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骨肽注射液对四肢骨折患者骨代谢、红细胞相关指标及炎症因子水平的影响

汪志举¹ 王俊生² 张 鹏² 赵 磊¹ 刘庆锴¹

(1 赤峰市医院创伤科 内蒙古 赤峰 024000; 2 长治市第二人民医院骨科 山西 长治 046099)

摘要 目的:研究骨肽注射液对四肢骨折患者骨代谢、红细胞相关指标及炎症因子水平的影响。**方法:**选取 2015 年 4 月-2017 年 4 月我院收治的四肢骨折患者 84 例,将其以随机数字表法分成研究组(n=42)与对照组(n=42)。对照组予以常规治疗,研究组则在常规治疗的基础上予以骨肽注射液治疗。分别比较两组骨折愈合时间、治疗前后骨代谢、红细胞相关指标以及炎症因子水平变化情况。**结果:**研究组上肢骨折、下肢骨折愈合时间分别少于对照组(P<0.05)。治疗 4 周后研究组骨碱性磷酸酶(BALP)、I 型前胶原羧基端前肽(PICP)、骨钙素(BGP)水平均高于对照组和治疗前,而 I 型胶原羧基端肽 β 特殊序列(β -CTX)水平低于对照组和治疗前(P<0.05)。治疗 4 周后研究组红细胞积聚指数(EAI)、红细胞电泳指数(EEI)水平均低于对照组和治疗前,而红细胞免疫促进因子(RFER)、直向肿瘤红细胞花环率(DTER)水平较对照组和治疗前均升高(P<0.05)。治疗 4 周后两组患者 C 反应蛋白(CRP)、白细胞介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平均低于治疗前,且研究组 CRP、TNF- α 水平较对照组降低(P<0.05)。**结论:**骨肽注射液应用于四肢骨折患者中可促进骨折愈合,改善骨代谢、红细胞相关指标以及炎症因子水平,值得临床应用。

关键词:四肢骨折;骨肽注射液;骨代谢;红细胞相关指标;炎症因子

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Influence of Ossotide Injection on Bone Metabolism, Erythrocyte Related Indexes and Inflammatory Factor Levels in Patients with Limb Fracture

WANG Zhi-ju¹, WANG Jun-sheng², ZHANG Peng², ZHAO Lei¹, LIU Qing-kai¹

(1 Department of Traumatology, Chifeng Municipal Hospital, Chifeng, Inner Mongolia, 024000, China;

2 Department of Orthopedics, Changzhi Second People's Hospital, Changzhi, Shanxi, 046099, China)

ABSTRACT Objective: To study influence of ossotide injection on bone metabolism, erythrocyte related indexes and inflammatory factor levels in patients with limb fracture. **Methods:** A total of 84 patients with limb fracture, who were treated in Chifeng Municipal Hospital from April 2015 to April 2017, were selected and randomly divided into study group (n=42) and control group (n=42). The control group was given routine treatment, the study group was given ossotide injection on the basis of routine treatment. The time of fracture healing, bone metabolism, erythrocyte related indexes and the levels of inflammatory factors in the two groups before and after treatment were compared. **Results:** The healing time of upper limb fracture and lower limb fracture in the study group was less than that of the control group (P<0.05). After 4 weeks of treatment, the levels of bone alkaline phosphatase (BALP), procollagen carboxyterminal propeptide (PICP) and bone gla protein (BGP) in the study group were higher than those in the control group and before treatment, but the levels of β -isomer of the C-terminal telopeptide of type I collagen (β -CTX) was lower than those in the control group and before treatment (P<0.05). After 4 weeks of treatment, the erythrocyte electrophoresis index (EAI) and erythrocyte electrophoresis index (EEI) were lower than those in the control group and before treatment, and rosette forming enhancing rate (RFER) and direct tumor erythrocyte rosette rate (DTER) were higher than those in the control group and before treatment (P<0.05). After 4 weeks of treatment, the levels of C reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in the two groups were all lower than those before treatment, and the levels of CRP and TNF- α in the study group were lower than those in the control group (P<0.05). **Conclusion:** The application of ossotide injection in the patients with limb fracture can promote fracture healing and improve bone metabolism, erythrocyte related indexes and inflammatory cytokines, which is worthy of clinical application.

