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羟考酮注射液对全髋关节置换术患者血清 TNF- α 、IL-6、IL-2 水平及镇痛效果的影响 *

徐 振¹ 何绍明² 周 宁¹ 单 鹏¹ 胡 凯¹

(1 解放军第四五四医院 麻醉科 江苏 南京 210000; 2 南京大学附属鼓楼医院 麻醉科 江苏 南京 210000)

摘要 目的:研究羟考酮注射液对全髋关节置换术患者血清肿瘤坏死因子- α (TNF- α)、白介素-6(IL-6)、IL-2 水平及镇痛效果的影响。**方法:**选取 2015 年 7 月至 2016 年 6 月我院收治的 84 例全髋关节置换术患者,根据患者入院顺序分为观察组和对照组,42 例每组。对照组在术后使用硫酸吗啡注射液,观察组在术后使用羟考酮注射液。比较两组患者治疗前后血清 TNF- α 、IL-6、IL-2 水平的变化、镇痛效果、术后主动直腿抬高 30° 时间、主动外展患肢达 45° 时间及不良反应的发生情况。**结果:**治疗后,两组患者血清 TNF- α 、IL-6、IL-2 水平较治疗前显著升高($P<0.05$),但观察组的血清 TNF- α 、IL-6、IL-2 水平明显低于对照组($P<0.05$)。术后 6、12、24、48、72 h,两组患者的 VAS 评分均呈不同程度的下降,观察组术后 6、12、24、48、72 h 明显高于对照组($P<0.05$)。治疗后,观察组主动直腿抬高 30° 时间、主动外展患肢达 45° 时间显著短于对照组($P<0.05$)。此外,观察组总的不良反应率显著低于对照组($P<0.05$)。**结论:**羟考酮注射液对全髋关节置换术患者血清 TNF- α 、IL-6、IL-2 水平的影响较小,且镇痛效果较好,安全性高。

关键词:羟考酮注射液;全髋关节置换术;肿瘤坏死因子- α ;白介素-6;白介素-2

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Influence of Oxycodone Injection on Serum TNF- α , IL-6 and IL-2 and Analgesic Effect of Patients with Total Hip Arthroplasty*

XU Zhen¹, HE Shao-ming², ZHOU Ning¹, SHAN Peng¹, HU Kai¹

(1 Department of Anesthesiology, the 454 Hospital of PLA, Nanjing, Jiangsu, 210000, China;

2 Department of Anesthesiology, Affiliated Drum Tower Hospital, Nanjing University, Nanjing, Jiangsu, 210000, China)

ABSTRACT Objective: To study the influence of oxycodone injection on the serum levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), interleukin-2(IL-2) and analgesic effect of patients with total hip arthroplasty. **Methods:** From July 2015 to June 2016, 84 patients with total hip arthroplasty were selected in our hospital and divided into the observation group and the control group. The control group was treated by morphine sulfate injection after the operation. The observation group was treated with oxycodone injection. The levels of serum TNF- α , IL-6 and IL-2 before and after treatment, analgesic effect prolonged by 30°, active progression of limb 45° time and the occurrence of adverse reactions were compared between two groups. **Results:** After treatment, the levels of serum TNF- α , IL-6 and IL-2 in both groups were significantly higher than those before treatment ($P<0.05$), but the levels of serum TNF- α , IL-6 and IL-2 in the observation group were significantly lower than those of the control group ($P<0.05$). The VAS scores of both groups were decreased at 6, 12, 24, 48 and 72 hours after operation. The levels of VAS in the observation group were significantly higher than those in the control group at 6, 12, 24, 48 and 72 hours after operation ($P<0.05$). After treatment, the rats in the observation group were raised by 30°, active extubation limb up to 45° time was significantly shorter than that of the control group ($P<0.05$). In addition, the overall adverse reaction rate of observation group was significantly lower than that of the control group ($P<0.05$). **Conclusion:** Oxycodone injection showed little effect on the levels of serum TNF- α , IL-6 and IL-2 of patients with total hip arthroplasty with good analgesic effect and high security.

