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滑膜炎颗粒联合玻璃酸钠治疗创伤性膝关节滑膜炎的疗效 及对患者血清炎症因子水平的影响 *

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摘要 目的:探讨滑膜炎颗粒联合玻璃酸钠治疗创伤性膝关节滑膜炎的疗效及对患者血清炎症因子水平的影响。**方法:**选取 2015 年 2 月~2017 年 12 月期间我院收治的创伤性膝关节滑膜炎患者 216 例为研究对象。根据随机数字表法将患者分为对照组(n=108)与研究组(n=108)。对照组患者给予玻璃酸钠治疗,研究组则在此基础上联合滑膜炎颗粒进行治疗,两组均治疗 5 周。比较两组治疗 5 周后(治疗后)的临床疗效及治疗前后血清白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、白介素-1 β (IL-1 β)水平,采用视觉模拟量表(VAS)评价患者治疗前后膝关节疼痛程度,美国特种外科医院量表(HSS)评价患者治疗前后膝关节功能,同时观察两组治疗期间不良反应发生情况。**结果:**研究组患者总有效率为 92.59%(100/108),高于对照组患者的 78.70%(85/108)($P<0.05$)。两组患者治疗后 IL-6、TNF- α 以及 IL-1 β 水平均较治疗前降低,且研究组低于对照组($P<0.05$)。两组患者治疗后 VAS 评分较治疗前降低,且研究组低于对照组,HSS 评分较治疗前升高,且研究组高于对照组($P<0.05$)。两组患者不良反应发生率对比差异无统计学意义($P>0.05$)。**结论:**滑膜炎颗粒联合玻璃酸钠治疗创伤性膝关节滑膜炎安全有效,可显著改善患者血清炎症因子水平以及膝关节功能,并减轻患者疼痛程度,具有一定的临床应用价值。

关键词:滑膜炎颗粒;玻璃酸钠;创伤性;膝关节滑膜炎;疗效;炎症因子

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Effect of Synovitis Granule Combined with Sodium Hyaluronate on Traumatic Synovitis of Knee Joint and its Influence on Serum Inflammatory Factors Level*

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ABSTRACT Objective: To investigate the effect of synovitis granule combined with sodium hyaluronate on traumatic synovitis of knee joint and its influence on serum inflammatory factors. **Methods:** 216 patients with traumatic synovitis of knee joint who were treated in our hospital from February 2015 to December 2017 were selected as the research subjects. According to the number table method, the patients were randomly divided into control group (n=108) and study group (n=108). The control group was treated with sodium hyaluronate, while the study group was treated with synovitis granules. The two groups were treated for 5 weeks. The clinical efficacy of two groups at 5 weeks after treatment (after treatment) and the levels of serum interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β) before and after treatment, visual analogue scale (VAS) was used to evaluate the degree of knee pain before and after treatment, the American special surgery hospital scale (HSS) was used to evaluate knee function before and after treatment, meanwhile, the adverse reactions of the two groups during treatment were observed. **Results:** The total effective rate of the study group was 92.59% (100/108), which was significantly higher than 78.70% (85/108) of the control group ($P<0.05$). The levels of IL-6, TNF- α and IL-1 β after treatment in the two groups were lower than those before treatment, and the study group was lower than that in the control group ($P<0.05$). The VAS score of the two groups decreased after treatment, and the study group was lower than that of the control group, the HSS score was higher than that before treatment, and the study group was higher than that of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Synovitis Granules Combined with sodium hyaluronate in the treatment of traumatic synovitis of knee joint is effective and safe. It can significantly improve the level of serum inflammatory factors, function of knee joint and relieve pain degree of patients, so it has certain clinical application value.

