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## 关节灌洗术联合透明质酸钠注射治疗颞下颌关节骨关节炎的疗效观察\*

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**摘要 目的:**评价关节腔灌洗联合透明质酸钠注射治疗颞下颌关节骨关节炎(TMJOA)的疗效及安全性。**方法:**选取我院 2014 年 5 月-2015 年 5 月收治颞下颌关节骨关节炎患者 68 例作为研究对象,根据入院时间先后顺序按照随机数字表法随机分为实验组和对照组各 34 例。所有患者在颞颌关节区域局麻下建立关节上腔的双通道灌洗系统,实验组用生理盐水反复冲洗关节腔后注射透明质酸钠,对照组只进行关节腔灌洗术,术后随访对比两组治疗前、治疗后 4 周、6 个月时患者非辅助最大开口度、侧向运动幅度、咀嚼时疼痛感;同时采用酶联免疫吸附法(ELISA)测定两组治疗前、治疗后 4 周血清中白细胞介素 6(IL-6)和肿瘤坏死因子  $\alpha$  (TNF- $\alpha$ )水平并进行比较。**结果:**实验组患者治疗后 4 周、治疗后 6 个月时颞下颌关节最大张口度和侧向活动距离明显增大,而咀嚼时疼痛感明显减轻,且优于同期对照组,差异具有统计学意义( $P<0.05$ );实验组患者治疗后 4 周时血清 IL-6、TNF- $\alpha$  水平较术前及同时期对照组均明显降低,差异具有统计学意义( $P<0.05$ )。**结论:**关节灌洗术联合透明质酸钠注射是治疗颞下颌关节骨关节炎的简单、安全有效治疗方法,治疗效果明显优于单纯关节腔灌洗,值得临床推广应用。

**关键词:**颞下颌关节骨关节炎;关节灌洗术;透明质酸钠;炎症

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## Effect of Sodium Hyaluronate Injection and Arthrocentesis for Patients with Temporomandibular Joint Osteoarthritis\*

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**ABSTRACT Objective:** To evaluate the effect of sodium hyaluronate injection and arthrocentesis for patients with temporomandibular joint osteoarthritis. **Methods:** 68 patients hospitalized with temporomandibular joint osteoarthritis from May 2014 to May 2015 were selected, and randomly divided into two groups with 34 cases in each. Observation group received underwent joint lavage combined with intra-articular injection of sodium hyaluronate by dual-channel irrigation system, but the patients only with joint lavage in control group. Compared the non-assisted maximum opening degree of mouth, degree of lateral movement and values of pain during chewing were measured at the baseline of two groups before treatment, 4 weeks and 6 months after treatment. The serum interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels of two groups were determined by enzyme-linked immunosorbent assay (ELISA) before treatment, 4 weeks and 6 months after treatment. **Results:** In observation group, the non-assisted maximum opening degree of mouth, degree of lateral movement were significantly increased and the value of pain was significantly reduced 4 weeks and 6 months after treatment, and better than the same period of the control group, the difference was statistically significant ( $P<0.05$ ). Compared with the preoperative and control group, postoperative levels of serum IL-6, TNF- $\alpha$  in observation group were reduced with significantly difference ( $P<0.05$ ). **Conclusion:** Arthrocentesis combined with intra-articular injection of sodium hyaluronate is a simple, effective means for temporomandibular joint osteoarthritis. Its therapeutic effect is superior to the simple joint cavity lavage, which is worthy of clinical application.

**Key words:** Temporomandibular joint osteoarthritis; Arthrocentesis; Sodium hyaluronate; Inflammation

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### 前言

骨关节炎(Osteoarthritis, OA)是累及膝关节和颞下颌关节

(Temporomandibular joint, TMJ)在内的所有滑膜关节的一种慢性退行性病变。颞下颌关节骨关节炎(Temporomandibular joint osteoarthritis, TMJOA)是口腔颌面部颞下颌关节紊乱疾病中最

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常见,最严重的疾病之一<sup>[1]</sup>,临床表现为严重的颞下颌关节疼痛、张口受限或出现张口绞锁,已严重危害患者的生活质量。临床上常采用关节灌洗治疗 TMJOA,虽然短期起到一定效果,但随着时间的延长,治疗效果不够理想<sup>[2]</sup>。透明质酸钠(sodium hyaluronate)是正常关节滑液的重要组分,对关节起到润滑、营养和保护的作用,临床上关节镜清理术联合注射透明质酸钠已广泛应用于膝关节骨性关节炎的治疗,取得了良好的治疗效果<sup>[3]</sup>。为此,本研究应用关节灌洗联合注射透明质酸钠治疗有张口受限、关节绞锁或急性疼痛的 TMJOA 患者,经过 6 个月的随访,观察并评定其治疗效果。

