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血流变学指标及血清学指标在骨折延迟愈合患者中的临床意义

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摘要 目的:探讨血流变学和血清学指标在骨折延迟愈合患者中的变化及其临床意义。**方法:**随机选取2010年1月~2016年6月在我院进行手术治疗的骨折延迟愈合及骨折正常愈合患者各90例,分别为观察组与对照组,对比分析两组患者术后第1、8、12周时血清可溶性血管细胞黏附分子1(sVCAM-1)、胰岛素样生长因子1(IGF-1)、血小板衍生生长因子(PDGF)及人可溶性细胞间黏附分子1(sICAM-1)和红细胞刚性指数、红细胞聚集指数、血浆黏度的差异。**结果:**术后第1、8、12周两组血清学及血流变学各指标整体相比差异均具有统计学意义(均 $P<0.05$),且组内两两比较均具有统计学差异(均 $P<0.05$)。术后8、12周观察组血清sICAM-1、sVCAM-1、红细胞刚性指数、红细胞聚集指数、血浆黏度均高于对照组,而血清PDGF、IGF-1均低于对照组,比较差异均具有统计学意义(均 $P<0.05$)。**结论:**骨折患者血清sICAM-1、PDGF、IGF-1、sVCAM-1及红细胞刚性指数、红细胞聚集指数、血浆黏度水平会随着病程进展发生变化,并且血清sICAM-1、sVCAM-1及红细胞刚性指数、红细胞聚集指数、血浆黏度水平的升高,血清PDGF、IGF-1水平的降低可能是引起骨折延迟愈合的重要因素,对于骨折患者的临床治疗具有重要临床意义。

关键词:骨折;延迟愈合;血清学;血液流变学

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Clinical Significance of Hemorheological Indexes and Serological Indexes in Patients with Delayed Fracture Healing

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ABSTRACT Objective: To explore the changes of hemorheology indexes and serological indexes in patients with delayed fracture healing and its clinical significance. **Methods:** 90 patients with delayed fracture healing and 90 patients with normal fracture healing who were treated with surgery in our hospital from January 2010 to June 2016 were randomly selected, they were divided into the observation group and the control group respectively. Then compared the serum soluble vascular cell adhesion molecule-1 (sVCAM-1), insulin-like growth factor-1 (IGF-1), platelet derived growth factor (PDGF), soluble intercellular adhesion molecule-1 (sICAM-1), erythrocyte rigidity index, erythrocyte aggregation index, plasma viscosity of two groups in the 1st, 8th, 12th weeks after surgery. **Results:** The serological indexes and hemorheological indexes in two groups were overall compared in the 1st, 8th, 12th weeks after surgery, the differences were statistically significant (both $P<0.05$), and the pairwise comparison of within each groups were statistically significant (both $P<0.05$). The serum sVCAM-1, sICAM-1, erythrocyte rigidity index, erythrocyte aggregation index, plasma viscosity of the observation group were higher than those of the control group in the 8th, 12th weeks after surgery, while the serum PDGF, IGF-1 of the observation group were lower than those in the control group, the differences were statistically significant (both $P<0.05$). **Conclusion:** The sICAM-1, PDGF, IGF-1, sVCAM-1, erythrocyte rigidity index, erythrocyte aggregation index, plasma viscosity level of patients with fracture will change alone with the disease progresses, the rise of serum sICAM-1, sVCAM-1, erythrocyte rigidity index, erythrocyte aggregation index, plasma viscosity, as well as the drop of serum PDGF, IGF-1 may be the important factors induced delayed fracture healing, which has important clinical significance for the treatment of patients with fracture.

Key words: Fracture; Delayed fracture healing; Serological; Hemorheological

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前言

骨折是临床常见的外科疾病,摔伤、砸伤、坠落、车祸等多种因素均可能导致骨折,因此其发病率一直较高^[1,2]。不同骨折患者由于创伤部位、性质、范围以及医源性因素等不同,导致部

分患者出现骨折延迟愈合,其发生率约在8~10%之间^[3]。骨折延迟愈合使患者的病程延长,增加经济负担,且在一定程度上增加了再次手术的可能性,严重影响患者预后。本研究通过分析骨折延迟愈合患者和骨折正常愈合患者在术后不同时间血液流变学和血清学指标差异,为临床诊疗提供参考,现报道如下。

