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仙灵骨葆胶囊联合透明质酸钠对膝骨关节炎患者关节功能、炎症因子及生活质量的影响*

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摘要 目的:观察仙灵骨葆胶囊联合透明质酸钠对膝骨关节炎(KOA)患者关节功能、炎症因子及生活质量的影响,为临床用药提供依据。**方法:**选取我院骨科于2014年12月-2016年12月间收治的72例KOA患者作为研究对象。采用随机数字表法将患者分为透明质酸钠组(采用透明质酸钠治疗,n=36)和联合组(采用仙灵骨葆胶囊与透明质酸钠联合治疗,n=36)。检测并比较两组患者治疗前及治疗1个月后的超敏C反应蛋白(hs-CRP)水平、肿瘤坏死因子-α(TNF-α)水平。分别于治疗前、治疗1个月后以及治疗6个月后采用生活质量调查表(SF-36)中文版评价患者生活质量,同时采用视觉模拟评估法(VAS)以及膝关节功能评定量表(Lysholm)对膝关节功能进行综合评定。治疗结束后随访半年,观察患者不良反应发生情况。**结果:**治疗1个月后,两组患者hs-CRP、TNF-α水平均明显下降,且联合组患者hs-CRP、TNF-α水平明显低于透明质酸钠组患者(*P<0.05*)。两组治疗6个月后的VAS评分明显低于治疗1个月后的VAS评分,Lysholm评分均明显高于治疗1个月后的Lysholm评分(*P<0.05*)。治疗1个月后和治疗6个月后,联合组患者VAS评分均明显低于透明质酸钠组患者同期VAS评分,而Lysholm评分均明显高于透明质酸钠组患者同期Lysholm评分(*P<0.05*)。两组治疗6个月后SF-36量表各维度评分均高于治疗1个月后的评分(*P<0.05*)。联合组患者治疗1个月后及治疗6个月后的躯体功能、躯体角色功能、躯体疼痛、总体健康、社会功能和心理健康评分均明显高于透明质酸钠组(均*P<0.05*)。两组均无严重不良反应发生,且不良反应发生情况无明显差异(*P>0.05*)。**结论:**仙灵骨葆胶囊联合透明质酸钠治疗膝骨关节炎对患者炎症反应、关节功能及生活质量有持续的改善作用,同时安全可靠,值得推广应用。

关键词:仙灵骨葆胶囊;透明质酸钠;膝骨关节炎;关节功能;炎症因子;生活质量

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Effect of Xianlinggubao Capsule Combined With Sodium Hyaluronate on Joint Function, Inflammatory Factors and Quality of Life in Patients With Knee Osteoarthritis*

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ABSTRACT Objective: To observe the effect of Xianlinggubao capsule combined with sodium hyaluronate on joint function, inflammatory factors and quality of life in patients with knee osteoarthritis (KOA),so as to provide the basis for clinical medication. **Methods:** 72 cases of patients with KOA treated in the department of orthopaedics in our hospital during December 2014 and December 2016 were selected as subjects. According to the random number table method, the patients were divided into sodium hyaluronate group (treated with sodium hyaluronate, n=36) and combination group (Xianlinggubao capsule combined with sodium hyaluronate treatment, n=36). The levels of hypersensitivity C reactive protein (hs-CRP) and tumor necrosis factor-α (TNF-α) were measured and compared between the two groups before treatment and 1 month after treatment. Before treatment, 1 month and 6 months after treatment, the quality of life was evaluated by the Chinese version of the quality of life questionnaire (SF-36), and the knee function was assessed by means of visual analogue assessment (VAS) and knee function rating scale (Lysholm). The patients were followed up for half a year after treatment, and the adverse reactions were observed. **Results:** After 1 months of treatment, the levels of hs-CRP and TNF-α in the two groups were obviously decreased, and the levels of hs-CRP and TNF-α in the combined group were significantly lower than those in the sodium hyaluronate group (*P<0.05*). The VAS scores of the two groups after treatment for 6 months were significantly lower than the VAS scores after 1 months treatment, and the Lysholm scores were significantly higher than the Lysholm scores after 1 months treatment (P<0.05). After 1 months of treatment and 6 months after treatment, the VAS scores of the combination group were significantly lower than those of the sodium hyaluronate group in the same period, and Lysholm score were significantly higher than those of the sodium hyaluronate group in the same period (*P<0.05*). The scores of each dimension of SF-36 scale 6 monts after treatment were higher than 1

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month after treatment in the two groups (*P<0.05*). The scores of body function, physical role, physical pain,general health, social function and mental health of the patients in the combination group were significantly higher than those in the sodium hyaluronate group 1 month and 6 months after treatment (*P<0.05*). There were no serious adverse reactions in the two groups, and there was no significant difference in the incidence of adverse reactions between the two groups (*P>0.05*). **Conclusion:** Xianlinggubao capsule combined with sodium hyaluronate in the treatment of knee osteoarthritis has a continuous improvement effect on inflammatory reaction, joint function and quality of life, and it is safe and reliable. It is worthy of popularization and application.

