

doi: 10.13241/j.cnki.pmb.2022.07.028

氨甲环酸在老年股骨转子间骨折伤后早期的应用研究*

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摘要 目的: 研究老年股骨转子间骨折伤后早期使用氨甲环酸(tranexamic acid, TXA)的有效性和安全性。**方法:** 2021年4月到2021年8月选择在本院诊治的符合纳入标准的老年股骨转子间骨折患者70例作为研究对象,根据随机数字表法把患者分为TXA组与对照组各35例。TXA组于伤后6小时内静脉滴注TXA 1g(与100 mL生理盐水配伍,半小时滴完),对照组伤后6小时内静脉滴注生理盐水100 mL。观察指标:入院即刻及伤后第1、2天和术前清晨红细胞压积(Hct)、红细胞(RBC)、血红蛋白(Hb)、纤维蛋白原(FIB)、D-二聚体(D-Dimer)。术前2小时、术后2周查下肢静脉血管B超明确有无下肢深静脉血栓形成。观察记录术后伤口感染、伤后出血并发症发生情况。疗效指标包括术前隐性失血量、术前输血率。安全性指标为围手术期深静脉血栓发生率、术后伤口并发症发生率。**结果:** (1)两组患者伤后第1、2天和术前清晨红细胞压积、红细胞、血红蛋白水平和D-二聚体随时间延长逐渐降低,纤维蛋白原逐渐增加($P<0.05$)。伤后第1、2天和术前清晨TXA组红细胞压积、红细胞、血红蛋白水平均高于对照组($P<0.001$)。 (2)伤后第1、2天和术前清晨两组隐性失血量随时间延长逐渐增加, TXA组隐性失血量均低于对照组($P<0.001$)。 (3)TXA组术前输血率显著低于对照组($P<0.001$)。**结论:** TXA伤后早期应用可有效降低老年股骨转子间骨折患者术前的隐性失血量,降低术前输血率,不增加围手术期深静脉血栓发生率,且减少术后伤口并发症。

关键词: 老年股骨转子间骨折; 伤后早期; 氨甲环酸; 术前隐性失血; 深静脉血栓

中图分类号: R683.42 **文献标识码:** A **文章编号:** 1673-6273(2022)07-1328-05

Study on the Early Application of Tranexamic Acid after Intertrochanteric Fracture in the Elderly*

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ABSTRACT Objective: To study the efficacy and safety of early use of tranexamic acid (TXA) after femoral intertrochanteric fracture in the elderly. **Methods:** From April 2021 to August 2021, 70 elderly patients with femoral intertrochanteric fracture who met the inclusion criteria were selected as the research objects. According to the random number table, the patients were divided into TXA group and control group, with 35 cases in each group. TXA group was intravenously injected with txa1g (compatible with 100 mL normal saline, half an hour) within 6 hours after injury, and the control group was intravenously injected with 100 mL normal saline within 6 hours after injury. Outcome measures: hematocrit (HCT), red blood cell (RBC), hemoglobin (HB), fibrinogen (FIB) and D-Dimer (D-dimer) immediately after admission, on the first and second days after injury and in the morning before operation. The venous vessels of lower limbs were examined by B-ultrasound 2 hours before operation and 2 weeks after operation to determine whether there was deep venous thrombosis of lower limbs. The complications of postoperative wound infection and bleeding were observed and recorded. The efficacy indexes included preoperative occult blood loss and preoperative blood transfusion rate. The safety indexes were the incidence of perioperative deep venous thrombosis and the incidence of postoperative wound complications. **Results:** (1) The hematocrit, red blood cell, hemoglobin level and D-dimer of the two groups of patients decreased gradually over time on the 1st and 2nd day after injury and early morning before operation, and fibrinogen gradually increased ($P<0.05$). The hematocrit, red blood cell and hemoglobin levels of TXA group were higher than those of the control group on the 1st and 2nd day after injury and early morning before operation ($P<0.001$). (2) The hidden blood loss of the two groups gradually increased with time on the first and second days after injury and the early morning before operation. The hidden blood loss of the TXA group was lower than that of the control group ($P<0.001$). (3) The preoperative blood transfusion rate in the TXA group was significantly lower than that in the control group ($P<0.001$). **Conclusion:** Early application of TXA after injury can effectively reduce the preoperative occult blood loss of elderly patients with femoral intertrochanteric fracture, reduce the preoperative blood transfusion rate, do not increase the incidence of perioperative deep venous thrombosis, and