1 资料与方法

1.1 一般资料

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随机选取我院 2010 月 1 月~2016 年 6 月收治的骨折延迟愈合患者 90 例(观察组),纳入标准:(1)具有明确长骨骨折外伤史,符合临床骨折诊断标准^[7],术后 4 月内骨折未痊愈;(2)影像学检查可见骨折断端无连续性骨痂形成,或可见断端明显间隙。排除标准:(1)患者合并有其他脏器损伤、重要神经损伤;(2)患者骨折部位为颅骨、骨盆、椎体等躯干部位而非长骨骨折,或患者为长骨骨折但合并有其他躯干骨折。观察组包括男性 53 例,女性 37 例;年龄 20~75 岁,平均(47.84±6.97)岁;开放性骨折 41 例,闭合性骨折 49 例;骨折部位:肱骨 18 例,胫腓骨 30 例,股骨 23 例,尺桡骨 19 例;按照 Muller 长骨骨折分类系统对骨折分型:A 型 33 例,B 型 43 例,C 型 14 例。同时选取同一时期骨折正常愈合患者 90 例(对照组),骨折愈合标准:局部无压痛、无叩击痛,局部活动无异常,X 线影像可见骨折线模糊,连续性骨痂形成通过骨折线。对照组包括男性 59 例,女性 31 例;年龄 19~73 岁,平均(45.93±7.41)岁;开放性骨折 34 例,闭合性骨折 56 例;骨折部位,肱骨 20 例,胫腓骨 29 例,股骨 25 例,尺桡骨 16 例;A 型 21 例,B 型 42 例,C 型 27 例。两组患者的性别、年龄、骨折部位、类型资料均不存在统计学差异(P>0.05),具有可比性。全部患者均被告知本研究相关内容,并签署知情同意书,本研究经伦理委员会审核通过。

1.2 研究方法

两组患者相似骨折部位均接受内固定治疗,治疗方法一致。患者术后第 1 周、8 周、12 周分别抽取清晨空腹静脉血 5 mL/管×2 管,1 管用 4000 r/min,离心 3 min,分离血清,置于-40℃环境下保存备用。血清可溶性血管细胞黏附分子 1(soluble

vascular cell adhesion molecule-1,sVCAM-1)、胰岛素样生长因子 1(insulin-like growth factor-1,IGF-1)、血小板衍生生长因子(platelet-derived growth factor,PDGF)及人可溶性细胞间黏附分子 1(soluble intercellular adhesion molecule-1,sICAM-1)使用酶联免疫吸附测定法(enzyme linked immunosorbent assay,ELISA)检测,试剂盒均购置自上海西唐生物科技有限公司,操作严格按照说明书进行。另 1 管用于血液流变学检测,包括红细胞刚性指数、红细胞聚集指数、血浆黏度,检测使用普利生 LBY-N6C 全自动血流变仪。

1.3 统计学处理

运用 SPSS19.0 统计软件进行数据分析,计量资料以($\bar{x} \pm s$)表示,两两比较采用 t 检验,多个时间点数据比较使用方差分析,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组患者血清 sICAM-1、PDGF、IGF-1、sVCAM-1 比较

组内比较,两组术后第 1、8、12 周血清 sICAM-1、PDGF、IGF-1、sVCAM-1 整体相比,差异均具有统计学意义(均 P<0.05);两组术后第 8、12 周上述指标与术后第 1 周相比,差异均具有统计学意义(均 P<0.05),两组术后第 8 周上述指标与第 12 周相比,差异均具有统计学意义(均 P<0.05)。组间比较,两组术后 1 周全部血清学指标比较,差异均无统计学意义(均 P>0.05);术后 8、12 周观察组血清 sICAM-1、sVCAM-1 高于对照组,PDGF、IGF-1 低于对照组,比较差异均具有统计学意义(均 P<0.05)。见表 1。

表 1 两组患者术后第 1 周、8 周、12 周各项血清学指标比较

Table 1 Comparison of serological indexes of two groups patients in the 1st, 8th, 12th weeks after surgery

Groups	Time	sICAM-1(μg/L)	PDGF(U/L)	IGF-1(mg/mL)	sVCAM-1(μg/L)
Observation group (n=90)	The 1st week	180.76±13.41	120.64±13.28	225.64±15.42	419.34±32.88
	The 8th week	358.22±30.91 ^{ab}	347.33±14.56 ^{ab}	250.14±19.55 ^{ab}	680.28±50.31 ^{ab}
	The 12th week	340.63±19.24 ^{abc}	220.41±12.76 ^{abc}	310.27±20.59 ^{abc}	571.22±16.37 ^{abc}
Control group(n=90)	The 1st week	177.23±13.47	121.82±12.49	229.53±15.78	418.55±33.23
	The 8st week	169.51±19.38 ^b	431.25±15.42 ^b	331.26±14.28 ^b	541.27±40.56 ^b
	The 12th week	121.89±13.28 ^{bc}	320.78±11.06 ^{bc}	410.29±16.37 ^{bc}	506.24±31.58 ^{bc}

Note: Compared with the same period of the control group, ^aP<0.05; Compared with the 1st week after surgery, ^bP<0.05; Compared with 8th week after surgery, ^cP<0.05.

