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丹红注射液联合玻璃酸钠关节腔内注射对胫骨骨折患者血清骨性标志物水平的影响 *

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摘要 目的:研究丹红注射液联合玻璃酸钠关节腔内注射对胫骨骨折术后血清骨性标志物水平的影响。**方法:**研究对象选取我院2015年5月到2016年8月间收治的胫骨骨折患者110例,所有患者均行切开复位内固定手术治疗。采用随机数字法将其分为对照组和观察组,每组各55例。对照组患者玻璃酸钠关节腔内注射治疗,观察组患者配合丹红注射液。比较两组患者的治疗疗效、治疗前后的视觉模拟评分法(VAS评分)、血清骨钙素(bone Glaprotein, BGP)、I型前胶原羧基端肽(carboxyterminal propeptide of type I procollagen, PICP)水平的变化。**结果:**治疗后1、3、7天患处疼痛VAS评分均明显低于对照组($P<0.05$),治疗后1、2、4周观察组患者关节活动度评分均明显高于对照组($P<0.05$),治疗后观察组患者血清BGP、PICP水平均明显高于对照组($P<0.05$)。**结论:**丹红注射液联合玻璃酸钠关节腔内注射能够促进胫骨骨折术后骨折愈合,提高临床疗效。可能与其有效提高患者血清BGP、PICP水平有关。

关键词:丹红注射液;胫骨骨折术后;临床疗效;血清骨钙素;I型前胶原羧基端肽

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Effects of Danhong Injection Combined with Sodium Hyaluronate Intra-articular Injection on Serum Levels of Bone Markers of Patients with Tibial Fracture*

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ABSTRACT Objective: To study the effects of Danhong injection combined with sodium hyaluronate intra-articular injection on the serum levels of bone markers of patients with tibial fracture. **Methods:** 110 cases of patients with tibial fracture in our hospital from May 2015 to August 2016 were randomly divided into the control group and the observation group, 55 cases in each group. The patients in the control group were treated with intra-articular injection of sodium hyaluronate treatment, the observation group were treated with Danhong injection on the basis of control group. The total efficiency, visual analogue score(VAS) and serum bone Glaprotein(BGP) and carboxyterminal propeptide of type I procollagen(PICP) before and after treatment were compared between two groups. **Results:** On the 1st, 3rd, 7th day after treatment, the pain VAS score were significantly lower than those of the control group ($P<0.05$); at 1, 2, 4 weeks after treatment, the joint mobility scores of observation group were significantly higher than those of the control group ($P<0.05$); the serum BGP and PICP levels of the observation group were significantly higher than those of the control group ($P<0.05$). **Conclusion:** Danhong injection can promote the fracture healing, improve the clinical efficacy, which may be related to the improvement of serum BGP and PICP levels.

Key words: Danhong injection; After tibial fracture; Clinical efficacy; BGP; PICP

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前言

胫骨骨折是由外伤所致,位于胫骨干或胫骨平台,多以小腿及膝盖疼痛,结构异常、活动受限为临床表现的骨折^[1]。在全身骨折中,仅胫骨骨折就占13.7%,同时易并发开放性骨折、粉碎性骨折等严重损害,容易引起患者肢体活动障碍,影响膝关

节活动,发生率约为5%~10%^[2]。既往多选择在切开复位内固定基础上进行关节腔内药物注射治疗胫骨骨折,玻璃酸钠为常用药物,其可以润滑关节、增加关节弹性作用,保护关节软骨,但作用时间短,常需持续性维持治疗,并且对于减轻患处疼痛效果不佳,不能明显缩短骨折愈合时间^[3]。

