

doi: 10.13241/j.cnki.pmb.2019.10.031

透明质酸钠联合硫酸氨基葡萄糖钾胶囊对踝关节损伤患者血清骨性标志物水平及关节功能的影响*

李 伟¹ 杨兴刚¹ 李大银¹ 徐杨博² 邓 勇²

(1 广元市第三人民医院外二科 四川 广元 628000; 2 西南医科大学附属医院足踝外科 四川 泸州 646099)

摘要 目的:探讨透明质酸钠联合硫酸氨基葡萄糖钾胶囊对踝关节损伤患者血清骨性标志物水平及关节功能的影响。**方法:**选择2015年1月至2017年1月在我院接受治疗的120例踝关节损伤患者,将其随机分为观察组和对照组,每组各60例。对照组患者采用透明质酸钠治疗,观察组则在对照组治疗方案的基础上联合硫酸氨基葡萄糖钾胶囊进行治疗。检测和比较两组患者治疗前后血清骨钙素(BGP)、I型前胶原羧基端肽(PICP)、骨源性碱性磷酸酶(BALP)水平及Baird-Jackson踝关节评分的变化情况及治疗后的临床疗效。**结果:**治疗后,观察组的总有效率(91.67%)明显高于对照组(78.33%, $P<0.05$)。两组患者治疗后的血清BGP、PICP、BALP水平及Baird-Jackson踝关节评分均较治疗前显著升高,且观察组明显高于对照组($P<0.05$)。两组治疗过程中均无明显不良反应发生。**结论:**透明质酸钠联合硫酸氨基葡萄糖钾胶囊治疗踝关节损伤患者的临床疗效显著优于单用透明质酸钠治疗,其可有效改善血清骨性标志物水平,且利于踝关节功能的恢复。

关键词:透明质酸钠;硫酸氨基葡萄糖钾胶囊;踝关节损伤;骨钙素;I型前胶原羧基端肽;骨源性碱性磷酸酶

中图分类号:R684 **文献标识码:**A **文章编号:**1673-6273(2019)10-1949-04

Effect of Sodium Hyaluronate Combined with Glucosamine Sulfate Glucose Potassium on the Serum Osteo-Marker and Joint Function of Patients with Ankle Joint Injury*

LI Wei¹, YANG Xing-gang¹, LI Da-yin¹, XU Yang-bo², DENG Yong²

(1 Surgical department, Guangyuan Third People's Hospital, Guangyuan, Sichuan, 628000, China;

2 Foot and ankle surgery, Southwest Medical University Affiliated Hospital, Luzhou, Sichuan, 646099, China)

ABSTRACT Objective: To study the effect of sodium hyaluronate combined with glucosamine Sulfate Glucose Potassium capsule on the serum bilirubin level and joint function of patients with ankle joint injury. **Methods:** 120 cases of patients with ankle injuries treated in our hospital from January 2015 to January 2017 were selected and randomly divided into the observation group and the control group, with 60 cases in each group. The control group was treated with sodium hyaluronate, while the observation group was treated with glucosamine potassium sulfate capsules on the basis of treatment regimen of the control group. The changes of serum osteocalcin (BGP), type I procollagen carboxyl-terminated peptide (PICP), osteogenic alkaline phosphatase (BALP) and baird-jackson ankle score before and after treatment and the clinical efficacy were measured and compared between the two groups. **Results:** After treatment, the total effective rate of observation group (91.67%) was significantly higher than that of the control group (78.33%, $P<0.05$). The serum BGP, PICP, BALP and baird-jackson ankle scores of both groups were significantly increased after treatment compared with those before treatment, which were significantly higher in the observation group than those of the control group ($P<0.05$). No obvious adverse reactions occurred during the treatment in both groups. **Conclusion:** The clinical efficacy of sodium hyaluronate combined with glucosamine potassium sulfate is significantly better than that of sodium hyaluronate alone in the treatment of patients with ankle joint injury.