Key words: Synovitis granule; Sodium hyaluronate; Traumatic; Synovitis of knee joint; Curative effect; Inflammatory factors

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前言

创伤性膝关节滑膜炎是指膝关节损伤后引起的滑膜非感染性炎症反应,临床表现为膝关节疼痛、肿胀以及功能障碍等。该病可引发滑膜水肿渗出、粘连以及肥厚,继而使软骨发生萎缩,膝关节积液反复出现,最终影响膝关节功能,对患者生活质量造成严重影响^[1-3]。现临床上针对创伤性膝关节滑膜炎的主要治疗方式为药物治疗,玻璃酸钠是一种高分子多糖体生物材料,其作为关节腔液的主要成分之一,对骨关节疾病有良好的治疗作用,可以补充关节内滑液,起到润滑关节、缓冲应力的作用,同时改善滑液的粘弹性,进一步抑制病情发展^[4-6]。近年来相关研究表明^[7,8],中药在治疗创伤性膝关节滑膜炎上具有一定的优势,滑膜炎颗粒是由多种中药制成的方剂,具有活血化瘀、清热利湿等作用。然而中药治疗具有一定局限性,如起效慢、患者耐受性差及治疗周期长等。因此,本研究通过探讨滑膜炎颗粒联合玻璃酸钠治疗创伤性膝关节滑膜炎的疗效及对患者血清炎症因子水平的影响,旨在为临床治疗提供数据支持,现作如下报道。

1 资料与方法

1.1 一般资料

选取 2015 年 2 月~2017 年 12 月期间我院收治的创伤性膝关节滑膜炎患者 216 例为研究对象。纳入标准:(1)所有患者均符合中医诊断标准《中医病证诊断疗效标准》、西医诊断标准《外科学》中有关创伤性膝关节滑膜炎相关诊断标准^[9,10];(2)近期关节腔内未注射激素者;(3)对本次研究使用药物不存在禁忌症者;(4)患者及其家属知情本研究并签署同意书。排除标准:(1)合并代谢性骨病患者;(2)患有精神疾病者;(3)合并心、肝、肾等脏器功能障碍者;(4)合并骨折、韧带损伤及脱位现象;(5)妊娠以及哺乳期妇女。根据随机数字表法将患者分为对照组(n=108)与研究组(n=108)。其中对照组男 56 例,女 52 例,年龄 26~68 岁,平均(42.43±5.12)岁;病程 14~26 d,平均(20.08±2.48)d;发病原因:急性挫伤 26 例,暴力打击 48 例,有劳损史 34 例;其中左膝 55 例,右膝 53 例。研究组男 58 例,女 50 例,年龄 25~71 岁,平均(43.28±4.65)岁;病程 15~29 d,平均(19.71±3.01)d;发病原因:急性挫伤 24 例,暴力打击 46 例,有劳损史 38 例;其中左膝 52 例,右膝 56 例。两组患者一般资料比较差异无统计学意义(P>0.05),提示组间均衡可比,所有研究过程均符合我院医学伦理委员会的相关规定。

1.2 治疗方法

对照组患者取仰卧位,膝关节弯曲呈 30° 角,常规消毒,选用普通 5 mL 注射器于髌骨中点外缘内侧刺入关节腔,回抽关节积液,回抽无血后,于关节腔内注入玻璃酸钠(上海昊海生物科技股份有限公司,国药准字:H20174089,规格:2.5 mL:25 mg) 20 mg,注入完毕拔针,同时使用无菌纱布盖住,5 min 后稍屈膝关节以使药液分布均匀,1 次/周。研究组在对照组基础上联合使用滑膜炎颗粒(神威药业(张家口)有限公司,国药准字:Z13020929)治疗,1 袋/次,3 次/d。两组均连续治疗 5 周,患者治疗期间均尽可能减少肢体以及负重等运动行为。