2.2 两组患者的血流变学指标比较情况

组内比较,两组术后第 1、8、12 周红细胞刚性指数、红细胞聚集指数、血浆黏度整体相比,差异均具有统计学意义(均 P<0.05);两组术后第 8、12 周上述指标与术后第 1 周相比,差异均具有统计学意义(均 P<0.05);两组术后第 8 周上述指标与第 12 周相比,差异均具有统计学意义(均 P<0.05)。组间比较,两组术后第 1 周全部血流变学指标比较,差异均无统计学意义(均 P>0.05),而术后第 8、12 周观察组各血流变学指标均高于对照组,比较差异均有统计学意义(均 P<0.05)。见表 2。

3 讨论

目前,针对影响骨折延迟愈合因素,研究显示^[9],影响骨折愈合的因素可以分为物理因素和体质内在因素。物理因素如骨折部位、骨折碎裂严重程度等,这类指标对骨折愈合的影响较为明确^[6,7];患者体质内在因素则包括患者的血液流变学指标和血清学指标,血液流变学指标包括红细胞聚集指数、红细胞刚性指数、血浆黏度等,血清学指标则包括血清 sVCAM-1、IGF-1、PDGF 及 sICAM-1 等。而对于患者体质等内在因素的研究相对较少,尤其是针对患者血清学指标的研究^[8-10]。骨折愈合

表 2 两组患者术后第 1 周、8 周、12 周各血流变学指标比较

Table 2 Comparison of hemorheological indexes of two groups patients in the 1st, 8th, 12th weeks after surgery

Groups	Time	Erythrocyte rigidity index	Erythrocyte aggregation index	Plasma viscosity
Observation group(n=90)	The 1st week	6.51± 0.88	4.20± 0.44	1.54± 0.15
	The 8th week	8.01± 0.92 ^{ab}	7.77± 0.56 ^{ab}	1.92± 0.14 ^{ab}
	The 12th week	8.72± 0.97 ^{abc}	6.74± 0.59 ^{abc}	1.88± 0.20 ^{abc}
Control group(n=90)	The 1st week	6.66± 0.90	4.18± 0.47	1.55± 0.12
	The 8th week	6.13± 0.69 ^b	5.02± 0.39 ^b	1.39± 0.15 ^b
	The 12th week	5.19± 0.51 ^{bc}	2.27± 0.37 ^{bc}	1.25± 0.11 ^{bc}

Note: Compared with the same period of the control group, ^aP<0.05; Compared with the 1st week after surgery, ^bP<0.05; Compared with 8th week after surgery, ^cP<0.05.

过程中如果患者营养状况欠佳,一些患者可能长期患有慢性疾病,特别是老年患者,可能同时伴有骨质疏松的情况,这类患者体内的钙磷代谢较紊乱,使得血液细胞携氧能力以及血流变学等指标等水平异常,引发骨折延迟愈合^[11-13]。

本组研究显示,术后第 1、8、12 周两组血清 sICAM-1、PDGF、IGF-1、sVCAM-1,血流变学指标红细胞刚性指数、红细胞聚集指数、血浆黏度整体相比,差异均具有统计学意义(P<0.05),且术后第 8、12 周上述指标与术后第 1 周相比,差异均具有统计学意义(P<0.05),说明无论是骨折延迟愈合患者还是骨折正常愈合患者,在疾病发展过程中上述各项指标均存在显著变化,从侧面反映出各项指标与骨折愈合具有密切的关系。组间比较,术后 8、12 周观察组血清 sICAM-1、sVCAM-1、红细胞刚性指数、红细胞聚集指数、血浆黏度均高于对照组,而血清 PDGF、IGF-1 低于对照组,比较差异均有统计学意义(P<0.05)。其中红细胞刚性指数、红细胞聚集指数、血浆黏度指标越高可能会直接导致患者血液循环受到影响,从而使患者骨折部位血液循环不畅,形成较多的湍流,血凝状态异常形成较多微型血栓等,从而影响骨折愈合^[14,15]。此处关于红细胞刚性指数的水平与部分文献研究结果有出入^[16],考虑原因可能是样本量不同导致,而本组研究样本量相对较大,因此保留本组研究的结果,并对此项差异在今后继续深入研究。sICAM-1 和 sVCAM-1 是作用于细胞间和细胞外基质的一类黏附因子^[17],能够在一定程度上诱导机体中炎症细胞的趋化作用和黏附作用,使得患者骨折部位炎症细胞聚集,引起过度炎症反应,最终导致骨折延迟愈合^[18]。可见,sICAM-1 和 sVCAM-1 浓度水平对骨折患者的愈合至关重要。PDGF、IGF-1 是非常重要的骨质生长刺激因子,在骨质受损后,其可以参与骨间充质细胞的增殖和分化,促进软骨和成骨细胞增生,诱导软骨内和骨膜内成骨形成^[19,20],因此,骨折延迟愈合患者血清 PDGF、IGF-1 浓度较正常愈合患者降低。

综上所述,骨折延迟愈合患者的红细胞刚性指数、红细胞聚集指数、血浆黏度增加,以及血清 sICAM-1、sVCAM-1 浓度升高和 PDGF、IGF-1 浓度降低,临床对于骨折患者的治疗过程中,能够对上述指标进行动态监测,评价患者预后,并及时根据监测结果进行早期干预,可以在一定程度上促进患者骨折愈合,减轻患者痛苦。

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