Key words: Sodium hyaluronate; Glucosamine potassium sulfate capsule; Ankle injury; Osteocalcin; Type I procollagen carboxyl-terminated peptide; Bone - derived alkaline phosphatase

Chinese Library Classification(CLC): R684 **Document code:** A

Article ID: 1673-6273(2019)10-1949-04

前言

踝关节的稳定性对人们的体育运动及日常活动意义重大^[1]。踝关节损伤是常见的骨科疾病,主要包括踝关节韧带损

伤、关节内骨折、关节内骨挫伤、关节周围肌腱钙化以及关节不稳定等。导致踝关节损伤因素较多^[2],如超负荷运动、骨质疏松、反复关节扭伤、肥胖、下肢生理力学改变等,其临床常见症状主要表现为关节疼痛肿胀、压痛、瘀血、不同程度的功能障碍等,

* 基金项目:四川省卫计委科研基金项目(150013)

作者简介:李伟(1982-),男,本科,主治医师,研究方向:足踝外科方向,E-mail: caoshuan000@163.com,电话:13419224003 / 0839-3450931

(收稿日期:2018-09-28 接受日期:2018-10-24)

一旦治疗不当,极易导致创伤性关节炎等并发症发生,进而加重肢体功能障碍,甚至发展成残疾。

近年来,临床大多数采用关节腔注射透明质酸钠对其进行治疗,可维持关节软骨组织的生理功能。但有研究显示^[9]透明质酸钠只能有效缓解患者疼痛,对患者的运动功能及生活质量改善微弱。研究表明^[10]氨基葡萄糖常用于骨科患者,且硫酸氨基葡萄糖钾胶囊总的有效成分硫酸氨基葡萄糖对关节疼痛感具有显著减轻作用。本研究主要探讨了透明质酸钠联合硫酸氨基葡萄糖钾胶囊对踝关节损伤患者血清骨性标志物水平及关节功能的影响。现报道如下。

1 材料与方法

1.1 一般资料

将我院 2015 年 1 月至 2017 年 1 月收治的踝关节损伤患者 120 例为研究对象,纳入标准^[9]:(1)踝关节受伤时间在 3 周以上,患处无明显血运障碍;(2)无大面积的软组织缺失;(3)未有其他严重复合损伤;(4)无明显开放性骨折及显著移位,且不需手术,患者及家属知情并签署同意书。排除标准^[9]:(1)有踝关节手术史者;(2)属于类风湿性或痛风性踝关节疼痛;(3)足部伴有先天性畸形者;(4)伴有类风湿、糖尿病、结核等病症者。将所纳入的 120 例患者随机将其均分为观察组(60 例)和对照组(60 例),观察组患者中男性 34 例,女性 26 例,年龄 24~60 岁,平均(40.14±8.97)岁,踝关节韧带损伤 34 例,关节内骨挫伤 26 例;而对照组患者中男性 32 例,女性 28 例,年龄 25~61 岁,平均(41.52±9.31)岁,踝关节韧带损伤 36 例,关节内骨挫伤 24 例。两组一般临床资料比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组患者治疗前均经抗炎、脱水等常规方法进行处理,对照组患者给予透明质酸钠(华熙福瑞达生物医药有限公司,规格:100 g/瓶,批号:20141123)进行治疗,先用空针将局部淤血吸出,分别于踝前(胫距关节线前下方皮肤)、踝后(内踝上方与跟腱内侧间)、外翻者加注踝内侧三角韧带(内踝下端 0.5 cm 处)、内翻者加注踝外侧三角韧带(距腓前韧带处)进针,使用注

射器将 2.5 mL 透明质酸钠缓慢注入关节腔内,拔针后使用无菌纱布将其覆盖,协助患者活动踝关节,以便透明质酸钠充分分布于关节腔滑膜及软骨表面,每周注射 1 次,连续注射 5 次;观察组患者则在对照组治疗方案的基础上联合硫酸氨基葡萄糖钾胶囊(山西康宝生物制品股份有限公司,规格:0.25 g/以硫酸氨基葡萄糖计,批号:20141209)进行口服治疗,3 次/1 d,每次 2 粒(500 mg),餐后服用,6 周为 1 疗程。