1.3 观察指标

观察两组患者治疗 5 周后(治疗后)的临床疗效。疗效判定标准^[11]:临床症状消失,关节功能恢复正常,对日常工作生活无影响为痊愈;临床症状基本消失,关节功能基本恢复正常,劳累后仍疼痛,可自行缓解为显效;临床症状有所缓解,关节功能有所改善,需经常服用镇痛药物为有效;临床症状无变化甚至加重为无效。总有效率=痊愈率+显效率+有效率。分别于治疗前后采集患者清晨空腹静脉血 5 mL,3000 r/min 离心 8 min,分离血清,采用酶联免疫吸附法检测白介素-6 (Interleukin-6, IL-6)、肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、白介素-1 β (Interleukin-1 β , IL-1 β)水平,试剂盒来源于上海雅培生物科技工程有限公司,严格按照试剂盒操作进行。采用视觉模拟量表(Visual analogue scale, VAS)评价患者治疗前后膝关节疼痛程度,分数根据疼痛程度由轻到重定义为 0~10 分;采用美国特种外科医院量表(hospital for special surgery, HSS)评价患者治疗前后膝关节功能,HSS 包括疼痛、稳定性、肌力、功能、活动度以及有无屈曲畸形,总分 100 分,分数越高提示膝关节功能越好。观察两组患者治疗期间不良反应发生情况。

1.4 统计学方法

研究数据录入 SPSS23.0 软件处理。计数资料以率(%)表示,采用卡方检验。计量资料用均数±标准差($\bar{x}$ ±s)表示,采用 t 检验。检验水准设置为 α =0.05。

2 结果

2.1 两组患者临床疗效比较

研究组患者总有效率为 92.59%(100/108),高于对照组患者的 78.70%(85/108),差异比较有统计学意义(P<0.05);详见表 1。

表 1 两组患者临床疗效比较(n,%)

Table 1 Comparison of clinical efficacy between the two groups(n,%)

Groups	Recovery	Excellent	Good	Invalid	Total efficiency
Control group(n=108)	29(26.85)	35(32.41)	21(19.44)	23(21.30)	85(78.70)
Study group(n=108)	53(49.07)	29(26.85)	18(16.67)	8(7.41)	100(92.59)
χ^2					8.474
P					0.004

2.2 两组患者治疗前后血清炎症因子水平比较

两组患者治疗前 IL-6、TNF- α 以及 IL-1 β 水平比较差异无

统计学意义(P>0.05);两组患者治疗后 IL-6、TNF- α 以及 IL-1 β 水平均较治疗前降低,且研究组低于对照组(P<0.05);详见表 2。

表 2 两组患者治疗前后血清炎症因子水平比较($\bar{x} \pm s$)Table 2 Comparison of serum inflammatory factors between two groups before and after treatment($\bar{x} \pm s$)

Groups	IL-6(pg/mL)		TNF- α (ng/mL)		IL-1 β (pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=108)	29.62 $\pm$ 6.48	18.62 $\pm$ 7.42*	2.74 $\pm$ 0.91	2.07 $\pm$ 0.52*	6.83 $\pm$ 1.57	5.71 $\pm$ 1.13*
Study group (n=108)	28.29 $\pm$ 6.27	12.75 $\pm$ 6.96*	2.85 $\pm$ 0.79	0.95 $\pm$ 0.16*	7.01 $\pm$ 1.81	2.02 $\pm$ 0.57*
t	1.533	5.996	0.949	21.394	0.781	30.299
P	0.127	0.000	0.344	0.000	0.436	0.000

Note: compared with before treatment, *P<0.05.

2.3 两组患者治疗前后 VAS、HSS 评分比较

两组患者治疗前 VAS、HSS 评分比较差异无统计学意义(P>0.05);两组患者治疗后 VAS 评分较治疗前降低,且研究组

低于对照组,HSS 评分较治疗前升高,且研究组高于对照组(P<0.05);详见表 3。

表 3 两组患者治疗前后 VAS、HSS 评分比较(分, $\bar{x} \pm s$)Table 3 Comparison of VAS, HSS scores between two groups before and after treatment(score, $\bar{x} \pm s$)

Groups	VAS		HSS	
	Before treatment	After treatment	Before treatment	After treatment
Control group(n=108)	6.41 $\pm$ 1.26	4.12 $\pm$ 0.68*	64.03 $\pm$ 10.49	69.12 $\pm$ 11.35*
Study group(n=108)	6.39 $\pm$ 1.31	2.16 $\pm$ 0.71*	65.08 $\pm$ 11.47	82.26 $\pm$ 10.42*
t	0.114	20.719	0.702	8.863
P	0.909	0.000	0.483	0.000

Note: compared with before treatment, *P<0.05.

