

氨甲环酸在髋关节翻修术中应用的研究进展

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摘要

由于全球预期寿命的增加, 关节置换术的总数也有所增加。全髋关节置换术(THA)通常用于髋关节骨关节炎患者, 而全髋关节置换术(THA)期间失血量达到1000至1500毫升之间, 输血率在21%到70%之间。尽管输血可以挽救生命, 但输血与已知的有时会危及生命的不良事件有关。氨甲环酸(TXA)是一种抗纤溶的药物, 广泛应用于接受THA的患者。而TXA在THA中的有效性及安全性已被证实, 这为骨科医生降低失血量, 输血率以及术后并发症更多的髋关节翻修术(RHA)的围手术期失血量及输血率而指了一条明路。本文对以氨甲环酸在全髋关节置换翻修术中的应用进行了综述。首先介绍了TXA的作用机制, 包括其抑制纤维蛋白溶解作用和减少纤维蛋白溶酶原激活的能力。随后, 回顾了已发布的研究, 探讨了TXA在全髋关节置换翻修术中的疗效和安全性。研究结果显示, TXA能够显著减少手术过程中的出血量和输血需求, 同时并不增加手术并发症的风险。一些研究还发现, 更早地应用TXA可以获得更好的止血效果。综上所述, 以氨甲环酸在全髋关节置换翻修术中的应用显示出良好的止血效果和安全性。然而, 我们仍然需要进一步的研究, 以进一步明确其最佳应用时间和剂量, 为临床实践提供更可靠的依据。

关键词

髋关节翻修术, 氨甲环酸, 全髋关节置换术, 围手术期出血量, 围手术期输血率

Research Progress on the Application of Tranexamic Acid in Revision Hip Arthroplasty

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Abstract

As global life expectancy rises, so does the number of joint replacement surgeries. Total Hip Arthroplasty (THA) is commonly performed on patients with hip osteoarthritis, with blood loss during surgery ranging from 1000 to 1500 milliliters and transfusion rates between 21% and 70%. Although blood transfusions can be lifesaving, they are associated with potentially life-threatening adverse events. Tranexamic Acid (TXA), an antifibrinolytic medication, has been widely used in patients undergoing THA. Its effectiveness and safety in THA have been confirmed, offering orthopedic surgeons a clearer path to reduce blood loss, transfusion rates, and postoperative complications in Revision Hip Arthroplasty (RHA). This article reviews the application of TXA in revision hip arthroplasty. It first introduces the mechanism of action of TXA, including its ability to inhibit fibrinolysis and reduce the activation of plasminogen to plasmin. Subsequently, it reviews published studies to discuss the efficacy and safety of TXA in hip revision surgeries. The findings indicate that TXA significantly reduces intraoperative blood loss and the need for blood transfusions without increasing the risk of surgical complications. Some studies have also found that earlier application of TXA can achieve better hemostatic effects. In summary, the application of tranexamic acid in RHA has shown good hemostatic effect and safety. However, further research is still needed to further clarify the optimal timing and dosage for clinical practice.

Keywords

Revision Hip Arthroplasty, Tranexamic Acid, Total Hip Arthroplasty, Perioperative Blood Loss, Perioperative Transfusion Rate

