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经皮椎体成形术对老年骨质疏松性胸腰椎压缩骨折患者血清 MMP-3、TIMP-1、IL-6 及疗效的影响 *

张 晶¹ 杜 耿¹ 刘 伟¹ 刘 冲¹ 卫宝宁¹ 王 震²

(1 榆林市第一医院 骨科 陕西 榆林 719000; 2 延安大学第二附属医院 骨科 陕西 延安 719000)

摘要 目的:探讨经皮椎体成形术对老年骨质疏松性胸腰椎压缩骨折患者血清基质金属蛋白酶-3(MMP-3)、基质金属蛋白酶抑制因子-1(TIMP-1)、白细胞介素-6(IL-6)及疗效的影响。**方法:**选择60例2016年10月到2017年3月我院接诊的老年骨质疏松性胸腰椎压缩骨折患者,依照随机数表法分为实验组和对照组,每组30例,在都给予常规药物治疗的基础上,对照组给予复位枕垫和康复训练治疗,实验组采用经皮椎体成形术治疗。**结果:**治疗前,两组血清MMP-3、TIMP-1、IL-6水平无差异($P>0.05$);治疗后,两组血清MMP-3、IL-6水平均降低,实验组下降幅度更大,两组血清TIMP-1水平均升高,实验组上升幅度更大($P<0.05$);治疗前,两组患者VAS评分无差异($P>0.05$),治疗1周及治疗后,实验组患者VAS评分均低于对照组($P<0.05$);治疗前,两组患者Cobb角无差异($P>0.05$),治疗后,两组患者Cobb角均明显下降,实验组较对照组下降更大($P<0.05$);治疗前,两组患者伤椎高度比无差异($P>0.05$),治疗后,两组伤椎高度比明显下降,实验组低于对照组($P<0.05$);治疗后,实验组有效率96.67%大于对照组的76.67%,差异显著($P<0.05$)。**结论:**经皮椎体成形术能有效降低患者血清MMP-3、IL-6水平,恢复TIMP-1水平,能显著提高治疗老年骨质疏松性胸腰椎压缩骨折的疗效

关键词:经皮椎体成形术;老年骨质疏松性胸腰椎压缩骨折;基质金属蛋白酶-3;基质金属蛋白酶抑制因子-1;白细胞介素-6

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Effects of Percutaneous Vertebroplasty on Serum MMP-3, TIMP-1, IL-6 and Efficacy in Elderly Patients with Osteoporotic Thoracolumbar Vertebral Compression Fracture*

ZHANG Jing¹, DU Geng¹, LIU Wei¹, LIU Chong¹, WEI Bao-ning¹, WANG Zhen²

(1 Department of orthopedics, Yulin First Hospital, Yulin, Shaanxi, 719000, China;

2 Department of orthopedics, the Second Affiliated Hospital of Yan'an University, Yan'an, Shaanxi, 719000, China)

ABSTRACT Objective: To investigate the effects of percutaneous vertebroplasty on serum levels of matrix metalloproteinase-3 (MMP-3), matrix metalloproteinase-1 (TIMP-1) and interleukin-6 (IL-6) and therapeutic effect. **Methods:** 60 cases of 2016 years in October 2017 to March 2017 in our hospital admissions of elderly osteoporotic thoracolumbar vertebral compression fractures, according to the random number table method is divided into experimental group and control group, each group of 30 cases, are given conventional On the basis of drug treatment, the control group was given conservative treatment such as reduction pillow and rehabilitation training, and the experimental group was treated by percutaneous vertebroplasty. **Results:** Before treatment, the levels of serum MMP-3, TIMP-1 and IL-6 were not significantly different between the two groups ($P>0.05$). After treatment, the levels of serum MMP-3 and IL-6 were decreased ($P<0.05$). Before treatment, There was no significant difference in VAS score between the two groups ($P>0.05$). After 1 week of treatment and after treatment, the VAS score of the experimental group was lower than that of the control group ($P<0.05$). Before treatment, there was no difference in Cobb angle between the two groups ($P>0.05$), after treatment, the Cobb angle of the two groups was significantly lower than that of the control group ($P>0.05$). There was no significant difference in the height ratio between the two groups before treatment ($P>0.05$), After treatment, the height of the two groups was significantly lower than that of the control group ($P<0.05$). After treatment, The effective rate was 96.67% in the experimental group and 76.67% in the control group, the difference was significant ($P<0.05$). **Conclusion:** Percutaneous vertebroplasty can effectively reduce the levels of serum MMP-3 and IL-6 and restore the level of TIMP-1, which can significantly improve the treatment of osteoporotic thoracolumbar vertebrae compression fractures.