## 1 资料与方法

### 1.1 临床资料

选取 2014 年 5 月-2015 年 5 月于我院就诊的 TMJOA 患者 68 例作为研究对象。纳入标准:符合 TMJOA 诊断标准<sup>[4]</sup>:关节区压痛,自主被动活动时关节疼痛,关节活动功能障碍(张口受限为主)、开闭口运动出现摩擦音、摩擦感等;颞下颌关节 MRI 检查证实关节为退行性病变表现;经保守治疗(热敷、理疗和牙合板等治疗)3 周以上,临床症状改善不佳者;参加本研究的患者,圆满完成 12 个月随访。排除标准:排除颞下颌关节外伤、肿瘤等器质性病变;排除关节感染,风湿、痛风等炎性病变。根据入院时间先后顺序按照随机数字表法将 68 例患者随机分为 2 组,各 34 例,即实验组男 16 例、女 18 例,年龄 39~71 岁,平均年龄(53.7±12.5)岁,病程 1.5 个月~48 个月,平均(7.5±1.5)个月。对照组男 17 例、女 17 例,年龄 41~73 岁,平均年龄(54.2±11.5)岁,病程 1.3 个月~43 个月,平均(7.2±2.0)个月。两组患者性别、年龄、病程差异无统计学意义( $P>0.05$ )。所有患者均签署治疗知情同意书,研究获得医院伦理委员会批准。

### 1.2 治疗方法

患者首先建立关节腔双通道灌洗系统,手术时患者取平卧位,头偏向健侧,嘱患者张口位,确定耳屏前髁状突外上方及耳屏切迹至外毗连线上耳屏前 1 cm 凹陷处两个穿刺点,分别作为颞下颌关节灌洗液的入口和出口。常规手术区皮肤消毒及局部浸润麻醉后,用两个 5 号注射针头分别于定位点缓慢穿入,当感觉有落空感或针孔有液体流出时代表已进入关节腔内。实验组患者利用 250 mL 生理盐水反复冲洗关节腔,可见有少量白色的絮状物冲出,灌洗结束后拔出出口针头,通过入口针

头缓慢注入 1.5 mL 透明质酸钠(别名施沛特,山东博士伦福瑞达制药有限公司生产,国药准字:H10960136),拔出入口针头,压迫数分钟后,再次消毒无菌敷料覆盖术口,然后嘱患者行开闭口运动及侧向运动,使透明质酸钠可均匀分布于关节腔内,每周 1 次,连续治疗 4 周。对照组患者只行颞下颌关节双通道灌洗术,具体操作同实验组,每周 1 次,连续治疗 4 周。所有患者术后嘱禁食坚硬及过于酸辣的食物,纠正不良习惯,避免开口过大、外力撞击等急性创伤。

### 1.3 观察指标

于治疗前、治疗后 4 周、治疗后 6 个月记录两组患者非辅助最大开口度、侧向运动幅度、咀嚼时疼痛感,分别与术前及两组同随访期指标之间进行比较。①非辅助最大开口度:利用游标卡尺测量患者在非辅助状态下最大开口时上下颌中切牙间距离( $\geq 35$  mm 为正常)<sup>[5]</sup>。②侧向运动幅度:侧向运动时上下颌中线间的最大距离( $\geq 6$  mm 为正常)<sup>[5]</sup>。③咀嚼时疼痛感:采用视觉模拟标尺法(visual analog scale, VAS)进行评价,即在医生指导下由患者在 0-10 cm 的标尺上主观评价疼痛程度,0 定义为“完全无痛”,10 cm 为“一生最强烈的疼痛”,由患者自我确定其疼痛程度在标尺上的相应位置,记录 VAS 疼痛评分<sup>[6]</sup>。于治疗前及治疗后 4 周监测血清中白细胞介素 6(IL-6)和肿瘤坏死因子  $\alpha$ (TNF- $\alpha$ )水平,分别与术前和两组间进行比较。所有患者于治疗前及治疗后 4 周时抽取清晨空腹静脉血 5 mL,置于不抗凝管内,自然沉淀 30 min 后,离心 10 min(3000 r/min),收集血清标本,立即保存低温冰箱中,待检。采取酶联免疫吸附法(ELISA)测定,试剂盒、酶标仪均由上海酶联生物科技有限公司提供,具体操作严格按照试剂厂家提供的说明书进行。