1.3 观察指标

1.3.1 临床疗效及踝关节功能的评定 采用 Baird-Jackson 评分评价疗效^[9]。优:评分在 96 分以上,踝关节可自由活动,劳累后无疼痛感;良:评分为 91~95 分,患者踝关节的活动范围受限制($<15^\circ$),劳累工作之后伴有轻微疼痛感;可:评分为 81~90 分,患者踝关节的活动范围受限制($<30^\circ$),只能接受轻微的体力劳动,且劳动后偶尔伴有疼痛感;差:评分为 0~80 分,患者踝关节活动范围受到较大限制,甚至是只能保持僵直状态,且经常伴有疼痛感,总有效率=优秀率+良好率。同时,分别于治疗前、治疗后 1 个月、治疗后 3 个月及治疗后 6 个月按照 Baird-Jackson 评分对患者踝关节功能进行评价,Baird-Jackson 评分越高,则表示踝关节功能越好。

1.3.2 血清骨性标志物水平的检测 两组患者于治疗前和治疗后 7 d 抽取清晨空腹静脉血 5 mL,采用离心机以 3000 r/min 的转速离心 5 min,分离血清,置于冰箱待检,冰箱温度设置为 -70°C ,采用酶联免疫吸附法对 BALP、PICP 及 BGP 水平进行检测。

1.4 统计学分析

采用统计学软件 SPSS18.0 分析数据,计量资料用均数±标准差表示,不同组间比较采用 t 检验,组间不同时间点比较采用重复测量方差分析,计数资料均用[例(%)]表示,组间比较采用 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者临床疗效的比较

治疗后,观察组的总有效率显著高于对照组 [91.67% vs. 78.33%]($P<0.05$),详见表 1。

表 1 两组患者临床疗效的比较[例(%)]

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

Groups	n	Excellent	Good	General	Poor	Total efficiency
Observation group	60	43(71.67)	12(20.00)	4(6.67)	1(1.67)	55(91.67)
Control Group	60	29(48.33)	18(30.00)	9(15.00)	4(6.67)	47(78.33)

2.2 两组患者治疗前后踝关节功能评分的比较

两组患者治疗后 1、3、6 个月的 Baird-Jackson 踝关节评分较治疗前显著升高,且观察组不同时间点 Baird-Jackson 踝关节评分均明显高于对照组($P<0.05$),详见表 2。

2.3 两组患者治疗前后血清 BGP、PICP 及 BALP 水平的比较

治疗前,两组的患者血清 BGP、PICP 及 BALP 水平比较差异无统计学意义($P>0.05$);治疗 7 d 后,观察组的血清 BGP、PICP 及 BALP 水平明显高于对照组($P<0.05$),详见表 3。

2.4 两组不良反应发生率的比较

观察组患者发生 1 例轻度胃腕部灼热,1 例关节局部肿胀不适,不良反应发生率为 3.33%;对照组患者发生关节局部肿胀不适 2 例,轻度胃腕部灼热 2 例,不良反应发生率为 6.67%,两组不良反应的发生率比较差异无统计学意义($P>0.05$)。

3 讨论

踝关节作为人体最大屈戌关节,是下肢最为重要的负重关节之一,承载着的重量人体体重的 5 倍,对人体的日常生活具有重要作用^[8]。但人体踝关节的结构尚存在不完整性,因此长期

表 2 两组治疗前后踝关节功能评分的比较 ($\bar{x} \pm s$)Table 2 Comparison of the ankle joint function score before and after treatment between two groups ($\bar{x} \pm s$)

Groups	n	Before treatment	At 1 month after treatment	At 3 months after treatment	At 6 months after treatment
Observation group	60	33.63± 5.42	61.48± 8.36*	78.75± 9.38*	87.67± 11.79*
Control Group	60	31.28± 5.15	46.24± 6.37	57.39± 7.95	64.39± 8.15

Note: Compared with the control group at 1, 3, and 6 months after treatment, * $p < 0.05$.