Key words: Percutaneous vertebroplasty; Elderly osteoporotic thoracic and lumbar vertebrae compression fractures; Matrix metalloproteinase-3; Matrix metalloproteinase-1; Interleukin-6

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作者简介:张晶(1983-2),男,硕士研究生,主治医师,研究方向:骨科,电话 15929989224, E-mail: 79988683@qq.com

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前言

腰椎压缩性骨折是指以椎体纵向高度被压扁为主要表现的一种脊柱骨折,前柱压缩而椎弓正常,是脊柱骨折中最常见的一种类型^[1]。临床多以第11、12胸椎和第1、2腰椎最为多见,老年人由于骨质疏松的缘故,发生率更高^[2]。有数据表明^[3],老年骨质疏松性胸腰椎压缩骨折的发病风险在持续上升,而传统的以功能锻炼并药物辅助的治疗方法,存在疗程长、疗效不稳定等缺点,故随着生物科学,材料学的发展,通过微创手术向体内注入内固定系统的外科治疗方法受到广泛重视^[4]。经皮椎体成形术(PVP)是利用穿刺将骨水泥从椎弓根注入椎体,提高伤椎强度,恢复椎体高度,达到治疗目的。但其总体疗效的报道不一^[5],仍需进一步的临床验证。在患者关节液中检测到多种含量异常的细胞因子,其中破骨细胞表达的基质金属蛋白酶-3(MMP-3)和白细胞介素-6(IL-6)在骨代谢中起重要作用,基质金属蛋白酶抑制因子-1(TIMP-1)可抑制性调控骨基质降解^[6,7],检测血清MMP-3、TIMP-1、IL-6水平变化具有监控免疫功能、骨代谢水平及反映骨密度的临床意义。本研究对对照组给予复位枕垫和康复训练治疗,实验组采用经皮椎体成形术治疗,探讨经皮椎体成形术对老年骨质疏松性胸腰椎压缩骨折患者血清MMP-3、TIMP-1、IL-6水平及疗效的影响。现报道如下:

1 资料与方法

1.1 一般资料

60例老年骨质疏松性胸腰椎压缩骨折患者均来自于我院2016年10月~2017年3月,依照随机数表法分为实验组和对照组,所有患者及其家属均被告知,同意参与该研究,并经得我院伦理委员会批准实施。入选标准:X射线片、MRI扫描或CT检查确诊为腰椎压缩骨折,年龄大于60岁,1个椎体损伤,无椎管内占位,脊髓和神经根无受损受压症状。排除标准:恶性肿瘤、骨病理性改变导致的胸腰椎压缩骨折患者,合并肝、肾、心等脏器病变患者,身体素质不宜手术者。对照组30例,男15例,女15例,年龄(64.25±4.10)岁,病程(10.50±4.75)天,损伤椎节段:T11 1例,T12 5例,L1 17例,L2 7例。实验组30例,男15例,女15例,年龄(65.45±3.75)岁,病程(10.16±4.38)天,损伤椎节段:T11 2例,T12 7例,L1 13例,L2 8例。两组患者基本资料无显著差异($P>0.05$)。

1.2 方法

在均给予止痛药,钙制剂,维生素D和阿仑膦酸钠(10mg/d)治疗的基础上,对照组采用保守法治疗,即入院时在受损椎体位置下放置复位矫正枕垫,随患者所能承受的最大高度而渐进升高,保证治疗1周内卧床,功能锻炼以上肢和下肢为主;1周后采用五点法,以头部、肘部和足跟部撑起全身,背部腾空,每日3~4次,每次40下;4~8周时在护腰保护下离床站立、行走。实验组采用经皮椎体成形术治疗,手术方法:病人俯卧,局麻后在C形臂X线机的引导下将椎体穿刺针经椎弓根敲进椎体,针尖位于椎体的前1/3处。搅拌混有显影剂的骨水泥(PMMA)及其溶剂,在稀粥状态注入椎体,胸椎3~4 mL,腰椎4~6 mL。正位透视图像观察骨水泥左右弥散,侧位图像观察前后弥散,若骨水泥出现渗漏立即停止注入。待骨水泥凝固,拔针,局部压迫

切口,无菌包扎。患者术后静卧30 min翻身。给予抗生素。治疗2周出院,随访6周。

1.3 观察指标

1.3.1 血清指标测定 分别取两组患者入院时和治疗8周的清晨空腹外周静脉血5 mL,3000 r/min离心15 min取得血清,ELISA法检测,采用上海雅吉公司的试剂盒检测血清MMP-3、TIMP-1和IL-6水平。

1.3.2 疗效观察 根据视觉模拟评分法(VAS)评价患者入院时,治疗1周和治疗后8周的疼痛程度,10分制,得分越高,疼痛程度越大;依据X射线片脊柱标准全长的正位相,伤椎上端椎上缘划一横线,伤椎下端椎下缘划一横线,两横线的垂线夹角为Cobb角,反映受损椎体高度恢复情况和治疗矫正情况;测量伤椎椎体高度,计算伤椎高度比,反映受损程度和恢复情况。