* 基金项目: 陕西省自然科学基金研究计划项目(2019JM-524)

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(收稿日期: 2021-09-07 接受日期: 2021-09-30)

reduce postoperative wound complications.

Key words: Femoral intertrochanteric fracture in the elderly; Early post injury; Tranexamic acid; Preoperative occult blood loss; Deep venous thrombosis

Chinese Library Classification(CLC): R683.42 **Document code:** A

Article ID:1673-6273(2022)07-1328-05

前言

股骨转子间骨折是老年人常见的髋部骨质疏松性骨折,致死、致残率高,老年股骨转子间骨折患者的死亡率与手术时机的选择、围手术期贫血等因素有关^[1-3]。老年股骨转子间骨折手术应尽早进行,推荐在入院 48 小时内手术,而延迟手术会增加病死率^[4-6]。贫血是引起死亡率增加的另一重要因素^[7]。老年股骨转子间骨折围术期失血量大,以隐性失血为主,输血率较高^[8,9]。有研究证实,老年股骨转子间骨折患者围术期的隐性失血主要发生在术前^[10]。目前除了输血,预防隐性失血的方法有 TXA 的应用。TXA 目前已广泛用于关节外科、脊柱外科、心胸外科等领域,创伤骨科医生对 TXA 在老年髋部骨折围手术期的使用没有完全达成共识,目前国外关于 TXA 在老年髋部骨折围手术期应用的研究很少,国内一些研究证实 TXA 的使用可降低老年股骨转子间骨折患者术后隐性失血量,降低输血率,但不增加术后深静脉血栓发生率^[10]。以往的研究往往都局限在术中及术后用药,对于 TXA 在存在大量隐性失血的伤后至术前

这段时间的应用研究报道很少。本研究以我院收治的符合纳入条件的老年股骨转子间骨折患者为研究对象,观察老年股骨转子间骨折伤后早期(6 小时内)使用 TXA 的有效性和安全性。现报道如下。

1 资料与方法

1.1 研究对象

2021 年 4 月到 2021 年 8 月选择在本院诊治的符合纳入标准的老年股骨转子间骨折患者 70 例作为研究对象。纳入标准:初次新鲜单侧老年股骨转子间骨折,患者年龄 ≥ 65 岁,伤后入院时间 ≤ 6 小时。患者知情同意本研究且得到医院伦理委员会的批准。排除标准:多发骨折、长期应用抗凝药物、血液性疾病,合并心肺脑等严重疾病,不能耐受手术者,入院即刻查下肢血管 B 超发现有下肢深静脉血栓形成者,既往有血栓形成病史者。根据随机数字表法把患者分为 TXA 组与对照组各 35 例。两组患者对隐性失血有影响因素的一般资料差异均无统计学意义($P>0.05$)。见表 1。

表 1 两组患者对隐性失血有影响因素的一般资料比较

Table 1 Comparison of general data on influencing factors on recessive blood loss between the two groups

Groups	Injury to surgery time (d)	Age (year)	Gender (male / female)	Fracture AO-typing (A1/A2/A3)	BMI(kg/m ²)
TXA Group(n=35)	2.25 $\pm$ 0.85	68.22 $\pm$ 4.19	21/19	10/16/14	21.87 $\pm$ 5.44
Control group(n=35)	2.45 $\pm$ 0.95	68.14 $\pm$ 3.89	18/22	11/17/12	21.13 $\pm$ 4.89

1.2 研究方法

TXA 组于伤后 6 小时内静脉滴注 TXA (山西普德药业有限公司,规格 0.5 g,国药准字 H14020888,生产批号 08200607) 1 g(与 100 mL 生理盐水配伍,半小时滴完),对照组于伤后 6 小时内静脉滴注生理盐水 100 mL。