表 3 两组治疗前后血清 BGP、PICP 及 BALP 水平的比较 ($\bar{x} \pm s$)Table 3 Comparison of the serum BGP, PICP and BALP levels before and after treatment between two groups ($\bar{x} \pm s$)

Groups	n	BGP($\mu\text{g/L}$)		PICP($\mu\text{g/L}$)		BALP(U/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	60	2.25± 0.29	4.86± 0.61* [#]	122.35± 14.71	158.27± 19.52* [#]	62.53± 7.64	319.27± 40.35* [#]
Control Group	60	2.31± 0.34	3.71± 0.45*	123.18± 15.23	136.24± 16.17*	61.83± 7.31	221.34± 27.59*

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

的巨大负重及外界原因皆易导致该关节受损。踝关节损伤治疗对患者生活质量意义重大,一旦治疗失误,将增加创伤性关节炎并发症的发生,加重肢体功能障碍,严重者出现残疾^[9,10]。因此,如何有效治疗踝关节损伤,且改善踝关节功能康复一直是临床研究及关注的焦点。

透明质酸钠是一种黏多糖,是关节滑液及软骨组织中的重要成分,具有毒副作用小、安全可靠、疗效持久的特点^[11]。相关研究显示对踝关节损伤患者进行关节腔内注射外源性透明质酸钠,不仅可显著预防关节软骨退化,而且对关节软骨的退化具有一定的改善修复作用^[12,13]。另外,透明质酸钠还可抑制机体产生肽类致痛物质,达到减缓患者疼痛的效果。硫酸氨基葡萄糖钾胶囊中的硫酸葡萄糖对缓解关节疼痛具有显著作用,且主要是通过形成蛋白聚糖胶体复合物附着在基质胶原网架之上,进而构成一个弹性体,以便于承载压力,充分保护软骨结构及下骨,促进损伤关节的功能恢复^[14,15]。本研究结果显示透明质酸钠联合硫酸氨基葡萄糖钾胶囊临床总有效率是 91.67%,而单一透明质酸钠治疗组的总有效率是 78.33%,提示透明质酸钠与硫酸氨基葡萄糖钾胶囊治疗踝关节损伤,可有效增强临床疗效。

在踝关节功能修复过程中,骨代谢较为活跃,多种标志物含量的将发生改变,可通过测定该类标志物的水平值反映其踝关节康复愈合情况^[16]。BGP 是由骨细胞合成分泌而来对骨矿物质具有结作用的特异性非胶原蛋白^[17],可反映骨细胞功能及软骨内骨化情况;PICP 作为特异性纤维胶原^[18],主要由前胶原形成胶原纤维裂解而来,且水平变化是检测骨细胞活性的灵敏性的重要指标,其水含量越高,则表明成骨细胞活性越高;BALP 是一种由骨化部位的成骨细胞分泌而来的碱性单脂酶,其比例占据血清总碱性磷酸酶的一半^[19],BALP 对磷酸盐离子和钙离子的合成具有促进作用,进而形成磷酸钙沉积于骨胶原的基质中,增加骨密度和强度。有报道表明^[20]机体血清 BALP 水平升高利于骨细胞增殖。本研究结果显示患者经透明质酸钠联合硫酸氨基葡萄糖钾胶囊治疗后,血清 BGP、PICP 及 BALP 水平显著升高,且高于单一透明质酸钠治疗组,同时,踝关节功能康

复情况亦优于单一透明质酸钠治疗组,患者无明显不良反应发生。分析原因是由于硫酸氨基葡萄糖钾胶囊能促进软骨细胞合成并保护其不受破坏性酶的损害,改善关节活动,缓解疼痛,对静止、运动及恢复中的软骨具有保护作用。

综上所述,透明质酸钠联合硫酸氨基葡萄糖钾胶囊治疗踝关节损伤患者的临床疗效显著优于单用透明质酸钠治疗,其可有效改善血清骨性标志物水平,且利于踝关节功能的恢复。

参考文献(References)