Key words: Xianlinggubao capsule; Sodium hyaluronate; Knee osteoarthritis; Joint function; Inflammatory factor; Quality of life

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前言

膝骨关节炎(Knee osteoarthritis,KOA)在临床上主要表现为膝关节的肿痛及屈伸活动限制，是一种退行性关节病变,多发于中老年人[1,2]。KOA 的发病原因较多,主要包括肥胖、炎症、关节过度使用、代谢障碍、遗传因素、年龄衰老等[3],疾病主要特征为膝关节软骨的变性和破坏、以及骨质增生等,同时多数患者膝关节伴随骨摩擦音,严重影响患者的生活质量[4,5]。目前,西医主要采用在患者关节腔内注射透明质酸钠方式对 KOA 患者进行治疗,并且取得了一定的效果,但仍有部分患者采用单独透明质酸钠治疗的疗效并不理想[6,7]。中医认为 KOA 病理病机为肝肾亏虚、筋脉痹阻,属于痹症、骨痹范畴[8]。而仙灵骨葆胶囊有补肝肾、强筋骨、温阳通络的功效,在 KOA 的治疗中也具有一定的疗效[9]。本研究将仙灵骨葆胶囊与关节腔内注射透明质酸钠联合用于 KOA 患者的治疗中,观察患者关节功能、炎症因子以及生活质量的影响,以期为临床用药提供依据。报道如下。

1 资料与方法

1.1 一般资料

选取我院骨科于 2014 年 12 月 -2016 年 12 月间收治的 72 例 KOA 患者作为研究对象。KOA 诊断标准[10]:患者年龄不低于 38 岁，膝部活动时伴随骨摩擦音且近两个月时常感觉到疼痛,晨僵时间不高于 30 min,同时经检查发现骨性肥大。排除标准:① 合并有恶性肿瘤,易发生感染及出血事件的患者;② 合并膝关节骨折、半月板损伤或关节结核的患者;③ 孕期或哺乳期妇女;④ 依从性差,不积极配合治疗的患者。采用随机数字表法将患者分为透明质酸钠组和联合组,各 36 例。透明质酸钠组男 13 例,女 23 例,年龄 40~65 岁,平均(51.78± 5.21)岁,病程 1~5 年,平均(2.33± 1.14)年,病变部位:右侧 19 例,左侧 17 例;联合组男 14 例,女 22 例,年龄 39~65 岁,平均(52.34± 5.47)岁,病程 1~5 年,平均(2.51± 1.27)年,病变部位:右侧 20 例,左侧 16 例。两组患者一般资料差异无统计学意义(*P>0.05*),可以比较。

1.2 治疗方法

透明质酸钠组患者取坐位,膝关节屈曲为直角,在髌上囊下外侧进行常规皮肤消毒后作为穿刺点。采用 2%的利多卡因进行局部麻醉后穿刺入关节腔,抽出积液后向关节腔内注射医用透明质酸钠凝胶（上海其胜生物制剂有限公司)2 mL,1 次 / 周,持续 4 周。联合组患者在透明质酸钠组的基础上联用仙灵骨葆胶囊（国药集团同济堂 (贵州) 制药有限公司，国药准字 Z20025337,规格 0.5 g/ 粒)口服,3 粒 / 次,2 次 / 日,持续 4 周。

1.3 观察指标及评价标准

分别于治疗前、治疗 1 个月后清晨采集患者空腹静脉血 3 mL，分离血清后采用免疫比浊法测定超敏 C 反应蛋白(hs-CRP)水平、采用酶联免疫吸附测定肿瘤坏死因子 -α(TNF-α)水平。治疗结束后随访半年,观察患者不良反应发生情况。分别于治疗前、治疗 1 个月后以及治疗 6 个月后采用生活质量调查表(SF-36)中文版评价患者生活质量,同时采用视觉模拟评估法(VAS)以及膝关节功能评定量表(Lysholm)对膝关节功能进行综合评定[11,12]。SF-36 量表共包含躯体功能、躯体角色功能、躯体疼痛、总体健康、生命活力、社会功能、情绪角色功能、心理健康八个维度的内容,各维度满分为 100 分,分值越高表明生活质量越好。VAS 评分总分为 10 分,分数越高表明疼痛程度越高。Lysholm 评分包括跛行、支撑、交锁、疼痛、肿胀、爬楼梯、关节不稳定和下蹲 8 个项目,共 100 分,分数越高表明膝关节功能越好。