2.4 两组患者不良反应发生情况

对照组治疗期间未出现不良反应现象,不良反应发生率为 0.00%(0/108);研究组则有 2 例出现不良反应现象,1 例恶心呕吐,1 例腹泻,并发症发生率为 1.85%(2/108);两组患者不良反应发生率对比无统计学差异($\chi^2=2.037$,P=0.154)。

3 讨论

中医认为创伤性膝关节滑膜炎属“痹病”、“伤筋病”范畴,其病机为跌打损伤致使气血紊乱,膝部淤血阻塞,致使新血不生,风寒湿邪入侵。其主要治疗原则为温经通络、驱寒除湿^[12,13]。有相关研究表明^[14-16],炎症因子参与了该病的发生发展过程,炎症因子破坏人体组织,形成水肿,加重创伤性膝关节滑膜炎病情。该病若未得到有效的控制治疗,易导致滑膜组织肥厚、粘连,进而发生关节退行性病变,给患者生活质量造成严重影响^[17-19]。因此,本研究侧重从血清炎症因子水平、膝关节功能状况等方面考察滑膜炎颗粒联合玻璃酸钠治疗的临床疗效。

玻璃酸钠在关节内主要由滑膜 β 细胞分泌,是关节滑液和软骨基质内的重要组成部分,具有润滑关节、保护软骨以及维持滑液、软骨粘弹性等作用^[20,21]。滑膜炎颗粒主要成分为夏枯草、川牛膝、丹参、当归、泽兰、薏苡仁、土茯苓、防己、女贞子、黄芪等,其中夏枯草可散结消肿,川牛膝可活血利湿,丹参可活血通经,当归、泽兰可活血通络,薏苡仁可健脾除湿,土茯苓、防己可利尿消肿,女贞子可滋阴补肾,黄芪可补气益胃,诸药合用发挥温经通络、驱寒除湿的功效^[22]。本研究结果表明,研究组患者

总有效率高于对照组,说明滑膜炎颗粒联合玻璃酸钠治疗较单用玻璃酸钠治疗效果更为显著。另外上述两种治疗方式均可有效降低血清炎症因子水平,而联合用药减轻炎症反应作用更为明显,这与阮文辉等人研究结果基本一致^[23]。IL-6 是一种白细胞趋化因子,可促进多种炎性细胞生长,并抑制正常细胞生长^[24]。TNF- α 是一种单核细胞因子,可促进炎性细胞聚集和分化,抑制软骨胶原生成,同时诱导软骨细胞产生过氧化反应^[25]。IL-1 β 是一种致炎细胞因子,正常情况下,机体含量较低,然而当机体处于病理状态时,其水平呈现异常升高,在创伤性膝关节滑膜炎的发生、发展中起重要作用^[26]。上述三种炎症因子经联合治疗后,均得到有效控制,分析其原因,可能是由于关节腔内注入玻璃酸钠,补充并提高了关节腔内玻璃酸钠含量,增加了关节的粘弹性及润滑性,减少了炎症介质与软骨的接触,同时玻璃酸钠进入软骨基质内与糖蛋白结合,有效改善关节腔内环境,发挥抗感染、补充软骨基质以及润滑等作用。再加上滑膜炎颗粒可减少白细胞浸润,降低炎症因子水平表达,有效减轻患者炎症反应,改善患者临床症状^[27-29]。同时比较两种治疗方式对膝关节功能状况的影响,研究组 VAS 评分低于对照组,研究组 HSS 则高于对照组,表明研究组患者膝关节功能得到显著改善,VAS 评分主要来源于患者自身主观疼痛感受,HSS 则是临床常用于评价膝关节功能的量表,上述两种量表信效度均较高。在不良反应考察方面,两组患者不良反应发生率对比无统计学差异,提示联合用药安全性好,这可能与滑膜炎颗粒为纯中药制剂,对患者刺激作用较小有关^[30]。

综上所述,滑膜炎颗粒联合玻璃酸钠治疗创伤性膝关节滑膜炎效果显著,可明显改善患者膝关节功能,减轻炎症反应,且安全性较好。

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