- [1] Arroyo-Hernández M, Mellado-Romero M, Páramo-Díaz P, et al. Chronic ankle instability: Arthroscopic anatomical repair[J]. Rev Esp Cir Ortop Traumatol, 2017, 61(2): 104-110
- [2] Shuai L, Yu GH, Feng Z, et al. Application of a paraplegic gait orthosis in thoracolumbar spinal cord injury [J]. Neural Regen Res, 2016, 11(12): 1997-2003
- [3] Wu Q, Sun X, Du L, et al. Association of fibulin-3 concentrations with the presence and severity of knee osteoarthritis: A cross-sectional study[J]. Knee, 2017, 24(6): 1369-1373
- [4] Xiang X, Ozkan A, Chiriboga O, et al. Techno-economic analysis of glucosamine and lipid production from marine diatom Cyclotella sp [J]. Bioresource technology, 2017, 244(2): 1480-1488
- [5] Steinberg N, Waddington G, Adams R, et al. Use of a Textured Insole to Improve the Association Between Postural Balance and Ankle Discrimination in Young Male and Female Dancers [J]. Med Probl Perform Art, 2015, 30(4): 217-223
- [6] Cuéllar-Avaroma A, Jambou S, De Lavigne C, et al. Minimal invasive anterolateral ankle stabilization with a modified Hemi-Castaing technique[J]. Acta Ortop Mex, 2015, 29(4): 212-217
- [7] Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis [J]. Ann Rheum Dis, 1957, 16(4): 494-502
- [8] Maffulli N, Longo UG, Locher J, et al. Outcome of ankle arthrodesis and ankle prosthesis: a review of the current status[J]. British medical bulletin, 2017, 124 (1): 91-112
- [9] Koshino Y, Ishida T, Yamanaka M, et al. Toe-in Landing Increases the

- Ankle Inversion Angle and Moment During Single-Leg Landing: Implications in the Prevention of Lateral Ankle Sprains[J]. *Journal of sport rehabilitation*, 2017, 26(6): 530-535
- [10] Fuglsang EI, Telling AS, Sørensen H, et al. Effect of Ankle Mobility and Segment Ratios on Trunk Lean in the Barbell Back Squat[J]. *Journal of strength and conditioning research*, 2017, 31(11): 3024-3033
- [11] Ryu YA, Jin M, Kang N, et al. Histological, Physical Studies after Xenograft of Porcine Ear Cartilage[J]. *Arch Craniofac Surg*, 2017, 18(3): 155-161
- [12] Brorsson A, Willy RW, Tranberg R, et al. Heel-Rise Height Deficit 1 Year After Achilles Tendon Rupture Relates to Changes in Ankle Biomechanics 6 Years After Injury[J]. *The American journal of sports medicine*, 2017, 45(13): 3060-3068
- [13] Akin D, Ozmen S, Yilmaz ME, et al. Hyaluronic Acid as a New Biomarker to Differentiate Acute Kidney Injury From Chronic Kidney Disease[J]. *Iran J Kidney Dis*, 2017, 11(6): 409-413
- [14] Meza-Morelos D, Fernandez-Maestre R. Caffeine and glucosamine mobility shifts by adduction with 2-butanol depended on interaction energy, charge delocalization, and steric hindrance in ion mobility spectrometry[J]. *Journal of mass spectrometry*, 2017, 52(12): 823-829
- [15] Passalacqua LFM, Jimenez RM, Fong JY, et al. Allosteric Modulation of the Faecalibacterium prausnitzii Hepatitis Delta Virus-like Ribozyme by Glucosamine 6-Phosphate: The Substrate of the Adjacent Gene Product[J]. *Biochemistry*, 2017, 56(45): 6006-6014
- [16] Steinberg N, Waddington G, Adams R, et al. Use of a Textured Insole to Improve the Association Between Postural Balance and Ankle Discrimination in Young Male and Female Dancers [J]. *Med Probl Perform Art*, 2015, 30(4): 217-223
- [17] Liu X, Brock KE, Brennan-Speranza TC. et al. Comment on Association between serum osteocalcin and body mass index: a systematic review and meta-analysis[J]. *Endocrine*, 2017, 58(3): 595-596
- [18] Berger PK, Pollock NK, Laing EM, et al. Zinc Supplementation Increases Procollagen Type 1 Amino-Terminal Propeptide in Premenarcheal Girls: A Randomized Controlled Trial[J]. *The Journal of nutrition*, 2015, 145(12): 2699-2704
- [19] Sun R, Wang J, Zheng Y, et al. Traditional Chinese medicine baixin decoction improves cardiac fibrosis of rats with dilated cardiomyopathy[J]. *Exp Ther Med*, 2017, 13(5): 1900-1906
- [20] Kang SJ, Choi BR, Kim SH, et al. Anti-climacterium effects of pomegranate concentrated solutions in ovariectomized ddY mice[J]. *Exp Ther Med*, 2017, 13(4): 1249-1266

