺样体肥大患儿 100 例为研究对象, 其中 50 例手术治疗者为等离子组, 同期保守药物治疗者 50 例为对照组。对照组给予孟鲁司特钠、糠酸莫米松鼻喷雾剂治疗, 等离子组行低温等离子射频消融术。比较两组治疗前后症状积分、通气功能、炎症因子水平的变化。**结果:**治疗前, 两组症状积分、通气功能指标呼吸紊乱指数(apnea hypopnea index, AHI)、最长呼吸暂停时间(longest apnea time, LAT)、氧减指数(oxygen reduction index, ODI)、最低夜间血氧饱和度(lowest nocturnal oxygen saturation, LSaO₂)、血氧饱和度小于 90% 时间所占睡眠时间百分比 (percentage of time when oxygen saturation lower than 90%, SLT90 %)以及血清肿瘤坏死因子- α (inflammatory mediators of tumor necrosis factor, TNF- α)、白介素-4(interleukin, IL-4)、嗜酸性粒细胞阳离子蛋白(eosinophil cationic protein, ECP)水平比较差异均无统计学意义($P>0.05$)。治疗后, 两组打鼾、鼻塞、张口呼吸等症状积分与治疗前相比均显著降低($P<0.05$), 且等离子组打鼾、鼻塞、张口呼吸各项积分均显著低于对照组($P<0.05$)。治疗后, 两组 AHI、LAT、ODI、SLT90 %、血清 TNF- α 、ECP、IL-4 水平均较治疗前显著降低($P<0.05$), LSaO₂ 水平均较治疗前显著升高($P<0.05$), 且等离子组 AHI、LAT、ODI、SLT90 %、血清 TNF- α 、ECP、IL-4 水平均显著低于对照组, LSaO₂ 水平显著高于对照组($P<0.05$)。**结论:**低温等离子射频消融术可显著缓解儿童腺样体肥大患儿的临床症状, 改善机体通气功能, 减轻炎症反应。

关键词:等离子射频消融术; 儿童腺样体肥大; 疗效; 通气功能; 炎症反应

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Effect of Plasma Radiofrequency Ablation on the Adenoid Hypertrophy in Children and Its Influence on the Ventilation and Inflammatory Reaction*

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ABSTRACT Objective: To investigate the curative effect of plasma radiofrequency catheter ablation on adenoid hypertrophy in children and its effect on ventilatory function and inflammatory response. **Methods:** 100 cases of adenoid hypertrophy in our hospital from December 2016 to August 2017 were selected, 50 cases patients treated with surgical treatment was in plasma group, and 50 patients treated with conservative treatment were in control group in the same period. The control group was given montelukast and Mometasone furoate nasal spray, and the plasma group was given low temperature plasma radiofrequency ablation. The symptom score, ventilation function and inflammatory cytokines levels in two groups before and after treatment were compared. **Results:** Before treatment, symptom score, apnea hypopnea index (AHI), longest apnea time (LAT), oxygen reduction index (ODI), minimum nocturnal oximetry Lowest nocturnal oxygen saturation (LSaO₂), percentage of time when oxygen saturation less than 90% (SLT 90%), and serum inflammatory mediators (TNF- α), interleukin-4 (IL-4) and eosinophil cationic protein (ECP) levels were not significantly different between the two groups ($P>0.05$). After treatment, the scores of snoring, nasal obstruction and mouth breathing were significantly decreased in both groups ($P<0.05$), and the scores of snoring, nasal obstruction and mouth breathing in plasma group were significantly lower than those in control group ($P<0.05$). After treatment, the levels of AHI, LAT, ODI and SLT90 % in both groups were significantly decreased ($P<0.05$), and the LSaO₂ level was significantly increased ($P<0.05$). After treatment, the levels of AHI, LAT, ODI, SLT90 % in the plasma group were significantly lower than those in the control group ($P<0.05$), and the LSaO₂ level was significantly higher than the control group ($P<0.05$). **Conclusion:** Low-temperature plasma radiofrequency ablation can significantly relieve the clinical symptoms of children, improve the body's ventilatory function and reduce the inflammatory response.