祖国医学治疗骨折可追溯到新石器时代,中药外敷、内服

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应用于骨折等外伤的治疗历史悠久,临床疗效肯定^[4]。目前,中药提取物注射液已广泛应用在胫骨骨折治疗中,且被证实具有疗效高、副作用小等优点^[5]。研究显示^[6]骨折后成骨细胞的活跃程度与血清骨性标志物含量具有正相关关系,尤其是血清骨钙素 (bone Gla-protein, BGP)、I 型前胶原羧基端肽(carboxyterminal propeptide of type I procollagen, PICP),其在临床检测过程中具有灵敏度高、特异性强的特点,是判断骨折愈合程度的常用检测指标。本研究主要探讨了对丹红注射液联合玻璃酸钠关节腔内注射对胫骨骨折术后血清骨性标志物水平的影响。

1 资料与方法

1.1 一般资料

研究对象收集本院骨科病区 2015 年 5 月~2016 年 8 月收治并确诊为胫骨骨折的患者 110 例。纳入标准:符合《临床骨科诊断指南》^[7]中关于胫骨骨折的诊断标准;采取相近方式进行切开复位内固定手术治疗^[8];年龄大于 20 岁且低于 60 岁;①患者清楚具体实验内容及过程并签署知情同意书。排除标准:胫骨开放性骨折、多处骨折、陈旧性骨折、病理性骨折或者骨质疏松的患者;合并有严重全身性疾病患者,如合并神经血管损伤、心肝肾功能及凝血功能异常、恶性肿瘤等;未行切开复位内固定手术治疗者。所有患者均采用随机数字法分为观察组和对照组,每组各 55 例。对照组中,男 34 例,女 21 例,平均年龄(38.14 ± 6.29)岁,胫骨干骨折、胫骨平台骨折患者数分别为 29 例、26 例。观察组中,男 32 例,女 23 例,平均年龄(36.68 ± 3.99)岁,胫骨干骨折、胫骨平台骨折患者数分别为 28 例、27 例。两组患者的性别组成、年龄分布、疼痛部位、骨折类型等一般资料对比差异均无统计学意义($P>0.05$),具可比性。

1.2 治疗方法

根据患者影像学资料及病情等采取适当方式进行切开复位内固定,术中行手法复位及钢板髓内钉螺钉固定,术后按照常规方法进行换药防治感染、镇痛、消肿、康复锻炼等治疗,两

组患者均关节腔内注射玻璃酸钠注射液 1 支^[9](2.5 mL:25 mg×1 支,北京前瑞制药有限公司, H20030364),注射后嘱患者活动膝关节,1 次/周。在此基础上,观察组关节腔内同时注射丹红注射液 1 支^[10](2.0 mL:20 mg×1 支,北京前瑞制药有限公司, H20030364),注射后嘱患者活动膝关节,1 次/周。均连续治疗 4 周。本次研究采用视觉模拟评分法^[11](即 Visual Analogue Scale/Score, 简称 VAS)划分患者患处疼痛程度,具体方法为,疼痛评分为 10 分制,患者根据自我感觉进行评分,0 和 10 分别表示无痛、剧痛,评分越高,疼痛越剧烈。统计膝关节内旋、外旋角度之和,旋转范围越大,代表膝关节活动度越高。治疗前后分别抽取研究对象一份 5.0 mL 外周静脉血,静置 10 min,采用酶联免疫吸附法(ELISA)检查检测血清中 BGP、PICP 水平,试剂盒由亿盛生物制药公司提供,所有步骤均严格参考操作说明书进行。

1.3 观察指标

①比较两组患者的治疗疗效;②比较两组患者治疗后 1、2、4 周膝关节活动度;③比较两组患者治疗前后血清 BGP、PICP 水平的变化。

1.4 统计学分析

采用 SPSS21.0 专业统计学软件进行数据分析,计量资料以均数±标准差($\bar{x} \pm s$)表示,两组间比较采用 t 检验,所有的计数资料以率(n%)表示,两组间比较采用 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者术后 1、3、7 天疼痛情况的比较