(上接第 1940 页)

- [18] Dong SL, Chen X, Tu ZX, et al. Aneurysm of the Anomalous Splenic Artery Arising from Superior Mesenteric Artery Treated by Coil Embolization: A Report of Two Cases and Literature Review[J]. *Ann Vasc Surg*, 2018, 48(251): e5-251.e10
- [19] Zoremba M, Kommann D, Vojnar B, et al. Recovery and prediction of postoperative muscle power - is it still a problem? [J]. *BMC Anesthesiol*, 2017, 17(1): 108
- [20] Venturini M, Marra P, Colombo M, et al. Endovascular Repair of 40 Visceral Artery Aneurysms and Pseudoaneurysms with the Viabahn Stent-Graft: Technical Aspects, Clinical Outcome and Mid-Term Patency[J]. *Cardiovasc Intervent Radiol*, 2018, 41(3): 385-397
- [21] Han K, Kim MD, Diffley M, et al. Safety and effectiveness of transarterial embolization for splenic artery hemorrhage in patients undergoing radical gastrectomy[J]. *Acta Radiol*, 2018, 59(8): 939-945
- [22] Akhtar MI, Sharif H, Hamid M, et al. Fast Track Extubation In Adult Patients On Pump Open Heart Surgery At A Tertiary Care Hospital [J]. *J Ayub Med Coll Abbottabad*, 2016, 28(4): 639-643
- [23] Alamri Y, Moon D, Yen DA, et al. Ten-year experience of splenic trauma in New Zealand: the rise of non-operative management [J]. *N Z Med J*, 2017, 130(1463): 11-18
- [24] Philips CA, Kumar L, Augustine P. Partial splenic artery embolization for severe hepatic myelopathy in cirrhosis [J]. *Hepatology*, 2018, 67(3): 1169-1171
- [25] Rao JH, Zhang F, Lu H, et al. Effects of multimodal fast-track surgery on liver transplantation outcomes [J]. *Hepatobiliary Pancreat Dis Int*, 2017, 16(4): 364-369
- [26] Ologun G, Sharpton K, Granet P. Successful use of resuscitative endovascular balloon occlusion of the aorta in the treatment of ruptured 8.5-cm splenic artery aneurysm[J]. *J Vasc Surg*, 2017, 66(6): 1873-1875
- [27] Seeber GH, Wijnen A, Lazovic D, et al. Effectiveness of rehabilitation after a total hip arthroplasty: a protocol for an observational study for the comparison of usual care in the Netherlands versus Germany[J]. *BMJ Open*, 2017, 7(8): e016020
- [28] Rasuli P, Moosavi B, French GJ, et al. Splenic Artery Embolization in Blunt Trauma: A Single-Center Retrospective Comparison of the Use of Gelatin Sponge Versus Coils[J]. *AJR Am J Roentgenol*, 2017, 209(6): W382-W387
- [29] Rana SS, Kumar A, Lal A, et al. Safety and efficacy of angioembolisation followed by endoscopic ultrasound guided transmural drainage for pancreatic fluid collections associated with arterial pseudoaneurysm[J]. *Pancreatology*, 2017, 17(5): 658-662
- [30] Senturk JC, Kristo G, Gold J, et al. The Development of Enhanced Recovery After Surgery Across Surgical Specialties [J]. *J Laparoendosc Adv Surg Tech A*, 2017, 27(9): 863-870