Key words: Oxycodone injection; Total hip arthroplasty; Tumor necrosis factor- α ; Interleukin-6; Interleukin-2

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前言

在中老年晚期髋关节疾病中,全髋关节置换术属于较为有效的一种治疗方式,能有效缓解疼痛感,并重建髋关节功能^[1]。

临床骨科急需为术后选取一种合理有效的镇痛方案,术后疼痛的解决有助于患者早日完成功能锻炼,促进髋关节活动度的恢复,避免肌肉萎缩和深静脉血栓的发生,减少住院时间^[2]。羟考酮注射液作为高纯度的阿片类镇痛药,模拟机体内源性镇痛物

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作者简介:徐振(1982-),男,本科,医师,研究方向:麻醉

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质功能,可阻碍中枢神经的痛觉传导,具有镇痛效果强、镇痛时间长等优势,同时能发挥抗焦虑和镇静的作用,并且能相应地避免咳嗽、恶心呕吐等不良反应的发生,减少患者对于此药物的依赖性,避免成瘾^[3]。为给临床在髋关节置换术中提供更多可借鉴之处,本研究主要探讨了羟考酮注射液对全髋关节置换术患者血清肿瘤坏死因子- α (TNF- α)、白介素-6(IL-6)、IL-2及镇痛效果的影响。

1 资料与方法

1.1 临床资料

选取2015年7月至2016年6月我院收治的84例全髋关节置换术患者。纳入标准:①意识清晰者,能配合医护人员完成本次研究;②近期内未使用过抗生素治疗者;③心、肝、肾功能齐全者。排除标准:①自身免疫系统疾病合并者;②长时间使用镇痛药物治疗者;③哺乳期或妊娠期妇女。本次研究已取得我院伦理委员会批准,及得到患者及家属同意。根据患者入院顺序分为观察组和对照组,42例每组。其中观察组中男性28例,女性14例;年龄为31~66岁,平均(45.24 $\pm$ 5.54)岁;体质量为55~74 kg,平均(64.36 $\pm$ 2.53)kg;ASA分级:I级27例,II级15例;股骨头缺血性坏死13例,股骨颈骨折22例,髋关节骨性关节炎7例。对照组中男性25例,女性17例;年龄为32~67岁,平均(45.31 $\pm$ 5.49)岁;体质量为54~75 kg,平均(64.29 $\pm$ 2.51)kg;ASA分级:I级24例,II级18例;股骨头缺血性坏死12例,股骨颈骨折21例,髋关节骨性关节炎9例。两组患者性别、年龄、体质量等方面比较无显著差异($P>0.05$),具有可比性。

1.2 治疗方法

所有患者手术均在同一组医师操作下完成,采取连续硬膜外麻醉,取患者侧卧位,入路途径为后外侧,根据标准关节置换技术将骨水泥型假体植入其中。对照组在术后使用5 mg的硫酸吗啡注射液(生产厂家:青海制药厂有限公司,规格:1 mL:10 mg,生产批号:20150204),给药方式为肌肉注射,4次/天,当VAS评分 $\leq$ 4分时,开启PCA泵,输注速度为0.5 mg/h,每次给药量为1 mg,给药时间间隔为5 min。观察组在术后将5 mL的

0.9%生理盐水和5 mg的盐酸羟考酮注射液(生产厂家:英国NAPP PHARMACEUTICALS LIMITED,规格:1 mg:10 mg,生产批号:20150309)混合后,行静脉推注的方式给药,在1~2 min内推注完毕,2次/天,当VAS评分 $\leq$ 4分时,开启PCA泵,每次给予0.03 mg/kg的药物,给药时间间隔5 min,持续输注速度为0.5 mg/h。若以上方案难以满足镇痛需求,可通过肌肉注射的方式给予50 mg/次盐酸哌替啶。所有患者均需连续治疗3天。

1.3 观察指标

1.3.1 血清 TNF- α 、IL-6、IL-2 水平分析 所有患者在术前及术后3天抽取5 mL的空腹静脉血,转速3000 r/min,离心15 min,分离血清后,提取上清液,采取酶联免疫吸附法检测血清TNF- α 、IL-6、IL-2水平。