1.4 统计学方法

采用 SPSS16.0 对本研究数据进行统计分析。其中计数资料以%的形式表示,采用卡方检验,炎性因子水平、SF-36 评分、Lysholm 评分等计量资料以($\bar{x}\pm s$)的形式表示,采用 t 检验。检验标准设置为 α=0.05。

2 结果

2.1 两组患者 hs-CRP、TNF-α 水平比较

两组患者治疗前 hs-CRP、TNF-α 水平比较差异无统计学意义(*P>0.05*)。治疗 1 个月后,两组患者 hs-CRP、TNF-α 水平均明显下降,且联合组患者 hs-CRP、TNF-α 水平明显低于透明质酸钠组患者(*P<0.05*)。见表 1。

2.2 两组患者膝关节功能变化情况

两组患者治疗前 VAS 评分、Lysholm 评分比较差异无统计学意义(*P>0.05*)。治疗 1 个月后及治疗 6 个月后,两组患者 VAS 评分明显降低,Lysholm 评分均明显升高，且两组治疗 6 个月后的 VAS 评分明显低于治疗 1 个月后的 VAS 评分,Lysholm 评分均明显高于治疗 1 个月后的 Lysholm 评分(均 *P<0.05*)。治疗 1 个月后和治疗 6 个月后,联合组患者 VAS 评分均明显低于透明质酸钠组患者同期 VAS 评分，而 Lysholm 评分均明显高于透明质酸钠组患者同期 Lysholm 评分（均 *P<0.05*)。见表 2。

2.3 两组患者生活质量变化情况

治疗前,两组患者 SF-36 量表各维度评分比较差异无统计

学意义（*P>0.05*）。治疗 1 个月后及治疗 6 个月后，两组患者 SF-36 量表各维度评分均明显升高，且两组治疗 6 个月后 SF-36 量表各维度评分均高于治疗 1 个月后的评分（均 *P<0.05*）。联合组患者治疗 1 个月后及治疗 6 个月后的躯体功能、躯体角色功能、躯体疼痛、总体健康、社会功能和心理健康评分均明显高于透明质酸钠组（均 *P<0.05*）。见表 3。

表 1 两组患者 hs-CRP、TNF-α 水平比较（$\bar{x}\pm s$）

Table 1 Comparison of hs-CRP and TNF- alpha levels between the two groups（$\bar{x}\pm s$）

Groups	Period	hs-CRP(mg/L)	TNF-α(pg/mL)
Sodium hyaluronate group (n=36)	Before treatment	9.23± 2.06	7.87± 0.94
	1 month after treatment	6.98± 0.89*	6.02± 0.63*
Combination group (n=36)	Before treatment	9.11± 1.97	8.01± 1.03
	1 month after treatment	5.23± 0.72*#	4.26± 0.57*#

Note: Compared with before treatment,**P<0.05*; compared with sodium hyaluronate group, #*P<0.05*.

表 2 两组患者 VAS 评分、Lysholm 评分比较（$\bar{x}\pm s$）

Table 2 Comparison of VAS score and Lysholm score between the two groups（$\bar{x}\pm s$）

Groups	Period	VAS score	Lysholm score
Sodium hyaluronate group (n=36)	Before treatment	7.74± 0.71	23.65± 8.43
	1 month after treatment	5.52± 0.83*	48.53± 10.21*
	6 month after treatment	3.35± 0.62*△	64.31± 11.76*△
Combination group (n=36)	Before treatment	7.79± 0.68	23.17± 9.16
	1 month after treatment	4.11± 0.73*#	67.74± 11.50*#
	6 month after treatment	2.64± 0.46*△ #	80.12± 12.37*△ #

Note: Compared with before treatment, **P<0.05*; compared with 1 month after treatment, △ *P<0.05*; compared with sodium hyaluronate group, #*P<0.05*.

表 3 两组患者 SF-36 评分变化情况（$\bar{x}\pm s$）

Table 3 Changes of SF-36 scores in the two groups（$\bar{x}\pm s$）

Items	Sodium hyaluronate group (n=36)			Combination group (n=36)		
	Before treatment	1 month after treatment	6 month after treatment	Before treatment	1 month after treatment	6 month after treatment
Physical function	47.31± 9.62	57.49± 8.32*	62.95± 7.94*△	46.54± 10.17	63.75± 8.96*#	69.43± 8.83*△ #
Role-physical	43.29± 8.43	58.31± 9.63*	64.09± 9.12*△	42.87± 8.92	65.27± 10.85*#	71.21± 9.54*△ #
Bodily pain	39.83± 10.44	51.54± 8.72*	58.10± 8.21*△	40.08± 11.21	57.43± 9.97*#	67.40± 10.75*△ #
General health	45.32± 12.75	55.92± 10.31*	62.95± 9.87*△	44.75± 11.86	62.41± 12.54*#	72.21± 13.08*△ #
Vitality	51.72± 9.42	60.93± 7.38*	68.33± 8.70*△	52.83± 8.74	62.83± 8.16*	70.19± 10.52*△
Social function	48.49± 7.52	55.41± 8.52*	61.32± 9.71*△	48.95± 8.01	60.37± 10.51*#	68.42± 10.29*△ #
Role-emotional	49.18± 10.21	61.05± 9.51*	70.23± 10.09*△	48.32± 9.54	62.37± 10.82*	72.54± 11.17*△
Mental health	53.23± 6.84	58.47± 6.32*	64.91± 8.22*△	54.38± 7.41	63.31± 8.14*#	71.85± 9.76*△ #