Key words: Plasma radiofrequency ablation; Adenoid hypertrophy in children; Curative effect; Ventilatory function; Inflammatory reaction

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前言

腺样体是咽淋巴环的重要组成部分之一, 又称咽扁桃体, 在出生后会随着年龄增长而增大。腺样体自身炎症或者鼻咽部及邻近部位发生炎症均可引起腺样体免疫功能异常, 若经反复刺激还可导致腺样体病理性增生, 出现张口呼吸、夜间打鼾等症状, 严重影响睡眠, 甚至造成阻塞性睡眠呼吸暂停低通气综合征^[1-3]。

在正常情况下, 6-7 岁时腺样体发育增长到最大, 至青春后期逐渐萎缩, 到成人阶段则基本消失^[4]。儿童腺样体肥大大多由炎症反复刺激出现持续性病理性增生肥大而引起; 炎症递质释放增高、血管通透性加强导致局部组织肿胀, 引起血清中炎症介质水平的改变, 造成患儿呼吸道堵塞, 出现暂停及夜间睡眠缺氧症状, 若患儿夜间睡眠过程中长期缺氧, 则会影响到正常呼吸通气和睡眠结构, 不利于儿童生长发育^[5-7]。

内窥镜辅助下低温等离子射频消融术是微创手术方式, 切割精准, 对邻近正常组织损伤小, 可显著降低手术对机体造成的炎症伤害^[8]。本研究观察等离子射频消融术治疗儿童腺样体肥大的疗效及对患儿通气功能、炎症反应的影响, 现将结果报道如下。

1 资料与方法

1.1 一般资料

以我院 2016 年 12 月至 2017 年 8 月治疗的腺样体肥大患儿 100 例为研究对象, 其中 50 例手术治疗者为等离子组, 同期保守药物治疗者 50 例为对照组。等离子组: 男 28 例, 女 22 例, 年龄 4-11 岁, 平均年龄 (8.1 ± 2.4) 岁; 病程 3 个月 -1.3 年。对照组: 男 26 例, 女 24 例, 年龄 5-12 岁, 平均年龄 (7.8 ± 2.2) 岁; 病程 5 个月 -1.2 年。两组患儿一般资料比较差异不显著 $(P>0.05)$, 具有可比性。本研究经本院医学伦理委员会批准通过, 获取患儿家属知情同意且签署同意书。

纳入标准: ①符合《诸福棠实用儿科学》^[9]中小儿腺样体肥大的诊断标准; ②患儿接受本研究治疗前未接受其他相关治疗。排除标准: ①伴有先天遗传性疾病; ②伴有支气管肺炎、支气管炎、扁桃体肥大、扁桃体炎等其他呼吸道疾病; ③对本研究所用药物有过敏反应。

1.2 治疗方法

1.2.1 对照组实施药物治疗 给予糠酸莫米松鼻喷雾剂(商品名: 内舒拿, 进口药品注册证号: H20140100, 50 μ g/ 揿)于清洗鼻腔后喷至患儿两侧鼻腔, 每次 1 喷, 每日 1 次。同时, 给予孟鲁司特(默沙东, H20120366, 规格 4 mg/ 片)口服治疗, 6 岁以下患儿每晚 4 mg, 6 岁以上患儿每晚 5 mg。治疗 3 个月。

1.2.2 等离子组实施鼻内窥镜下低温等离子射频消融术治疗 以 Evac70° 刀头行鼻内镜下腺样体切除术, 使用等离子刀止血, 以细软导尿管穿入鼻腔至口腔拉出, 软腭稍系紧并暴露鼻咽部, 在口腔置入 70° 鼻窦内窥镜, 在内窥镜下用 Evac70° 刀头对肥大腺样体进行逐步消融。在消融过程中保持同步止血,

术中尽量不接触正常组织, 检查确认腺样体切除干净并无出血后, 手术完毕。

1.3 检测指标及方法

1.3.1 症状积分 分别于治疗前后对两组患儿打鼾、鼻塞以及张口呼吸进行记分: 无症状记为 0 分, 发作间歇记为 1 分, 发作频繁记为 2 分, 症状持续记为 3 分。