1.3.3 总体疗效评价 在术后进行总体评价,基本治愈:临床症状基本消退,疼痛基本消失,恢复正常生活能力;显著有效:临床症状显著减轻,躯体功能显著恢复,疼痛存在;一般有效:临床症状有所减轻,躯体功能有所改善,疼痛有所缓解;基本无效:临床症状无减轻,躯体功能障碍,需卧床,疼痛无缓解。

1.4 统计学分析

本文数据处理采用SPSS18.0,均数±标准差($\bar{x} \pm s$)表示计量资料,t检验用于两组间比较,[(例)%]表示计数资料,用 χ^2 检验比较,秩和检验进行等级资料的比较, $P<0.05$ 有统计学意义。

2 结果

2.1 两组治疗前后血清MMP-3、TIMP-1、IL-6比较

治疗前,两组血清MMP-3、TIMP-1、IL-6水平无差异($P>0.05$);治疗后,两组血清MMP-3、IL-6均降低,实验组下降幅度更大,两组血清TIMP-1均升高,实验组上升幅度更大($P<0.05$),具体数据见表1。

2.2 两组VAS评分比较

治疗前,两组患者VAS评分无差异($P>0.05$),治疗1周及治疗后,实验组患者VAS评分均低于对照组,差异有统计学意义($P<0.05$),具体数据见表2。

2.3 两组Cobb角比较

治疗前,两组患者Cobb角无差异($P>0.05$),治疗后,两组患者Cobb角均明显下降,实验组较对照组下降更大,差异有统计学意义($P<0.05$),具体数据见表3。

2.4 两组伤椎高度比比较

治疗前,两组患者伤椎高度比无差异($P>0.05$),治疗后,两组伤椎高度比明显下降,实验组低于对照组,组间差异显著($P<0.05$),具体数据见表4。

2.5 两组总体疗效比较

实验组有效率96.67%大于对照组的76.67%,差异显著($P<0.05$),具体数据见表5。

3 讨论

骨质疏松是一种以低骨量和骨组织微结构破坏为特征,导致骨质脆性增加和易于骨折的全身性骨代谢性疾病^[8]。椎体是脊柱的承重部位,松质骨是其主要构成,因而是骨质疏松性骨折的高风险部位^[9]。据报道^[10],我国老年骨质疏松性骨折发病率

超过 20%，严重危害老年人健康。近年来经皮椎体成形术 (PVP) 的应用逐渐推广，除了脊椎血管瘤、骨髓瘤、溶骨性转移瘤外，更多应用于骨质疏松性椎体压缩骨折伴有顽固性疼痛的患者并体现出了极大的优越性^[11]。PVP 继承了椎体成形术的优

表 1 两组治疗前后血清 MMP-3、TIMP-1、IL-6 比较($\bar{x} \pm s$)Table 1 Comparison of serum MMP-3, TIMP-1, IL-6 before treatment and after treatment between two groups ($\bar{x} \pm s$)

Groups	Time	MMP-3(mmol/L)	TIMP-1(μ g/L)	IL-6(mmol /L)
Control group(n=30)	before treatment	25.18 $\pm$ 3.09	137.62 $\pm$ 10.45	3.85 $\pm$ 0.57
	after treatment	30.56 $\pm$ 4.13	121.40 $\pm$ 18.36	7.05 $\pm$ 0.82
Treatment group(n=30)	before treatment	29.87 $\pm$ 4.50	124.71 $\pm$ 15.43	7.14 $\pm$ 0.96
	after treatment	22.58 $\pm$ 2.47	143.990 $\pm$ 8.92	2.29 $\pm$ 0.34
t/pControl group value		5.7130,0.0000	4.2053,0.0001	17.5508,0.0000
t/pTreatment group value		7.7784,0.0000	5.8974,0.0000	26.0838,0.0000
t/p values befroe treatment		0.6187,0.5385	0.7559,0.4527	0.3904,0.6976
t/p Value after treatment.		3.5999,0.0007	2.5035,0.0151	12.8740,0.0000

表 2 两组 VAS 评分比较($\bar{x} \pm s$)Table 2 Comparison the VAS score between two groups($\bar{x} \pm s$)

Groups	Before treatment	After treatment 1 week	Before treatment 8 weeks
Control group(n=30)	8.10 $\pm$ 1.02	4.89 $\pm$ 0.88	2.45 $\pm$ 0.21
Treatment group(n=30)	8.12 $\pm$ 0.94	3.75 $\pm$ 0.71	2.29 $\pm$ 0.26
t	0.0790	5.5222	2.6221
P	0.9373	0.0000	0.0111

