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氨甲环酸联合罗哌卡因对全髋关节置换术后患者凝血功能、失血量和血清 CRP、PCT 的影响 *

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摘要 目的:观察氨甲环酸联合罗哌卡因对全髋关节置换术(THA)后患者凝血功能、失血量和血清 C 反应蛋白(CRP)、降钙素原(PCT)的影响。**方法:**纳入我院 2019 年 1 月到 2021 年 6 月期间接收的髋关节骨关节炎或股骨头坏死行 THA 治疗的患者共 100 例作为研究对象,采用信封抽签的形式分组,分为对照组和研究组,各 50 例。对照组在缝合手术切口时,采用注射器抽取等量的生理盐水注射于关节腔处。研究组在缝合手术切口时,接受氨甲环酸联合罗哌卡因处理。对比两组凝血功能、失血量、血常规、疼痛情况和血清 CRP、PCT,记录两组术后深静脉血栓发生率。**结果:**研究组的隐性失血量、显性失血量、输血量均少于对照组($P<0.05$)。两组术后 3 d 血红蛋白、红细胞比容较术前下降,但研究组术后 3 d 血红蛋白、红细胞比容高于对照组($P<0.05$)。两组术后 3 d 凝血酶原时间(PT)、活化部分凝血活酶时间(APTT)、D-二聚体(D-D)、纤维蛋白原(FIB)较术前升高,但研究组术后 3 d 的 PT、APTT、D-D、FIB 低于对照组($P<0.05$)。两组术后 3 d 疼痛视觉模拟评分(VAS)评分较术后 12 h 下降,CRP、PCT 较术前升高,研究组术后 3 d VAS 评分、CRP、PCT 均低于对照组($P<0.05$)。两组术后深静脉血栓发生率对比差异无统计学意义($P>0.05$)。**结论:**氨甲环酸联合罗哌卡因可有效减少 THA 术后患者的失血量,减轻术后疼痛,控制全身炎症反应,同时减轻手术对机体凝血功能的影响。

关键词:氨甲环酸;罗哌卡因;全髋关节置换术;凝血功能;失血量;C 反应蛋白;降钙素原

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Effects of Tranexamic Acid Combined With Ropivacaine on Coagulation Function, Blood Loss, Serum CRP and PCT after Patients with Total Hip Arthroplasty*

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ABSTRACT Objective: To observe the effects of tranexamic acid combined with ropivacaine on coagulation function, blood loss, serum C-reactive protein (CRP) and procalcitonin (PCT) after patients with total hip arthroplasty (THA). **Methods:** A total of 100 patients with hip osteoarthritis or femoral head necrosis treated with THA who were received in our hospital from January 2019 to June 2021 were included as the research objects. They were divided into control group and study group by envelope lottery, with 50 cases in each group. In the control group, the same amount of normal saline was injected into the joint cavity with a syringe when the incision was closed. The study group was treated with tranexamic acid combined with ropivacaine when the surgical incision was sutured. The coagulation function, blood loss, blood routine, pain, serum CRP and PCT were compared between the two groups, and the incidence of postoperative deep vein thrombosis was recorded. **Results:** The recessive blood loss, dominant blood loss and blood transfusion in the study group were less than those in the control group ($P<0.05$). The hemoglobin and hematocrit in the two groups at 3 d after operation decreased than those before operation, but the hemoglobin and hematocrit in the study group at 3 d after operation were higher than those in the control group ($P<0.05$). Prothrombin time (PT), activated partial thromboplastin time (APTT), D-Dimer (D-D) and fibrinogen (FIB) in the two groups at 3 d after operation were higher than those before operation, but PT, APTT, D-D and FIB in the study group were lower than those in the control group ($P<0.05$). The visual analogue scale (VAS) of pain in the two groups 3 d after operation was lower than that at 12 h after operation, and the CRP and PCT were higher than those before operation. The VAS score, CRP and PCT in the study group at 3 d after operation were lower than those in the control group ($P<0.05$). There was no significant difference in the incidence of postoperative deep venous thrombosis between the two groups ($P>0.05$). **Conclusion:** Tranexamic acid combined with ropivacaine can effectively reduce blood loss in patients with THA, reduce postoperative pain, control systemic inflammatory reaction, and reduce the impact of operation on blood coagulation function.