治疗后 1、3、7 天,观察组患者患处疼痛 VAS 评分分别为(7.33 ± 0.78)分、(5.34 ± 1.12)分、(2.76 ± 0.61)分,对照组患者患处疼痛 VAS 评分分别为(6.98 ± 0.72)分、(3.94 ± 0.98)分、(1.15 ± 0.56)分,观察组患者治疗后 1、3、7 天患处疼痛 VAS 评分均明显低于对照组($P<0.01$),详情见表 1。

表 1 两组患者术后第 1、3、7 天患处疼痛 VAS 评分的比较($\bar{x} \pm s$)

Table 1 Comparison of the VAS score 1st, 3rd, 7th day after treatment($\bar{x} \pm s$)

Groups	1st day	3rd day	7th day
Control group(n=55)	7.33 ± 0.78	5.34 ± 1.12	2.76 ± 0.61
Observation group(n=55)	6.98 ± 0.72	3.94 ± 0.98	1.15 ± 0.56
P	0.02	0.00	0.00

2.2 两组患者术后 1、2、4 周膝关节活动度比较

术后 1、2、4 周,观察组患者关节活动度评分分别为(41.58 ± 4.76)分、(59.12 ± 5.74)分、(89.54 ± 7.55)分,对照组患者关节活

度评分分别为(44.21 ± 5.29)分、(70.21 ± 6.21)分、(107.10 ± 7.21)分,观察组患者治疗后 1、2、4 周关节活动度评分均明显高于对照组($P<0.01$),详情见表 2。

表 2 两组术后第 1、2、4 周膝关节活动度的比较($\bar{x} \pm s$)

Table 2 Comparison of the knee joint activity at 1, 2 and 4 weeks after the operation($\bar{x} \pm s$)

Groups	1st week	2nd week	4th week
Control group(n=55)	41.58 ± 4.76	59.12 ± 5.74	89.54 ± 7.55
Observation group(n=55)	44.21 ± 5.29	70.21 ± 6.21	107.10 ± 7.21
P	0.01	0.00	0.00

2.3 两组患者治疗前后血清 BGP、PICP 水平的比较

治疗前,两组患者的血清 BGP、PICP 水平比较差异无统计

学意义($P>0.05$);治疗后,实验组患者血清 BGP、PICP 水平均明显高于对照组($P<0.05$),详见表 3。

表 3 两组患者治疗前后的血清 BGP、PICP 水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum BGP and PICP levels before and after treatment between the two groups($\bar{x} \pm s$)

Groups	BGP		PICP	
	Before treatment	After treatment	Before treatment	After treatment
Control group(n=55)	2.25 $\pm$ 0.34	3.12 $\pm$ 0.48 ^⓪	123.25 $\pm$ 14.21	138.26 $\pm$ 16.42 ^⓪
Observation group(n=55)	2.29 $\pm$ 0.32	4.24 $\pm$ 0.63 ^⓪	117.12 $\pm$ 13.47	149.87 $\pm$ 18.72 ^⓪
P	0.52	0.00	0.42	0.00

Note: ⓪ compared with before treatment, $P<0.05$.

3 讨论

胫骨由胫骨平台、胫骨骨干组成,二者均是骨折发生的常见部位^[12]。胫骨平台为膝关节与股骨下段形成的关节面,是膝关节的重要负荷结构,主要作用为增加膝关节的稳定性。骨折对膝关节内、外平台的影响不同,两者受力程度有差异,从而对邻近的韧带和半月板造成伤害,因此胫骨骨折特别是胫骨平台骨折常导致患者膝关节活动不利^[13]。胫骨骨折的治疗目的主要为恢复关节活动,在条件允许的情况下可进一步调整外表的美观性,轻度骨折通常行外固定术或者手法复位治疗即可,但在以下情况时需行切开复位内固定术,如胫骨平台骨折伴平台塌陷、不稳定骨折经非手术疗法无效者、骨折移位明显、手法复位失败、严重粉碎性骨折或双段骨折等^[14]。