手术时机:根据老年股骨转子间骨折诊疗指南要求及本院实际情况两组患者手术时间均在伤后 3 天左右。

手术方式:所有患者的手术均由同一组医生完成,给予股骨近端防旋髓内钉(PFNA)内固定治疗:硬膜外麻醉成功后,患者仰卧于牵引床上,C 型臂透视下患肢先外展牵引,再内收 15° 左右,轻度内旋使骨折复位,闭合复位满意后,微创小切口行 PFNA 内固定治疗。

围手术期基础治疗:所有患者均按照快速康复理念治疗。入院后注意超前、多模式镇痛,健康教育。积极完善术前检查及术前准备,必要时心内、呼吸、内分泌、营养科等多学科会诊,积极改善患者全身情况,积极治疗患者存在的糖尿病、高血压、心脏病等内科疾患,营养评估,积极改善患者的营养情况,必要时肠内营养。积极纠正低蛋白血症、电解质紊乱。常规应用低分子量肝素抗凝治疗,伤后 8 小时开始应用,预防血栓形成,术前

12 小时停用,术后 12 小时再开始应用。

1.3 观察指标

(1)实验室检查指标:入院即刻及伤后第 1、2 天和术前清晨红细胞压积(Hct)、红细胞(RBC)、血红蛋白(Hb)、纤维蛋白原(FIB)、D-二聚体(D-Dimer)。(2)根据身高、体重、Hct 差值应用 Gross 方程计算术前的隐性失血量:术前隐性失血量 = 理论失血量 + 输血量,理论失血量 = 总红细胞丢失量 / Hct₀,总红细胞丢失量 = 血容量 $\times$ [Hct₀-Hctn],血容量 = $K_1 \times$ 身高(m)³ + $K_2 \times$ 体重(kg) + K_3 ,其中女性: $K_1=0.3561$, $K_2=0.03308$, $K_3=0.1833$;男性: $K_1=0.3669$, $K_2=0.03219$, $K_3=0.6041$ 。Hct₀为伤后入院即刻红细胞压积,Hctn 为伤后第 1、2 及术前清晨所测得的红细胞压积。(3)术前输血率、围手术期深静脉血栓发生率计算:血红蛋白低于 100 g/L 为输血指征。术前输血患者例数占该组患者的比例为术前输血率。术前 2 小时、术后 2 周行下肢静脉 B 超检查,发现深静脉血栓者,纳入计算围手术期深静脉血栓发生率,若患者临床有考虑下肢深静脉血栓形成及肺栓塞的症状,及时完善检查,明确诊断者纳入计算围手术期深静脉血栓发生率。围手术期下肢深静脉血栓发生及肺栓塞患者例数占该组患者的比例为围手术期深静脉血栓发生率。(4)观察记录术后伤口

感染、伤后出血并发症发生情况。

1.4 统计学处理

使用 SPSS24.00 应用软件,计数资料以百分率(%)表示,采用卡方(χ^2)检验分析比较,计量资料以均数 $\pm$ 标准差($\bar{x}\pm s$)表示,两两比较采用 t 检验,多组间比较采用方差分析; $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者伤后各时间点凝血指标水平比较

表 2 两组患者伤后各时间点凝血指标水平比较

Table 2 Comparison of coagulation index levels at various time points after injury between the two groups