Key words: Limb fracture; Ossotide injection; Bone metabolism; Erythrocyte related index; Inflammatory factor

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前言

作者简介:汪志举(1975-),男,硕士,副主任医师,从事创伤骨科方面的研究, E-mail: edmhur@163.com

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骨折属于临床上最为常见的疾病之一,而四肢骨折在骨折疾病中较为多见,对患者的肢体功能具有极大的损害,并且对患者日常工作、学习以及生活造成严重的不良影响^[1,2]。骨折的愈合过程相对缓慢,因此对治疗效果与康复速度均有不同程度

的要求。有研究报道显示^[3,4],骨折的愈合是从组织和细胞两方面同时进行修复的过程,在整个复杂而连续的过程中,骨代谢指标水平的表达情况对骨折愈合的速度以及效果会产生直接影响。另有研究报道表明,机体在发生骨折后由于应激反应会分泌炎症因子,因此这些炎症因子可作为临床上反映疾病转归的指标^[5-7]。此外,在骨折发生时红细胞相关指标表达存在明显的异常,因此在临床治疗中如何有效改善其表达水平亦是主要治疗目标之一^[8]。既往,临床上主要采用手术内固定治疗,术后予以常规抗感染治疗以及相关功能锻炼,但该治疗方式效果并不十分理想。骨肽注射液主要成分为活性肽,同时还富含多种促进骨生长的微量元素和骨生长因子,可刺激细胞分裂、增殖以及趋向运动,进而促进骨骼的愈合^[9,10]。鉴于此,本文通过研究骨肽注射液对四肢骨折患者骨代谢、红细胞相关指标及炎症因子水平的影响,以期临床治疗提供数据支持。结果如下。

1 资料与方法

1.1 一般资料

选取 2015 年 4 月 -2017 年 4 月我院收治的四肢骨折患者 84 例。纳入标准:(1)所有患者均经临床 X 线片检查确诊为骨折;(2)骨折部位存在不同程度的疼痛、肿胀及功能障碍者;(3)近期骨折者;(4)年龄在 20-60 岁之间;(5)临床病历资料完整者。排除标准:(1)合并心、肝、肾等脏器功能严重障碍者;(2)伴有炎症疾病或恶性肿瘤者;(3)对本研究相关药物过敏者;(4)妊娠期或哺乳期妇女。将所有患者以随机数字表法划分成研究组(n=42)与对照组(n=42)。其中研究组男性 26 例,女性 16 例;年龄 21-58 岁,平均年龄(40.38± 10.58)岁;骨折部位:上肢骨折 19 例,下肢骨折 23 例;致伤原因:交通事故 18 例,高空坠落 14 例,其他原因 10 例;病程 1-5d,平均病程(2.18± 0.55)d。对照组男性 25 例,女性 17 例;年龄 22-58 岁,平均年龄(40.39± 10.61)岁;骨折部位:上肢骨折 17 例,下肢骨折 25 例;致伤原因:交通事故 19 例,高空坠落 15 例,其他原因 8 例;病程 2-5d,平均病程(2.23± 0.49)d。两组患者一般资料比较均无统计学差异(P>0.05),均衡可比。两组患者均签署了知情同意书,我院伦理委员会已批准此次研究。

1.2 研究方法

对照组入院后采用手术内固定进行治疗,综合患者病情严重程度以及骨折类型选择切开复位交锁髓内针固定术或锁定

钢板内固定术,术后给患者以抗感染治疗,同时进行的相关肢体功能锻炼。研究组则在对照组的基础上予以骨肽注射液(通化惠康生物制药有限公司,国药准字:H22024576,规格:2 mL:10 mg)治疗,即取 20 mL 的骨肽注射液加入 250 mL 生理盐水注射液中混匀,行静脉滴注,1 次/d,两组均连续治疗 4 周。

1.3 观察指标

分别采集两组患者空腹状态下的静脉血 5 mL,采集时间点为治疗前与治疗 4 周后的清晨,随后进行离心处理(转速 3000 r/min,时间 10 min),分离血清与血浆,取上血清置于 -80℃ 冰箱中保存待检。骨代谢相关指标检测:采用琼脂糖凝胶电泳测定骨碱性磷酸酶(bone alkaline phosphatase, BALP)、I 型前胶原羧基端肽(carboxyterminal propeptide of type I procollagen, PICP)水平,采用酶联免疫吸附法检测骨钙素(bone gla protein, BGP)、I 型胶原羧基端肽β 特殊序列(β-isomer of the C-terminal telopeptide of type I collagen, β-CTX)水平。相关试剂盒均购自上海酶联生物科技有限公司,具体操作遵循试剂盒操作指南进行。红细胞相关指标检测:采用 LB-2A 血流变分析仪(购自深圳山智紧密仪器科技有限公司)以及郭峰法检测红细胞积聚指数(erythrocyte aggregation index, EAI)、红细胞电泳指数(erythrocyte electrophoresis index, EEI)、红细胞免疫促进因子(rosette forming enhancing rate, RFER)、直向肿瘤红细胞花环率(direct tumor erythrocyte rosette rate, DTER)水平。炎症因子水平检测:采用酶联免疫吸附法(相关试剂盒均购自上海酶联科技有限公司)检测肿瘤坏死因子-α(tumor necrosis factor-α, TNF-α)、白细胞介素-6(interleukin-6, IL-6)C 反应蛋白(C reactive protein, CRP)水平,具体操作遵循试剂盒操作指南进行。