表 3 两组 Cobb 角比较($\bar{x} \pm s$)Table 3 Comparison the cobb Angle between two groups($\bar{x} \pm s$)

Groups	Before treatment	After treatment	t	P
Control group(n=30)	25.67 $\pm$ 2.80	18.26 $\pm$ 3.30	9.3780	0.0000
Treatment group(n=30)	25.74 $\pm$ 2.59	11.54 $\pm$ 3.55	17.6991	0.0000
t	0.1005	7.5939		
P	0.9203	0.0000		

表 4 两组伤椎高度比比较($\bar{x} \pm s$)Table 4 Comparison the injured vertebral height between two groups($\bar{x} \pm s$)

Groups	Before treatment	After treatment	t	P
Control group(n=30)	63.08 $\pm$ 4.36	16.42 $\pm$ 6.25	33.5368	0.0000
Treatment group(n=30)	62.91 $\pm$ 4.50	8.46 $\pm$ 5.47	42.1049	0.0000
t	0.1486	5.2493		
P	0.8824	0.0000		

表 5 两组总体疗效比较[(例)%]

Table 5 Comparison the clinical efficacy between two groups[(n)%]

Group	Basic cure	Significantly effective	Generally effective	Basic invalid	Effective rate
Control group(n=30)	10(33.33)	7(23.33)	8(26.67)	7(23.33)	23(76.67)
Treatment group(n=30)	15(50.00)	10(33.33)	4(13.33)	1(3.33)	29(96.67)
u/χ^2		2.3325			2.2596
P		0.0197			0.0238

点而无与开放手术有关的并发症。PVP 是一种微创脊柱外科手术,创伤小,适合大多老年患者耐受。据报道 PVP 能够缓解疼痛并且在结构上加强被溶骨破坏的椎体,使得患者的痛苦减轻并且能够继续日常的负重活动^[12]。

聚甲基丙烯酸甲酯(PMMA)是骨水泥主要成分,术中应使骨水泥均匀弥散填充在骨小梁中,增加其力学性能,减少应力损伤。据报道^[13],患者疼痛缓解机制可能和 PMMA 的直接细胞毒性对神经末梢的损伤和其聚合放热对神经末梢的热损伤作用有关。骨水泥渗漏是术中常见的并发症,若发生渗漏,需立即停止注入,其带来的影响不仅是压迫,还有聚合放热对神经根、脊髓的不可回复性损伤。本研究术中有未出现骨水泥渗漏。

基质金属蛋白酶(MMP)是一组锌与钙离子依赖性的肽链内切酶,它们的生物学功能主要是降解细胞外基质蛋白质^[14]。其中 MMP-3 由破骨细胞表达,是骨破坏的重要调节因素,参与骨质疏松炎症^[15]。Valimäki J 等人的研究证实^[16],骨与关节的不稳定性能刺激 MMP-3 的分泌。基质金属蛋白酶抑制因子-1 (TIMP-1)是一种糖蛋白,可抑制 MMP 活性,调节骨代谢,维护细胞外基质的稳定,其血清水平过低提示骨代谢异常,骨破坏活跃,骨密度低^[17]。IL-6 是促炎因子,骨折患者血清有高表达特征,因此可以用来辅助判断骨折和监视骨质疏松炎症水平。有研究发现^[18],IL-6 与 VAS 评分存在微弱关联。本研究二组患者血清 MMP-3、IL-6 均降低,TIMP-1 均升高,PVP 治疗组变化幅度更大,提示 PVP 对骨代谢平衡恢复程度影响较大。

保守法配合药物辅助治疗随避免了手术风险,但其疗效经大量实践论证^[19],有效率大体在 70%之下,张向阳等人在配合功能锻炼治疗下^[20],随访 14 月,有 85%的有效率。本研究亦获得了 76%的有效率。靳丹等人总结了 130 例老年骨质疏松性胸腰椎压缩骨折患者应用 PVP 治疗的结果^[21],患者 VAS 评分大大降低,1 年的随访时间内,85%以上的患者疼痛完全缓解,疗效显著,且未见复发。根据 Elapavaluru S 等人的研究发现^[22],PVP 治疗的患者疼痛缓解率可超过 90%。本研究发现,PVP 治疗组患者 VAS 评分、Cobb 角、伤椎高度比均显著下降,较保守法治疗组差异较大,有效率达到 96%,其中达到疼痛显著缓解,躯体功能显著恢复者占 83%以上,患者术后 2 周即可出院,临床疗效确切,和临床报道结果相似。

综上所述,经皮椎体成形术能有效降低患者血清 MMP-3、IL-6 水平,恢复 TIMP-1 水平,能显著提高治疗老年骨质疏松性胸腰椎压缩骨折的疗效。

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