1.3.2 通气功能指标检测 分别于治疗前后, 采用多导睡眠图对两组患儿通气功能指标呼吸紊乱指数(AHI)、最长呼吸暂停时间(LAT)、氧减指数(ODI)、最低夜间血氧饱和度(LSaO₂)、血氧饱和度小于 90% 时间所占睡眠时间百分比(SLT90 %)进行监测, 多导睡眠仪型号为 PSG 多导睡眠监测仪, 购自广州一尚医疗器械有限公司。

1.3.3 炎症因子检测 分别于治疗前后清晨采集两组患儿空腹静脉血 10 mL, 以 3000 r/min 离心 10 min 后取上清液备测。采用酶联免疫吸附法(ELISA)检测血清炎症介质肿瘤坏死因子- α (TNF- α)、白介素-4(IL-4)水平, 试剂盒购自上海哈灵生物公司, 批号 20150605, 20170510。采用 Pharmacia CAP System ECP FEIA 荧光酶标法检测血清中嗜酸性粒细胞阳离子蛋白(ECP)水平。

1.4 统计学处理

本研究中, 两组患儿症状积分、通气功能指标 AHI、LAT、ODI、LSaO₂、SLT90% 水平以及炎症因子 TNF- α 、ECP、IL-4 水平均服从正态分布, 以 $(\bar{x} \pm s)$ 表示, 治疗前后组内比较、治疗后组间比较采用 t 检验。数据分析工具采用统计学软件 SPSS18.0, 以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患儿治疗前后症状积分的比较

治疗前, 两组症状积分比较差异无统计学意义 $(P>0.05)$ 。治疗后, 两组打鼾、鼻塞、张口呼吸等症状积分与治疗前相比均显著降低 $(P<0.05)$, 且等离子组打鼾积分 (1.44 ± 0.43) 、鼻塞积分 (1.34 ± 0.31) 、张口呼吸积分 (1.33 ± 0.37) 均显著低于对照组, 差异有统计学意义 $(P<0.05)$ 。见表 1。

2.2 两组患儿治疗前后通气功能的比较

治疗前, 两组 AHI、LAT、ODI、LSaO₂、SLT90 % 水平比较差异无统计学意义 $(P>0.05)$ 。治疗后, 两组 AHI、LAT、ODI、SLT90 % 水平均显著降低 $(P<0.05)$, LSAO₂ 水平均显著升高 $(P<0.05)$, 等离子组 AHI、LAT、ODI、SLT90 % 水平均显著低于对照组, LSAO₂ 水平显著高于对照组, 差异有统计学意义 $(P<0.05)$ 。见表 2。

2.3 两组患儿治疗前后血清炎症因子水平的比较

治疗前, 两组血清 TNF- α 、ECP、IL-4 水平比较差异无统计学意义 $(P>0.05)$ 。治疗后, 两组血清 TNF- α 、ECP、IL-4 水平与治疗前相比均显著降低 $(P<0.05)$, 且等离子组血清 TNF- α 水平 (0.94 ± 0.11) ng/mL、ECP 水平 (2.82 ± 0.31) μ g/L、IL-4 水平 (204.02 ± 15.36) ng/L 均显著低于对照组, 差异有统计学意义 $(P<0.05)$ 。见表 3。

表 1 两组患儿治疗前后症状积分比较(n=50, $\bar{x} \pm s$)

Table 1 Comparison of the symptom scores between two groups before and after treatment(n=50, $\bar{x} \pm s$)

Groups	Time	Snoring (points)	Nasal obstruction (points)	Mouth breathing (points)
Plasma group	Before treatment	2.62± 0.33	2.55± 0.62	2.44± 0.44
	After treatment	1.44± 0.43* [#]	1.34± 0.31* [#]	1.33± 0.37* [#]
Control group	Before treatment	2.61± 0.34	2.62± 0.71	2.42± 0.52
	After treatment	2.27± 0.48*	2.07± 0.35*	1.84± 0.57*

注:与本组治疗前相比, * $P<0.05$;与对照组同时时间相比, [#] $P<0.05$ 。

Note: Compared with pretreatment, * $P<0.05$; compared with the control group at the same time, [#] $P<0.05$.