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前言

全髋关节置换术(THA)是指对髋关节疾病患者采用低强度的金属所制的人工股骨头以及高分子聚乙烯所制的髋臼进行取代治疗,以求实现假体的生物性永久固定^[1,2],被认为是髋关节晚期病变有效的治疗方法^[3]。但是由于THA创伤较大,围术期失血量较多,同时围术期引起应激反应也可导致严重的术后疼痛。此时,给予相应的处理措施对于改善THA患者预后具有积极的意义。氨甲环酸是一种抗纤溶蛋白溶解氨基酸,是目前最常用的止血药物之一^[4-6]。罗哌卡因是长效酰胺类局麻药,可有效阻滞分离感觉和运动神经,可为患者提供良好的镇痛效果^[7,8]。我院尝试给予THA患者术后使用氨甲环酸联合罗哌卡因,获得了较好的疗效,整理报道如下。

1 资料与方法

1.1 一般资料

纳入我院2019年1月到2021年6月期间接收的髋关节骨关节炎或股骨头坏死患者共100例作为研究对象,患者行THA治疗,研究方案通过我院伦理学委员会批准进行。纳入标准:(1)患者符合手术指征,诊断标准参考《外科学》^[9]的标准:髋关节骨关节炎诊断标准:髋内旋、髋外旋小于15°,1个月内大多数时间有髋痛,血沉小于45 mm/h,髋晨僵小于60 min。股骨头坏死诊断标准:通过X射线、磁共振成像诊断;(2)美国麻醉医生协会(ASA)分级^[10]: I~II级;(3)所有患者均签署知情同意书。排除标准:(1)术前存在贫血、凝血功能异常者;(2)对氨甲环酸、罗哌卡因等药物存在过敏者;(3)术前伴有心血管系统疾病患者;(4)既往有动静脉栓塞、下肢感染病史的患者;(5)既往存在恶性肿瘤者。采用信封抽签的形式分组,分为对照组和研究组,各50例。两组的一般资料对比无差异($P>0.05$),均衡可比,见表1。

表1 两组患者的一般资料

Table 1 General information of two groups of patients

Groups	Male/female	Age(years)	Body mass index (kg/m ²)	ASA classification(n)		Disease type(n)	
				Class I	Class II	Hip osteoarthritis	Femoral head necrosis
Control group (n=50)	22/28	58.69± 6.81	26.94± 2.38	29	21	27	23
Study group (n=50)	23/27	58.24± 7.32	26.75± 2.49	30	20	25	25
χ^2/t	0.040	0.318	0.390	0.041		0.160	
P	0.841	0.751	0.697	0.839		0.689	

1.2 方法

入院后完善血常规、凝血功能检查、血糖、心电图检查、肝肾功能和电解质指标等相关检查,患髋关节行正侧位X线片检查,同时所有患者均行下肢血管彩色多普勒超声检查排除血栓形成的可能,明确手术指征,择期行手术治疗。所有手术均由同一组医师完成,假体选择德国Link公司生产的Gemini人工髋关节假体,麻醉方式选用气管内全身麻醉,术前常规禁食、水,入室后均采取侧卧位,常规消毒铺巾,切口采用髋关节后外侧入路,行THA手术。研究组患者在缝合手术切口时,接受注射用氨甲环酸(广西梧州制药(集团)股份有限公司,国药准字H20030587,规格:0.5 g)联合盐酸罗哌卡因注射液(广东嘉博制药有限公司,国药准字H20173194,规格:20 mL: 200 mg(按盐酸罗哌卡因计))治疗,将0.5 g氨甲环酸与10 mL的罗哌卡因溶于50 mL的生理盐水后关节腔注射。对照组则给予注射器抽取等量的生理盐水注射于关节腔。两组均在术前10 min和术后静脉滴注氨甲环酸0.5 g(溶于50 mL的生理盐水中)。

1.3 观察指标

(1)观察两组隐性失血量、显性失血量、输血量,其中隐性失血量根据Gross方程计算^[11]:患者术前总血容量= $k_2 \times g + k_1 \times$

$h + k_3$ (其中h表示身高(m),g表示重量(kg),男: k_1, k_2, k_3 分别为0.3669、0.03219、0.6041,女: k_1, k_2, k_3 分别为0.3561、0.03308、0.1833),总隐性失血量= $[(\text{红细胞比容的变化量}) \times \text{血容量} / \text{术前红细胞比容}] - \text{显性减少量}$ 。(2)术前、术后3 d抽取两组患者肘静脉血4 mL,术前、术后3 d采用美国库尔特公司生产的GENS全自动五分类血液细胞分析仪检测两组血常规指标:血红蛋白和红细胞比容。术前、术后3 d采用法国STA-COMPACT全自动凝血分析仪检测凝血酶原时间(PT)、活化部分凝血活酶时间(APTT)、D-二聚体(D-D)、纤维蛋白原(FIB)。经2800 r/min离心12 min,离心处理后取上清液保存于低温冰箱中待测。采取酶联免疫吸附法检测C反应蛋白(CRP)、降钙素原(PCT)水平,试剂盒购自上海酶联科技有限公司。(3)术后12 h、术后3 d采用疼痛视觉模拟评分(VAS)评价患者疼痛情况,VAS评分0~10分,分数越高,痛感越剧烈。(4)记录两组术后深静脉血栓发生率。