2.4 两组不良反应发生情况

联合组出现局部关节肿痛 1 例，恶心 1 例，透明质酸钠组出现 2 例局部关节肿痛，经对症治疗后得到缓解，两组均无严重不良反应发生。两组不良反应发生情况无明显差异（*P<0.05*）。

3 讨论

KOA 多发于中老年人，有报道表明[13]，中国 40 岁以上人群原发性骨关节炎总体患病率超过 40%，且患病率随着年龄的增加而增加。KOA 致残率可高达 53%，是导致老年人残疾的重要原因之一，严重影响患者的生活质量[14]。现代医学研究表明[15,16]，KOA 的发病机制与关节软骨变性、生物力学改变以及软骨下骨质改变密切相关。西医治疗 KOA 的主要目的是减轻或消除患者疼痛、矫正畸形、改善患者关节功能等，并最终改善患者的生活质量[17,18]。KOA 在中医看来属于骨痹、筋痹、痹证等，研究证实，采用中医治疗 KOA 可以直接影响患者骨内压、氧自由基、细胞因子、组织形态学，临床效果良好[19]。

近年来，炎症因子在 KOA 中的介导作用在临床中越来越

受到重视。hs-CRP 参与软骨基质的降解作用以及滑膜组织的炎症病变，其主要由肝细胞分泌，当 hs-CRP 在血清中的含量升高时，可导致 KOA 患者关节软骨的退行性病变加剧[20]。TNF-α 参与骨关节的炎性反应同时在软骨破坏的过程中起着重要作用，其主要由单核巨噬细胞分泌，当 TNF-α 在血清中含量升高时，患者软骨胶原的合成受到抑制，从而引发软骨细胞外基质变性、降解[21,22]。本研究中，治疗 1 个月后两组 KOA 患者血清 hs-CRP、TNF-α 水平均明显下降，且联合组患者血清 hs-CRP、TNF-α 水平明显低于透明质酸钠组患者，提示仙灵骨葆胶囊联合透明质酸钠对患者的炎症反应抑制效果更为明显。同时本研究比较两组患者治疗前、治疗 1 个月后及治疗 6 个月后的 VAS 评分、Lysholm 评分结果发现，两组患者的疼痛情况以及关节功能均得到持续改善，且联合组的改善作用更为明显，提示仙灵骨葆胶囊联合透明质酸钠对 KOA 患者膝关节功有持续的改善作用。透明质酸钠具有多种生理功能，包括润滑关节、参与修复、抵御感染等，是软骨基质和关节滑液的重要组成部分[23,24]。与正常人相比，KOA 患者关节滑液中透明质酸钠的含量、浓度均较低[25]。通过补充外源性透明质酸钠，KOA 患者关节滑液的粘弹性得到恢复，并使软骨组织的自我修复功能重新激活，蛋白糖聚集，软骨基质分解得到抑制，同时诱导内源性透明质酸钠的产生[26-28]。仙灵骨葆胶囊的主要成分包括续断、淫羊藿、知母、地黄、丹参等，其中续断可续筋骨、补肝肾，淫羊藿能祛风湿、补肾阳，知母、地黄、丹参则有活血化瘀、温筋通络的功效[29]。仙灵骨葆胶囊以补肾壮骨为主，活血化瘀为辅，能明显抑制患者患处炎症、肿胀，同时能改善患者局部血液循环，促使软骨细胞成熟，切合 KOA 病理病机[30]。本研究中采用 SF-36 量表对患者治疗前、治疗 1 个月后及治疗 6 个月后的生活质量进行评价，发现两组患者的生活质量均得到持续改善，且在躯体功能、躯体角色功能、躯体疼痛、总体健康、社会功能和心理健康评方面，联合组改善效果更为明显，提示仙灵骨葆胶囊联合透明质酸钠对患者生活质量的改善作用更为明显。同时治疗及随访过程中两组患者均仅出现轻微不良反应，说明两种治疗方法均具有较好的安全性。

综上所述，仙灵骨葆胶囊联合透明质酸钠治疗膝骨关节炎对患者炎症反应、关节功能及生活质量有持续的改善作用，同时安全可靠，值得推广应用。

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