1.3.2 镇痛效果评估 分别在术后6、12、24、48、72 h检测两组患者镇痛情况,使用视觉模拟评分(VAS)法评价患者的疼痛程度,标准如下:剧痛则为10分,重度疼痛则为7~9分,中等疼痛则为4~6分,轻微疼痛则为1~3分,无痛则为0分。

1.3.3 术后情况 比较两组患者仰卧位能主动行直腿抬高30°时间、主动外展患肢达45°时间。

1.3.4 不良反应分析 从恶心呕吐、头晕嗜睡、皮肤瘙痒、免疫抑制方面分析两组患者的不良反应。

1.4 统计学处理

选取SPSS11.5软件包对本次实验数据予以处理,用($\bar{x}\pm s$)对计量资料进行表示,采用t检验,用[n(%)]表示计数资料,予以 χ^2 检验,以 $P<0.05$ 提示差异存在统计学意义。

2 结果

2.1 两组治疗前后血清 TNF- α 、IL-6、IL-2 水平比较

治疗前,两组患者血清TNF- α 、IL-6、IL-2水平比较差异无统计学意义($P>0.05$);治疗后,两组患者血清TNF- α 、IL-6、IL-2水平均较治疗前显著升高($P<0.05$),但对对照组相比,观察组的血清TNF- α 、IL-6、IL-2水平较低($P<0.05$),见表1。

表1 两组治疗前后血清 TNF- α 、IL-6、IL-2 水平的比较($\bar{x}\pm s$)

Table 1 Comparison of the serum TNF- α , IL-6 and IL-2 levels before and after treatment between two groups($\bar{x}\pm s$)

Items	Observation group(n=42)		Control group(n=42)	
	Before treatment	After treatment	Before treatment	After treatment
TNF- α (ng/mL)	391.21 $\pm$ 32.56	428.78 $\pm$ 41.25* [#]	392.02 $\pm$ 32.49	468.31 $\pm$ 37.54*
IL-6(ng/L)	35.43 $\pm$ 3.46	41.24 $\pm$ 3.02* [#]	35.47 $\pm$ 3.48	48.98 $\pm$ 4.12*
IL-2(ug/mL)	12.43 $\pm$ 1.27	13.21 $\pm$ 1.34* [#]	12.46 $\pm$ 1.25	14.56 $\pm$ 1.52*

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

2.2 两组手术后疼痛情况比较

术后6、12、24、48、72 h,两组患者的VAS评分均呈不同程度上的下降,和观察组相比,对照组在术后6、12、24、48、72 h的VAS评分显著降低($P<0.05$),见表2。

2.3 两组患者术后情况比较

观察组的主动直腿抬高30°时间、主动外展患肢达45°时间显著短于对照组,差异具有统计学意义($P<0.05$),见表3。

2.4 两组患者不良反应发生情况比较

观察组不良反应发生率显著低于对照组($P<0.05$),见表4。

3 讨论

目前,临床上在治疗类风湿性关节炎、股骨头坏死方面较为常见的方式是髋关节置换术^[4]。一旦病变的髋关节予以替换后,能促使患者的生理功能向正常状态恢复,同时有利于患

者生活质量的提高^[5]。但此类患者需考虑术后剧烈疼痛的问题, 功能造成严重影响, 并且剧烈疼痛会导致患者术后难以接受康
术后疼痛会给患者术后功能锻炼造成影响, 给患者生理及心理 复训练, 进而出现关节僵直及肌肉萎缩^[6,7]。

表 2 两组手术后 VAS 评分比较($\bar{x} \pm s$)Table 2 Comparison of VAS scales after operation between two groups($\bar{x} \pm s$)

Groups	6 h after operation	12 h after operation	24 h after operation	48 h after operation	72 h after operation
Observation group(n=42)	2.25± 0.28*	2.16± 0.19*	2.06± 0.15*	1.87± 0.13*	1.24± 0.08*
Control group(n=42)	2.68± 0.27	2.37± 0.23	2.19± 0.21	2.02± 0.17	1.53± 0.11

Note: Compared with control group, *P<0.05.