Index	Groups	Immediate admission	Day 1	Day 2	Early in the morning before surgery
Hematocrit levels were (%)	TXA Group(n=35)	42.22 $\pm$ 2.35	39.85 $\pm$ 2.54*	36.23 $\pm$ 3.17*	31.45 $\pm$ 3.51*
	Control group(n=35)	42.30 $\pm$ 2.20	36.80 $\pm$ 2.76	31.45 $\pm$ 3.19	27.22 $\pm$ 3.68
Erythrocyte levels ($10\times 10^{12}/L$)	TXA Group(n=35)	4.03 $\pm$ 0.54	3.58 $\pm$ 0.55*	3.35 $\pm$ 0.46*	3.15 $\pm$ 0.37*
	Control group(n=35)	4.04 $\pm$ 0.52	3.20 $\pm$ 0.57	3.05 $\pm$ 0.69	2.86 $\pm$ 0.64
Hemoglobin levels (g/L)	TXA Group(n=35)	122.75 $\pm$ 10.44	112 $\pm$ 12.54*	104 $\pm$ 15.65*	100 $\pm$ 13.51*
	Control group(n=35)	121.86 $\pm$ 10.20	105 $\pm$ 15.60	100 $\pm$ 14.30	95.30 $\pm$ 15.50
Fibrinogen(g/L)	TXA Group(n=35)	3.70 $\pm$ 1.70	3.90 $\pm$ 1.25	4.04 $\pm$ 1.17	4.45 $\pm$ 1.51
	Control group(n=35)	3.90 $\pm$ 1.75	4.05 $\pm$ 1.76	4.20 $\pm$ 1.59	4.30 $\pm$ 1.48
D-dimer(mg/L)	TXA Group(n=35)	6.50 $\pm$ 4.70	5.90 $\pm$ 4.25	4.05 $\pm$ 3.17	3.45 $\pm$ 3.20
	Control group(n=35)	6.40 $\pm$ 4.75	6.05 $\pm$ 4.76	4.50 $\pm$ 4.29	4.05 $\pm$ 3.48

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

2.2 两组患者术前隐性失血量比较

伤后第 1、2 天和术前清晨两组隐性失血量随时间延长逐

两组患者入院即刻红细胞压积、红细胞、血红蛋白比较无明显差异($P>0.05$)。

两组患者伤后第 1、2 天和术前清晨红细胞压积、红细胞、血红蛋白水平和 D-二聚体随时间延长逐渐降低,纤维蛋白原逐渐增加($P<0.05$)。伤后第 1、2 天和术前清晨 TXA 组红细胞压积、红细胞、血红蛋白水平均高于对照组($P<0.001$)。两组各时间点纤维蛋白原、D-二聚体比较差异无统计学意义($P>0.05$)。见表 2。

渐增加, TXA 组隐性失血量均低于对照组($P<0.001$)。见表 3。

表 3 两组患者术前隐性失血量比较(mL)

Table 3 Comparison of preoperative recessive blood loss in the two groups (mL)

Groups	Day 1	Day 2	Early in the morning before surgery
TXA Group(n=35)	200.50 $\pm$ 30.45*	340 $\pm$ 40.75*	450 $\pm$ 46.65*
Control group(n=35)	350.40 $\pm$ 50.50	550 $\pm$ 45.67	750 $\pm$ 42.74

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

2.3 两组患者术前输血率、围手术期深静脉血栓发生率、伤口并发症情况比较

TXA 组术前输血率显著低于对照组($P<0.05$);而两组并发症发生率相比差异无统计学意义($P>0.05$)。上述结果见表 4。

3 讨论

老年股骨转子间骨折围术期隐性失血量大, Smith 等研究证实,老年股骨转子间骨折患者围手术期的隐性失血主要发生在术前^[1]。本研究两组患者伤后第 1、2 天和术前清晨红细胞压积、红细胞、血红蛋白水平随时间延长逐渐降低($P<0.001$),隐性失血量随时间延长逐渐增加($P<0.001$),对照组术前隐性失血约 790 mL 左右。同样证明老年股骨转子间骨折术前存在大

量隐性失血。TXA 目前已广泛用于关节外科、脊柱外科、心胸外科等领域预防隐性失血,取得了良好疗效^[12-14]。TXA 的药理作用是抑制体内纤溶系统从而预防隐性失血,它理论上增加了深静脉血栓事件的风险,因此关于其给药时机、给药方式、如何序贯治疗以及深静脉血栓事件发生的风险均还存在争议^[15,16]。