1.4 统计学方法

采用SPSS20.0软件进行数据处理,所有资料经正态性分析,符合正态分布的计量资料如隐性失血量、血红蛋白用($\bar{x} \pm s$)表示,采用t检验,术后深静脉血栓发生率为计数资料用[n(%)]

表示,采用 χ^2 检验,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组患者失血量对比

研究组的隐性失血量、显性失血量、输血量均少于对照组($P<0.05$),详见表2。

表2 两组患者失血量对比($\bar{x}\pm s$)

Table 2 Comparison of blood loss between the two groups($\bar{x}\pm s$)

Groups	Recessive blood loss(mL)	Dominant blood loss(mL)	Blood transfusion(mL)
Control group(n=50)	661.04±64.28	745.28±46.24	736.68±61.42
Study group(n=50)	497.23±51.75	502.69±53.56	664.74±87.36
t	14.036	24.242	4.763
P	0.000	0.000	0.000

2.2 两组患者血常规指标对比

两组术前血红蛋白、红细胞比容对比无统计学差异($P>0.05$),研究组术后3 d 血红蛋白、红细胞比容高于对照组($P<0.05$)。

05)。两组术后3 d 血红蛋白、红细胞比容较术前下降($P<0.05$)。见表3。

表3 两组患者血常规指标对比($\bar{x}\pm s$)

Table 3 Comparison of blood routine indexes between the two groups($\bar{x}\pm s$)

Groups	Hemoglobin(g/L)		Hematocrit	
	Before operation	3d after operation	Before operation	3d after operation
Control group(n=50)	144.73±15.51	98.96±17.61*	0.56±0.06	0.36±0.05*
Study group(n=50)	143.58±16.47	122.79±15.42*	0.58±0.07	0.47±0.06*
t	0.359	-7.199	-1.534	-9.595
P	0.720	0.000	0.128	0.000

Note: compared with before operation, * $P<0.05$.

2.3 两组患者凝血功能指标对比

两组术前PT、APTT、D-D、FIB对比无统计学差异($P>0.05$),

研究组术后3 d PT、APTT、D-D、FIB 低于对照组($P<0.05$)。两组术后3 d PT、APTT、D-D、FIB 较术前升高($P<0.05$)。见表4。

表4 两组患者凝血功能指标对比($\bar{x}\pm s$)

Table 4 Comparison of coagulation function indexes between the two groups($\bar{x}\pm s$)

Groups	PT(s)		APTT(s)		D-D(ng/mL)		FIB(g/L)	
	Before operation	3d after operation	Before operation	3d after operation	Before operation	3d after operation	Before operation	3d after operation
Control group (n=50)	9.89±1.45	14.91±1.37*	26.72±4.31	39.51±4.38*	192.03±27.24	471.62±29.25*	2.86±0.42	3.97±0.56*
Study group (n=50)	9.96±1.18	11.73±1.25*	26.65±3.75	33.24±4.29*	193.98±30.28	256.12±32.74*	2.91±0.45	3.48±0.63*
t	-0.265	12.125	0.087	7.231	-0.339	34.709	-0.574	4.111
P	0.792	0.000	0.931	0.000	0.736	0.000	0.564	0.000

Note: compared with before operation, * $P<0.05$.

2.4 两组患者疼痛评分、CRP、PCT 对比

两组术前VAS评分、CRP、PCT对比无统计学差异($P>0.05$),研究组术后3 d VAS评分、CRP、PCT均低于对照组($P<0.05$)。两组术后3 d VAS评分较术后12 h下降,CRP、PCT较术前升高($P<0.05$)。见表5。

2.5 两组术后深静脉血栓发生率对比

研究组发生术后深静脉血栓的患者1例,发生率为2.00%;对照组发生术后深静脉血栓的患者2例,发生率为4.00%,组间发生率对比无差异($\chi^2=0.344$, $P=0.558$)。

3 讨论

THA是骨科手术之一,可有效阻止疾病进展、矫正下肢畸形及促进关节功能,疗效肯定^[12,13]。但THA术中对软组织剥离多,创伤大,术中不可避免的损伤一些细小血管,导致组织纤溶酶原激活物释放,激活纤维蛋白溶解过程,从而增加局部血液循环,导致局部失血量增多^[14,15]。以往的研究证实THA患者还存在一定量的隐性失血,致使患者术后多出现不同程度的贫血^[16],而术后贫血可导致伤口恢复延迟、并发症发生风险增加。