表 2 两组患儿治疗前后通气功能水平的比较(n=50, $\bar{x} \pm s$)

Table 2 Comparison of the ventilation function between two groups before and after treatment(n=50, $\bar{x} \pm s$)

Groups	Time	AHI (h)	LAT(s)	ODI(h)	LSaO ₂ (s)	SLT90 %(%)
Plasma group	Before treatment	32.01± 8.84	45.75± 7.32	26.93± 7.31	71.35± 9.82	23.54± 5.04
	After treatment	9.97± 4.28* [#]	17.91± 4.11* [#]	7.83± 4.29* [#]	87.44± 10.31* [#]	10.83± 2.37* [#]
Control group	Before treatment	34.14± 9.01	44.62± 6.88	27.32± 8.39	70.82± 10.02	24.02± 6.12
	After treatment	14.81± 5.24*	24.83± 3.95*	14.62± 5.82*	78.97± 9.65*	16.24± 4.57*

注:与本组治疗前相比, * $P<0.05$;与对照组同时时间相比, [#] $P<0.05$ 。

Note: Compared with pretreatment, * $P<0.05$; compared with the control group at the same time, [#] $P<0.05$.

表 3 两组患儿治疗前后血清炎症因子水平的比较(n=50, $\bar{x} \pm s$)

Table 3 Comparison of the serum inflammatory factors levels between two groups before and after treatment(n=50, $\bar{x} \pm s$)

Groups	Time	TNF- α (ng/mL)	ECP(μ g/L)	IL-4(ng/L)
Plasma group	Before treatment	1.95± 0.21	5.28± 0.51	264.61± 18.57
	After treatment	0.94± 0.11* [#]	2.82± 0.31* [#]	204.02± 15.36* [#]
Control group	Before treatment	1.93± 0.24	5.32± 0.48	261.67± 18.49
	After treatment	1.34± 0.15*	3.20± 0.27*	240.93± 15.02*

注:与本组治疗前相比, * $P<0.05$;与对照组同时时间相比, [#] $P<0.05$ 。

Note: Compared with pretreatment, * $P<0.05$; compared with the control group at the same time, [#] $P<0.05$.

3 讨论

腺样体是人体淋巴组织,位于鼻咽部顶部和咽后壁之间,又称咽扁桃体,可产生 T 淋巴细胞、B 淋巴细胞,同腭扁桃体、舌扁桃体共同构成人体最前沿免疫防线,是阻挡致病菌的第一道防线,可生成多种免疫活性物质。腺样体部位较深,无纤维组织包膜,可防御咽部感染,通常最先接触各种损伤要素,如冷空气刺激、呼吸道病毒、空气污染等,在机体免疫功能降低、鼻咽部及其邻近部位发生炎症反应并反复刺激腺样体时,可导致其病理性肥大,且有时能与扁桃体肥大同时发生^[10,11]。腺样体异常肥大能对咽鼓管口、鼻孔造成压迫、堵塞,导致呼吸障碍^[12]。腺样体在婴儿出生后便开始发育,随着年龄增大而生长变大,在 2-6 岁时增殖旺盛,6-7 岁长至最大,10 岁后逐渐萎缩变小。研究表明腺样体肥大发病机制与腺样体局部免疫功能失调、炎性介质反复释放刺激腺样体导致其病理性增生有关^[13]。感冒、鼻炎、慢性扁桃体炎等疾病的反复炎症刺激导致腺样体病理性增生,引发儿童鼻塞、张口呼吸、打鼾等症状,阻碍肺通气功能,造成患儿被迫性张口呼吸、打鼾,严重时甚至出现呼吸暂停或呼吸困难,对患儿身体与智力发育产生极大影响^[14]。