TXA 在老年髋部骨折围手术期的使用现国内研究较多,但主要局限在术中及术后用药,且没有达成共识。2019 年《中华骨与关节外科杂志》发表的“中国骨科手术加速康复围手术期 TXA 与抗凝血药应用的专家共识”给出创伤骨科包括股骨转子间骨折围手术期的 TXA 应用建议^[17]。根据 4 篇 meta 分析及 2 篇前瞻性随机对照研究报道^[18-23],建议 TXA 给药方式主要为单次静脉滴注或多次静脉滴注。单次应用在手术切开皮肤前

表 4 两组患者术前输血率及并发症情况比较

Table 4 Comparison of preoperative blood transfusion rate and complications between the two groups

Groups	Pre-operative transfusion rate	The occurrence of the complications		
		Rate of perioperative deep venous thrombosis	Wound complications	Total incidence
TXA Group(n=35)	3/35(8.5%)*	3/35(8.5%)	1(2.8%)	4(11.3%)
Control group(n=35)	10/35(28.5%)	2/35(5.7%)	5(14.0%)	7(19.7%)

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

15~30 min, 剂量 1~2 g。多次应用首次同单次应用, 3 h 后或关闭切口前追加 1 次(每次 1~2 g)。但 2020 年《中华创伤骨科杂志》发表的“老年股骨转子间骨折诊疗指南”没有提出围手术期 TXA 的使用^[24]。之所以没有达成共识, 结合李杰^[29]和 Zhou S^[26]等研究分析, 可能与以下因素有关: 老年股骨转子间骨折患者年龄大, 围手术期卧床时间长, 合并高血压病、糖尿病、心血管疾病等基础疾病多, 处于高凝状态, 所以血栓形成的风险较一般患者高。

目前对于 TXA 在老年股骨转子间骨折存在大量隐性失血的伤后至术前这段时间的应用研究报道很少。研究表明 TXA 伤后早期应用可有效降低老年股骨转子间骨折患者术前隐性失血量, 降低术前输血率, 且不增加术前深静脉血栓发生率^[27,28]。本研究伤后第 1、2 天和术前清晨 TXA 组红细胞压积、红细胞、血红蛋白水平均高于对照组($P < 0.001$), TXA 组术前输血率显著低于对照组($P < 0.05$); 而两组并发症发生率相比差异无统计学意义($P > 0.05$), 说明: 老年股骨转子间骨折伤后早期使用 TXA 具有显著有效性和安全性, 即可改善凝血指标, 且不会增加围手术期深静脉血栓发生率以及术后伤口并发症的发生率。另外, 本研究中, 两组患者伤后随时间延长, 纤维蛋白原逐渐增加, D-二聚体逐渐减少, 说明伤后早期存在明显纤溶亢进, 也证实了伤后早期使用 TXA 抑制体内纤溶系统从而预防隐性失血的必要性。Carroll K^[29]和 Zhou XD^[30]等研究显示: 伤后早期使用 TXA 可降低老年股骨转子间骨折术前输血率, 并且术后伤口并发症也显著降低, 从而也证实了术后伤口并发症的发生与输血率的上升有关。

本研究存在不足之处, 这些患者都接受了综合的深静脉血栓形成预防措施, 而深静脉血栓属于小概率事件, TXA 对老年股骨转子间骨折深静脉血栓事件的影响需要更高质量、更大样本的、多中心的随机临床试验来进行研究。而且本研究仅对老年股骨转子间骨折患者伤后早期单次使用 TXA, 未追加序贯干预, 研究组后期将进一步对 TXA 在老年股骨转子间骨折患者围手术期使用的给药时机、给药方式、如何序贯治疗以及深静脉血栓事件发生的风险进行深入研究报道。

综上所述, 本研究创新性将 TXA 应用于老年股骨转子间骨折后入院至术前阶段, 结果发现: TXA 早期应用可有效减少老年股骨转子间骨折患者术前的隐性失血量, 并降低术前输血率, 且不会增加围手术期深静脉血栓发生率以及术后伤口并发症的发生率, 安全性较好, 可考虑应用于临床。

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(上接第 1327 页)

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