1.4 统计学方法

采用 SPSS24.0 进行统计分析,性别构成等计数资料以率表示,实施 χ^2 检验,炎症因子水平、骨代谢指标水平、红细胞相关指标水平、骨折愈合时间等计量资料以($\bar{x} \pm s$)表示,实施 t 检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者骨折愈合时间比较

研究组上肢骨折、下肢骨折愈合时间分别少于对照组(P<0.05),见表 1。

表 1 两组患者骨折愈合时间比较($\bar{x} \pm s$)

Table 1 Comparison of fracture healing time between the two groups($\bar{x} \pm s$)

Groups		n	Fracture healing time(weeks)
Study group	Upper limb fracture	19	7.10± 0.94*
	Lower limb fracture	23	10.12± 1.24*
Control group	Upper limb fracture	17	9.22± 1.14
	Lower limb fracture	25	12.28± 1.52

Note: compared with the control group, *P<0.05.

2.2 两组患者血清骨代谢指标水平比较

治疗前研究组患者 BALP、PICP、BGP、β-CTX 水平相比对照组差异无统计学意义(P>0.05),治疗 4 周后研究组 BALP、

PICP、BGP 水平均对照组和治疗前升高,而 β-CTX 水平较对照组和治疗前降低(P<0.05),见表 2。

表 2 两组患者血清骨代谢指标水平比较($\bar{x} \pm s$)Table 2 Comparison of serum bone metabolism indexes in two groups ($\bar{x} \pm s$)

Indexes	Time	Study group(n=42)	Control group(n=42)	t	P
BALP(%)	Before treatment	3.11± 1.55	3.12± 1.57	0.029	0.977
	4 weeks after treatment	5.92± 1.44*	4.08± 1.58*	5.578	0.000
PICP($\mu\text{g/L}$)	Before treatment	94.21± 58.27	94.09± 58.31	0.009	0.993
	4 weeks after treatment	147.40± 36.13*	127.84± 40.23*	2.344	0.022
BGP($\mu\text{g/L}$)	Before treatment	2.06± 0.91	2.05± 0.88	0.051	0.959
	4 weeks after treatment	5.21± 0.90*	3.94± 0.87*	6.575	0.000
β -CTX(ng/mL)	Before treatment	0.58± 0.12	0.58± 0.11	0.000	1.000
	4 weeks after treatment	0.30± 0.10*	0.47± 0.13*	6.717	0.000

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

2.3 两组患者红细胞相关指标水平比较

治疗前研究组患者 EAI、EEI、RFER、DTER 水平相比如对照
组差异无统计学意义(P>0.05),治疗 4 周后研究组 EAI、EEI 水

平均较对照组和治疗前降低,而 RFER、DTER 水平较对照组和
治疗前升高(P<0.05),见表 3。

表 3 两组患者红细胞相关指标水平比较($\bar{x} \pm s$)Table 3 Comparison of erythrocyte related indexes in two groups ($\bar{x} \pm s$)

指标 Index	时间 Time	研究组 Study group (n=42)	对照组 Control group (n=42)	t	P
EAI	Before treatment	5.93± 0.38	5.94± 0.37	0.122	0.903
	4 weeks after treatment	2.55± 0.21*	4.10± 0.27*	29.367	0.000
EEI	Before treatment	8.41± 0.55	8.40± 0.58	0.081	0.936
	4 weeks after treatment	5.21± 0.38*	7.31± 0.42*	24.029	0.000
RFER(%)	Before treatment	46.91± 3.55	46.88± 3.57	0.039	0.969
	4 weeks after treatment	52.81± 4.01*	47.33± 3.72*	6.493	0.000
DTER(%)	Before treatment	30.61± 2.57	30.66± 2.59	0.089	0.930
	4 weeks after treatment	33.74± 3.06*	28.95± 2.44*	7.932	0.000