目前,腺样体异常肥大的临床治疗以手术切除为主,传统手术虽可迅速缓解腺样体肥大重症患儿打鼾、鼻塞、张口呼吸等症状,但对肥大腺体不能彻底清除,术后仍不能保证鼻腔完全通畅,需进行再次手术,且传统术式复发率、相关并发症发生率较高。另一方面,许多轻症患儿并无手术指征^[15,16]。临床药物治疗包括白三烯受体拮抗剂、鼻喷激素等,其中鼻喷激素有丙酸氟替卡松、糠酸莫米松等对机体局部炎症反应、变态反应有较好的抑制作用,可调节炎症细胞因子水平,促进抗炎蛋白合成,缓解鼻腔内黏膜充血,达到缩小腺样体体积的目的^[17-19]。常用白三烯受体拮抗剂孟鲁司特可阻断病因诱导白三烯途径,降低炎症反应,减轻气道高反应性,从而缓解患儿鼻塞症状,改善肺通气功能、上呼吸道通气功能^[20,21]。近年来,鼻内窥镜技术发展进步为腺样体肥大手术提供了有效辅助手段,鼻内窥镜可实现在多角度直视条件下进行手术,视野清晰、不留死角,手术程序简化,可有效避免对周边正常组织的损伤,明显降低术后并发症的发生率^[22]。低温等离子消融术是近年发展的微创手术,通过低温等离子打开分子键,使手术目标局部组织发生融解而达到切除目的,等离子体温度设为 40℃-70℃,可控制手术过程中对周围正常组织热损伤,同时在鼻内窥镜辅助下操作,切

割精准度较高,有损伤范围小、手术温度低、术中止血效果好等优点^[23]。

本研究结果显示两组治疗后打鼾、鼻塞、张口呼吸等症状积分与治疗前相比均显著降低,且等离子组打鼾、鼻塞、张口呼吸各项积分均显著低于对照组,表明鼻内窥镜辅助低温等离子射频消融术可显著改善腺样体肥大患儿临床症状,比药物治疗疗效更显著。这可能是因为手术切除腺样体后,气道障碍物清除彻底,相比药物治疗的患儿气道更加通畅,因此对于通气不足所引起打鼾、鼻塞、张口呼吸等症状,可以在气道恢复正常功能后得到减轻或消除。此外,两组治疗后 AHI、LAT、ODI、SLT90%水平均显著降低,LSaO₂ 水平均显著升高,等离子组治疗后 AHI、LAT、ODI、SLT90 %水平均显著低于对照组,LSaO₂ 水平显著高于对照组,表明鼻内窥镜辅助低温等离子射频消融术对患儿通气功能的改善更加显著,原因可能是在排除腺样体肥大引起的病理反应后,术后气道功能得到纠正、呼吸暂停时间缩短,且呼吸节律得到有效调节,因此通气功能得到明显改善。

炎症因子是导致机体炎症应激反应的重要因素,临床上炎症介质 TNF- α 、ECP、IL-4 均具有较高敏感度^[24,25]。TNF- α 有多种生物学活性,在细胞免疫中起到重要作用,可刺激辅助性 T 淋巴细胞参与细胞免疫,在 Th1 细胞与 Th2 细胞的平衡过程中、特异性免疫反应中起到关键作用。机体在缺氧状态下, TNF- α 水平增高,腺样体肥大导致机体气道堵塞,引发组织缺氧,从而促进细胞释放大量的 TNF- α ,导致 TNF- α 水平异常升高^[26]。ECP 由嗜酸粒细胞分泌,机体发生过敏反应时,激活嗜酸粒细胞释放,是一种毒性蛋白,可造成机体病理性损害^[27]。研究显示^[28,29]ECP 在气道炎症中起到基础作用,可引起气道上皮细胞脱落,损伤气道上皮,导致机体启动气道自我修复机制,而在组织修复过程中胶原沉积易诱发气道重塑,因此造成气道功能改变,产生病理症状。IL-4 由 Th2 细胞分泌,对机体细胞免疫和体液免疫均有联系作用,可促进 T 细胞、B 细胞增殖参与体液免疫,是促炎症细胞因子^[30,31]。本研究中,两组治疗后血清 TNF- α 、ECP、IL-4 水平与治疗前相比均显著降低,且等离子组 TNF- α 水平、ECP 水平、IL-4 水平均显著低于对照组相应水平,表明腺样体肥大患儿经鼻内窥镜辅助低温等离子射频消融术治疗后,炎症反应显著降低,其原因考虑为腺样体病理性肥大时,患儿炎症反应水平高,因此血清中 TNF- α 、ECP、IL-4 处于高水平状态,治疗后机体气道恢复正常,缓解炎症刺激,因此炎症因子水平显著降低。

综上所述,鼻内窥镜下低温等离子射频消融术可显著缓解患儿临床症状,改善机体通气功能,减轻炎症反应,其远期疗效有待于扩大样本展开进一步研究。

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(上接第 3079 页)

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