表 5 两组患者疼痛评分、CRP、PCT 对比($\bar{x} \pm s$)Table 5 Comparison of pain score, CRP and PCT between the two groups($\bar{x} \pm s$)

Groups	VAS(scores)		CRP(mg/L)		PCT(ng/mL)	
	12h after operation	3d after operation	Before operation	3d after operation	Before operation	3d after operation
Control group (n=50)	6.84±1.03	3.31±0.89 [#]	62.73±4.05	138.21±11.34*	1.28±0.31	4.69±0.91*
Study group(n=50)	6.89±1.12	2.57±0.71 [#]	62.48±5.36	94.85±7.25*	1.32±0.27	2.15±0.68*
t	-0.232	4.596	0.263	22.780	-0.688	15.810
P	0.817	0.000	0.793	0.000	0.493	0.000

Note: compared with before operation, * $P<0.05$; compared with 12h after operation, [#] $P<0.05$.

输血虽可有效纠正这一情况,但也常因血源紧张及输血后的变态反应等风险受到一定的限制。因此,需寻找一种更为安全有效的治疗方法来控制 THA 围术期失血。氨甲环酸是一种人工合成的赖氨酸衍生物和同系物,现不少研究将氨甲环酸应用于关节置换围手术期止血,取得了一定的疗效^[17-19]。除了失血量外,降低 THA 患者术后康复效果的另一个因素则为疼痛。THA 作为创伤较大的外科手术,术中不可避免的损伤关节周围神经末梢,进而导致术后持续剧烈的疼痛,同时还可能导致机体处于不同程度的应激状态^[20,21]。罗哌卡因是临床中常用的麻醉药,具有强效的痛觉阻滞作用^[22,23]。舒波等^[24]学者认为罗哌卡因用于 THA 患者,可降低血清疼痛与炎症因子水平。

研究结果显示,研究组的隐性失血量、显性失血量、输血量均少于对照组,说明氨甲环酸联合罗哌卡因可有效减少 THA 患者失血量。同时也有学者提出,THA 术后可使患者血液处于高凝状态,从而增加血栓栓塞等并发症^[25]。血常规化验常作为疾病诊断的一种辅助手段,通过解读血常规化验数据,可以初步确定患者的病情^[26]。本次研究结果显示,两组处理方式下的患者均出现不同程度的凝血功能障碍和血常规异常,但氨甲环酸联合罗哌卡因处理的 THA 患者其凝血功能障碍和血常规异常程度明显更轻,这可能是由于氨甲环酸可与纤溶酶的赖氨酸结合位点强烈吸附,从而有效阻止纤维蛋白与纤溶酶原、纤溶酶结合,产生了一定的抗凝作用、抗血栓作用^[27]。此外,围术期出血量与炎症因子的分泌与表达有关,CRP 是一种急性时相反应蛋白,PCT 是降钙素的前肽,与细菌感染内毒素和炎症介质的释放密切相关^[28]。THA 围术期可导致组织损伤,促使炎症介质释放,导致 CRP、PCT 水平升高。本次研究结果表明,氨甲环酸联合罗哌卡因可有效控制 THA 患者术后炎症反应。氨甲环酸的抗炎作用主要是:通过减少纤溶酶对血小板膜糖蛋白受体的降解作用,进而有效抑制白细胞的聚集及内皮细胞活化,发挥控制炎症的效果^[29,30]。而有关罗哌卡因的抗炎作用尚不明确,体外实验证实^[31],局麻药可抑制前列腺素 E₂ 释放和脂蛋白磷脂酶 A2 活性,从而间接影响炎症因子的释放。同时观察两组术后疼痛情况可知,氨甲环酸联合罗哌卡因可有效减少 THA 患者术后疼痛,这是由于局麻药物可以减少神经纤维膜对钠离子的通透性,阻断神经兴奋与传导,从而提高镇痛效果^[32]。深静脉血栓是 THA 患者常见的并发症发生率,是由于血管内血小板的聚集或凝血因子异常所致。本研究中研究组患者其术后深静脉血栓发生率虽更低,但与对照组相比未见明显差异,其具体

结论有待进一步的大样本量论证。

综上所述,氨甲环酸联合罗哌卡因可有效减少 THA 患者失血量,减轻术后疼痛以及手术对机体凝血功能的影响,同时还可控制机体的炎症反应,临床应用价值较好。

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