### 1.4 统计学方法

结果数据采用 SPSS19.0 软件包进行处理,研究结果为计量资料以均数±标准差( $\bar{x}\pm s$ )表示,采用 t 检验进行组间比较,以  $P<0.05$  为差异有统计学意义。

## 2 结果

### 2.1 两组临床指标比较

治疗前比较两组患者的非辅助最大开口度、侧向运动幅度、咀嚼时疼痛值的差异均无统计学意义( $P>0.05$ ),实验组患者在治疗后 4 周、治疗后 6 个月时颞下颌关节最大张口度、侧向活动距离较术前明显增大,咀嚼时疼痛感较治疗前明显减轻,同时各指标值均优于同期对照组( $P<0.05$ ),见表 1。

表 1 两组临床指标比

Table 1 Comparison of clinical indicators

| Groups            |                          | Degree of maximum mouth opening(mm) | Degree of lateral movement(mm) | VAS(points)              |
|-------------------|--------------------------|-------------------------------------|--------------------------------|--------------------------|
| Observation group | Before treatment         | 26.70± 3.40                         | 4.50± 0.60                     | 7.02± 1.22               |
|                   | 4w after treatment       | 33.40± 2.70* <sup>#</sup>           | 7.30± 0.90* <sup>#</sup>       | 1.33± 1.00* <sup>#</sup> |
|                   | 6 months after treatment | 37.00± 2.20* <sup>#</sup>           | 8.90± 0.70* <sup>#</sup>       | 1.02± 0.59* <sup>#</sup> |
| Control group     | Before treatment         | 26.33± 3.71                         | 4.61± 0.52                     | 7.11± 1.19               |
|                   | 4w after treatment       | 30.22± 3.87*                        | 5.56± 0.39*                    | 6.22± 0.67*              |
|                   | 6 months after treatment | 32.12± 2.91*                        | 5.89± 0.42*                    | 5.35± 0.79*              |

Note: Compared with before treatment, \* $P<0.05$ , compared with control group, \*\* $P<0.05$ .

## 2.2 两组治疗前后血清 IL-6、TNF- $\alpha$ 水平比较

治疗前比较两组患者的血清 IL-6、TNF- $\alpha$  水平差异无统计学意义( $P>0.05$ ),实验组患者在治疗后 4 周时血清 IL-6、TNF- $\alpha$

水平较治疗前明显降低,同时炎症改善程度优于同期对照组( $P<0.05$ ),见表 2。

表 2 治疗前后血清 IL-6、TNF- $\alpha$  水平的比较

Table 2 Comparison of the levels of IL-6 and TNF- $\alpha$  before and after treatment

| Groups            | Time               | IL-6( pg/mL )       | TNF- $\alpha$ ( mg/mL ) |
|-------------------|--------------------|---------------------|-------------------------|
| Observation group | Before treatment   | 167.25 $\pm$ 4.19   | 18.14 $\pm$ 1.00        |
|                   | 4w after treatment | 127.25 $\pm$ 8.69** | 9.14 $\pm$ 0.76**       |
| Control group     | Before treatment   | 160.88 $\pm$ 7.35   | 18.14 $\pm$ 1.00        |
|                   | 4w after treatment | 141.25 $\pm$ 6.29*  | 12.14 $\pm$ 0.19*       |

Note: Compared with before treatment, \* $P<0.05$ . compared with control group, \*\* $P<0.05$ .

## 3 讨论

TMJOA 是口腔颌面部所有关节中最常见的退变性疾病,病理表现以关节软骨变性损伤,滑膜增生、以及出现关节软骨下硬化囊性变,关节液变性等<sup>[7]</sup>。临床上部分患者还会出现颞下颌关节盘半脱位,表现关节区疼痛,关节绞索,主动张口活动严重受限,给患者带来巨大痛苦。传统保守治疗如康复锻炼,理疗,口服药物等在缓解疼痛和炎症,改善关节功能方面效果不甚明显。临床上采用的关节介入治疗手段(如关节灌洗术),取得了良好的治疗效果<sup>[8]</sup>。但是,相关研究也表明,单纯行关节腔灌洗可能导致关节液大量丢失,引起关节内透明质酸缺失,反而刺激性的引起滑膜和软骨炎性渗出物明显增加,进一步导致滑膜炎性增生、软骨退变和周围软组织反应性水肿<sup>[9]</sup>。本研究中我们尝试进行颞下颌关节灌洗后向关节腔内注射透明质酸钠,快速构建类似于生理性关节液的内环境稳态,润滑和保护滑膜和关节软骨面,治疗效果明显优于单纯关节腔灌洗<sup>[10]</sup>。