表 3 两组患者术后情况比较($\bar{x} \pm s$)Table 3 Comparison of the postoperative condition between two groups($\bar{x} \pm s$)

Groups	Active straight leg raised 30 ° time(h)	Active extubation limb up to 45 ° time(h)
Observation group(n=42)	1.94± 0.19*	2.17± 0.25*
Control group(n=42)	3.76± 0.32	4.78± 0.43

Note: Compared with control group, *P<0.05.

表 4 两组患者不良反应发生情况比较[例(%)]

Table 4 Comparison of the incidence of adverse reaction between two groups[n(%)]

Groups	Nausea and vomiting	Dizzy drowsiness	Skin itching	Immunosuppressive	Total
Observation group(n=42)	0(0.00)	1(2.38)	2(4.76)	1(2.38)	4(9.52)*
Control group(n=42)	5(11.90)	3(7.14)	4(9.52)	2(4.76)	14(33.33)

Note: Compared with control group, *P<0.05.

羟考酮注射液主要来自于生物碱,属于极高纯度的阿片类镇痛药,模拟机体内源性抗痛物质功能,激动阿片受体,阻碍中枢神经的痛觉传导,具有镇痛效果强、镇痛时间长等优势^[8,9]。除此之外,羟考酮注射液能发挥抗焦虑和镇静的作用,可相应地避免咳嗽、恶心呕吐等不良反应的发生,减少患者对于此药物的依赖性,避免成瘾^[10-13]。当羟考酮发挥药理作用后,此药物会随着尿液而排除体外,有着较高的排泄率,并不会给人体带来集聚性损伤^[14-16]。

本研究通对全髋关节置换术患者在术后分别予以羟考酮注射液和硫酸吗啡注射液治疗后,结果显示经羟考酮注射液治疗的患者术后 6、12、24、48、72 h 的疼痛评分显著低于硫酸吗啡注射液治疗者,提示羟考酮注射液的作用更强,有着较高的生物利用度,具备良好的镇痛效果,能满足镇痛需求。在全髋关节置换术后,患者通过羟考酮注射液治疗后,主动直腿抬高 30° 时间、主动外展患肢达 45° 时间显著短于硫酸吗啡注射液治疗者,有利于患者临床症状的提高。除此之外,经羟考酮注射液治疗的患者,其恶心呕吐、头晕嗜睡、皮肤瘙痒、免疫抑制不良反应率显著低于硫酸吗啡注射液治疗者。

在传统观念中,只有发生镇痛时才会使用镇痛药物,然而此时的疼痛已经产生,难以达到理想的效果,还会增加镇痛药物的使用量,出现副反应^[17-19]。手术创伤所导致的炎症反应及周围神经末梢损伤和镇痛的出现存在着密切关联性,神经末梢会出现伤害性信号,经神经纤维会传递至大脑皮层,出现痛觉反应,炎症反应所导致的各种炎症介质和细胞因子,会对中枢神经发挥作用,降低外周和中枢神经的痛阈,增加伤害性刺激反应,出现痛觉^[20-22]。

TNF- α 、IL-6 作为促进炎症反应的细胞因子,痛觉刺激以及手术创伤会对巨噬细胞、单核细胞、淋巴细胞等造成影响,进而释放出 TNF- α 、IL-6 等细胞因子,TNF- α 、IL-6 不但会加重炎症反应,而且和疼痛的发生存在着密切关联性,相关研究者提出 TNF- α 、IL-6 会诱使中枢神经系统和周围组织的痛觉敏化,加重疼痛感^[23-25]。本次研究结果显示通过对全髋关节置换术患者予以羟考酮注射液后 TNF- α 、IL-6、IL-2 炎症因子水平均得到显著升高,但相对于硫酸吗啡注射液治疗者,上述指标升高的幅度较小,提示羟考酮注射液能阻碍患者术后细胞因子水平的增加,进而缓解炎症反应。

总之,羟考酮注射液对全髋关节置换术患者血清 TNF- α 、IL-6、IL-2 水平的影响较小,且镇痛效果较好,安全性高。

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