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

2.4 两组患者炎症因子水平比较

治疗前研究组患者 CRP、IL-6、TNF- α 水平相比如对照组差
异无统计学意义(P>0.05),治疗 4 周后研究组和对照组组患者

CRP、IL-6、TNF- α 水平均较治疗前降低,且研究组 CRP、TNF- α
水平较对照降低(P<0.05),而治疗 4 周后两组 IL-6 水平比较差
异无统计学意义(P>0.05),见表 4。

表 4 两组患者炎症因子水平比较($\bar{x} \pm s$)Table 4 Comparison of levels of inflammatory factors of two groups ($\bar{x} \pm s$)

Groups	CRP(mg/L)		IL-6($\mu\text{g/mL}$)		TNF- α (ng/mL)	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Study group(n=42)	45.58± 13.48	12.02± 5.33*	62.55± 1.19	41.33± 15.02*	560.38± 79.02	429.74± 82.16*
Control group (n=42)	45.62± 13.50	21.47± 5.41*	62.59± 1.20	46.16± 15.27*	560.49± 78.84	488.01± 76.38*
t	0.014	8.064	0.153	1.461	0.006	3.366
P	0.989	0.000	0.879	0.148	0.995	0.001

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

3 讨论

四肢骨折属于临床上较为常见的骨科疾病,此类患者均会出现不同程度的疼痛、骨折部位肿胀和畸形、活动受限等,给患者带来极大的心理负担,影响其生活质量^[11-13]。目前临床上治疗

四肢骨折的方式较多,并且取得了一定的治疗效果,但骨折的愈合是一个漫长且复杂的组织修复过程,在正确复位以及合理固定的前提下,骨愈合快慢还与多种骨生长因子的参与有关^[14-16]。因此,对四肢骨折患者予以适当的药物治疗可促进软组织损伤的修复、增加骨折愈合速度。另有研究报道证实^[17-19],随着

骨折的发生、发展,多种红细胞指标水平亦会随之改变,特别是与红细胞黏滞度指标变化尤为明显,随着其水平的不断升高,会对机体各器官血流速率、营养供应产生影响,进一步引发或加重一系列临床症状。因此,红细胞相关指标不但对骨折创伤本身具有良好的反映作用,同时对治疗效果亦有积极的作用^[20,21]。因此,临床上对红细胞指标水平进行改善是治疗四肢骨折的主要目标之一。

本研究结果发现,研究组上肢骨折、下肢骨折愈合时间分别少于对照组($P<0.05$)。这提示了将骨肽注射液应用于四肢骨折的治疗中可有效促进患者骨折的愈合,效果明显。究其原因,笔者认为可能与骨肽注射液的药理机制有关。具体而言,骨肽注射液可以调节钙、磷、骨代谢,增加骨钙沉积,从而有利于促进骨细胞的增殖,进一步达到新骨形成的目的^[22]。此外,治疗后研究组 BALP、PICP、BGP 水平均高于对照组,而 β -CTX 水平低于对照组($P<0.05$),这提示骨肽注射液可显著改善患者骨代谢指标水平。分析原因,我们认为骨肽注射液是一种为微黄色至淡黄色的澄明液体,其一般从猪骨以及蝎子中提取制备而成,内含大量的骨生长必需微量元素、有机钙、磷等,这些成分可促进骨生长因子的合成,进一步影响骨细胞的细胞活动,从而使间质细胞转变为具有功能性的成软骨细胞,进而促进骨骼愈合^[23]。另外,治疗后研究组 EAI、EEI 水平均低于对照组,而 RFER、DTER 水平均高于对照组($P<0.05$),这提示骨肽注射液能够有效改善患者的红细胞相关指标。其中主要原因在于骨肽注射液具有改善患者微循环的作用,可以为骨折愈合提供充足的血供,同时对患者的免疫功能具有积极的调节功效,从而有效促进红细胞相关指标水平的改善。本研究结果还显示,治疗后研究组 CRP、TNF- α 水平均低于对照组($P<0.05$),这和陈安刚等人的研究报道相似^[24],说明了骨肽注射液应用于四肢骨折的治疗中具有减轻炎症反应的作用。其中主要原因可能是与骨肽注射液具有消炎作用有关,其可达到促进损伤修复以及消炎镇痛的目的^[25]。另外,陈安刚等人的研究结果也显示了骨肽注射液应用于四肢骨折患者中有利于促进骨折愈合,同时改善红细胞相关指标水平,与本文研究相一致。

综上所述,骨肽注射液对四肢骨折患者的骨折愈合具有显著的促进作用,同时有利于骨代谢、红细胞相关指标水平的改善,且可有效减轻炎症反应。具有较高的临床推广应用价值。

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