本研究结果发现,我们建立关节腔双通道系统反复冲洗关节腔后,无论在实验组还是对照组患者在治疗后 4 周、治疗后 6 个月时颞下颌关节最大张口度、侧向活动距离和咀嚼时疼痛感较治疗前均有明显改善,同时患者治疗 4 周后血清 IL-6、TNF- $\alpha$  水平较治疗前也有所降低。与国外 Rahal A<sup>[11]</sup>等试验研究结果大体一致,提示双通道反复冲洗关节腔治疗 TMJOA 效果值得肯定。我们分析其原因认为:反复生理盐水冲洗颞下颌关节腔,一方面可消除滑液中的代谢副产物,研究发现,退行性骨关节炎的关节液发生变性,各种炎性细胞(如粒细胞及巨噬细胞)、炎性因子(如肿瘤坏死因子、前列腺素 E、白三烯 B4、IL-1、IL-6 等)、变性的关节软骨的撕脱碎片、血凝块等明显增多,冲洗清除代谢废物尤其清除大量的炎性因子,可减轻其对关节的炎性刺激,缓解疼痛和滑膜增生<sup>[12-14]</sup>。另一方面,关节腔内的快速流动的灌洗液,改善关节腔内压及关节液的黏稠度,可使关节内的纤维粘连得到充分松解,从而消除或减轻疼痛,改善颞下颌运动功能<sup>[15,16]</sup>。

研究结果显示,实验组患者随访期内颞下颌关节最大张口度、侧向活动距离和咀嚼时疼痛感的改善程度明显优于单纯关节腔灌洗。这提示透明质酸钠在治疗 TMJOA 时发挥重要作用。分析原因,正常的滑膜关节液中存在较高浓度的透明质酸钠,其由滑膜 B 细胞分泌,分布到软骨和韧带表面,可渗透到软

骨层,主要起到营养软骨、润滑关节以及保持滑液和软骨的黏弹性的作用<sup>[17]</sup>,而多项研究得出颞下颌关节骨关节炎患者的关节液中透明质酸钠浓度、相对分子量以及弹性度均明显低于正常水平<sup>[18]</sup>。另外临床研究表明,关节腔内注射透明质酸钠在治疗膝关节骨性关节炎方面已取得良好的治疗效果,明显减轻关节疼痛,改善关节活动度。本研究应用透明质酸钠注射治疗颞下颌关节炎,可以快速补充内源性透明质酸钠的不足,改善关节液内环境稳态,同时透明质酸钠黏附于灌洗后关节软骨表面,形成保护层润滑关节,营养关节盘,改善颞下颌关节活动,消除关节弹响、摩擦感,并且透明质酸钠是关节滑液的主要成分之一,无抗原性,无趋化作用,安全有效<sup>[19]</sup>。

此外,本文研究结果发现,实验组患者在治疗后 4 周时血清 IL-6、TNF- $\alpha$  水平较治疗前明显降低,同时炎症改善程度优于同随访期对照组。我们分析认为,关节腔反复冲洗后立即注射透明质酸钠改善了关节内环境,抑制关节腔内炎症介质形成,减轻对滑膜的炎性刺激,减少炎性渗出及增生,明显减轻关节肿胀,而且可中和血浆金属蛋白酶,减轻其对软骨的破坏和阻止蛋白多糖的丧失<sup>[20]</sup>。总之,透明质酸钠缓解、阻断了关节退行性病变的恶性循环趋势,在颞下颌关节炎治疗中取得了良好而稳定的治疗效果。

综上所述,关节灌洗术联合注射透明质酸钠是治疗颞下颌关节骨关节炎的简单、安全有效治疗方法,可以明显缓解症状,有效改善关节活动功能,提高患者生活质量,治疗效果明显优于单纯关节腔灌洗,值得临床推广应用。

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