胫骨骨折固定术后患者由于紧张、担忧等不良情绪及局部疼痛等不良影响,常不愿进行术后功能锻炼,可能出现疗效降低、恢复时间延长等不良反应,对患者的手术疗效及生活品质造成较大的影响^[15]。针对这种情况,临床上通常应用玻璃酸钠关节腔内注射起润滑、弹性作用,缓冲应力对关节软骨的损害,方便患者早期进行关节锻炼,促进骨折的愈合。研究显示^[16]关节腔内注射玻璃酸钠注射液相对于单纯固定的骨折治疗,可明显缩短骨折愈合时间,是固定术后有效的辅助治疗方法。但药理研究显示^[17]玻璃酸钠不参与骨折愈合的生物学过程,对于促进骨折愈合多发挥的是物理作用,疗效有限,对于减轻局部疼痛效果不佳,从而影响长期预后。

中医治疗骨伤由来已久,并且可以在促进骨折愈合过程中减轻患者局部疼痛、肿胀等症状,使患者更易配合治疗。中医认为骨的断裂常引起局部筋脉受损,进一步导致全身气血流通,气机凝滞,血脉瘀阻,"瘀不去,则新血不得生",因此在术后如果在常规治疗的基础上局部应用活血化瘀药物能有效改善骨折局部血供,减轻局部疼痛,促进骨折的修复与再生,恢复骨折部位的功能^[18]。丹红注射液是由中药红花和丹参的有效提取物制成,丹参具有活血止痛,祛瘀通经,凉血消痈之功,广泛应用于跌打损伤、血脉瘀阻等瘀血症症;红花尤擅长活血祛瘀、止痛消肿,是跌打损伤、瘀滞肿痛的必需药^[19]。临床上已有较多关于玻璃酸钠关节腔内注射对胫骨骨折术后愈合影响的研究报道,对于玻璃酸钠的作用机制研究较清晰,但对于中药促进骨折术后愈合的研究少见报道,因此本研究着重探讨中药对于骨折愈合的影响。丹红注射液为中药的有效提取物,主要发挥活血化

瘀,舒经通脉的作用,可明显改善患肢疼痛、活动障碍等临床症状,本研究结果显示:观察组患处的 VAS 评分明显低于对照组,并且观察组患者膝关节的活动度明显高于对照组,表明胫骨骨折内固定后进行丹红注射液联合玻璃酸钠关节腔内注射可以明显改善局部疼痛症状,提高临床疗效,促进局部功能恢复^[20]。

在骨折术后的自我修复过程中,外界刺激大大激活了大量成骨细胞的活性并促进了骨形成,为断端的再愈合形成了有利条件^[21]。在此过程中,多种反应骨代谢的标志物的含量发生了变化,通过测定该标志物就能有效了解骨折的愈合情况^[22]。BGP 来源于成骨细胞,主要功能是结合骨矿物质,保持骨的矿化速率,其水平是成骨细胞活性的灵敏反映物,是成骨细胞功能的良好标志物。PICP 是一种特异性表达的纤维胶原,主要来源于前胶原,其合成速率受成骨细胞的活动及骨生成的影响, PICP 既是成骨细胞活动的灵敏反应物,也是骨代谢的特异性指标。血清 BGP、PICP 水平能够灵敏反映成骨细胞功能,由此评价胫骨骨折的愈合情况。既往已有研究显示丹红注射液可促进胫骨骨折愈合,但具体机制尚不明确。本研究结果显示:观察组的血清标志物 BGP、PICP 水平均显著高于对照组,提示丹红注射液是通过增加成骨细胞活性,加速骨折的愈合。但本研究的研究对象数目有限,仅在一家医院进行统计,样本采集不够广泛,因此研究结果可能存在偏差,仍需大量数据对本研究进行验证。

综上所述,丹红注射液联合玻璃酸钠关节腔内注射能够促进胫骨骨折术后骨折愈合,提高临床疗效。可能与其有效提高患者血清 BGP、PICP 水平有关。

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