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1. 引言

全髋关节置换术(Total Hip Arthroplasty, THA)拥有着较高的病人满意度,是最经典、最成熟的,效果肯定持久的人工关节手术。当前,因骨性关节炎、类风湿性关节炎、股骨颈骨折和股骨头坏死进行全髋关节置换术(THA)的患者人数逐年增加[1] [2]。同样,由于感染、假体松动和假体磨损的原因,髋关节翻修术(Revision Hip Arthroplasty, RHA)的数量也在增加[3] [4] [5]。据估计,到2030年,RHA的数量可能超过97,000例。髋关节置换术的年翻修率约为19.05%,增长速度为137% [6]。围手术期出血性贫血是骨科手术的主要问题,关节置换术后输血的数量占骨科手术患者总数的40% [7] [8] [9]。RHA手术在围手术期仍被认为是血液损失和输血率较高的手术[10]。尽管如此,外科医生和麻醉师已采取了许多措施来减少围手术期的血液损失和输血,包括控制性低血压、局部麻醉、术中血液回收和促红细胞生成素[11] [12]。同种异体输血可以迅速纠正术后贫血,但显然伴有一些相关并发症,包括输血相关传染病、血管内溶血、输血相关急性肺损伤和迟滞恢复等[7] [13] [14]。作为赖氨酸类似物的人工合成物,氨甲环酸(Tranexamic Acid, TXA)通过阻断赖氨酸结合位点的抗纤溶作用能够减少血液丢失量[15]。最近对THA的研究表明,单次或多次应用TXA (10~20 mg/kg)能够减少术后出血,并且不增加深静脉血栓形成(DVT)或肺栓塞的风险[16] [17] [18]。其他研究也显示,静脉注射TXA能够减少人工髋关节置换术的出血量[19]。然而,在髋关节翻修术中使用TXA是否能够减少围术期失血量以及是否会增加患者罹患DVT和肺栓塞的风险还

需要进一步的临床研究。因此，我们进行了一项汇总相关文献分析，以确定 TXA 在人工髋关节置换术中的临床效果与安全性。

2. 氨甲环酸在全髋关节置换术中的作用机制

氨甲环酸(TXA)是一种人工合成的赖氨酸衍生物，在 20 世纪 50 年代由日本药物学家冈本歌子(Utako Okamoto)发现，后于 60 年代初首次作为药物引入临床，在经历 CRASH-2 trail 研究后于 2011 年正式纳为世界卫生组织(WHO)规定的基本药物，在临床上常用于止血(抗纤溶作用)。纤维蛋白原是凝血过程中的关键蛋白，在凝血酶的作用下分解为纤维蛋白，在凝血过程中形成网状聚集血小板后形成血栓，且能够被纤溶酶分解。围术期失血不仅影响患者预后、增加住院时长和经济负担，同时也增加了失血及输血相关的不良反应。在美国，2001 年有 1390 万单位红细胞(RBC)输注给 490 万患者，而在 2001/02 年，加拿大血液服务机构的支出总额达 6.388 亿加元[20] [21] [22]。Laurent G 等人纳入 10,100 例接受非心脏手术患者的回顾性研究结果表明：输血患者的 30 天死亡率为 6.44% 高于而未接受输血的患者的 4.26% [23]。根据北新英格兰心血管研究组的一项研究，接受一到两单位红细胞的心脏手术患者死亡的长期风险增加了 16% [24]。而预防手术或创伤导致大面积组织损伤后的纤溶亢进，也成为了骨科医生高度关注的问题。氨甲环酸通过竞争性结合纤溶酶原与纤溶酶上的 4~5 个赖氨酸结合位点，从而抑制纤维蛋白的分解、降低纤溶活性，进而发挥抗纤溶作用。此过程减少了纤溶酶原向纤溶酶的转化，阻止了纤维蛋白的降解，并保留了纤维蛋白的基质结构框架[25]。研究支持全身和局部使用氨甲环酸以减少失血和输血需求，而不会明显增加关节置换术期间发生深静脉血栓形成(DVT)或肺栓塞(PE)的风险[26]。目前，大量研究均已证实氨甲环酸可有效减少骨科手术围术期的失血量并降低输血率，且不增加术后静脉血栓栓塞症(VTE)的发生风险[27]。氨甲环酸的止血效果与其应用剂量和应用次数有关，但随着剂量或次数的增加，VTE 的发生风险也可能增大[28]。

3. 氨甲环酸在髋关节置换术中的应用现状

3.1. 氨甲环酸在髋关节置换术中的应用

TXA 在初次关节置换术患者中的使用已得到临床实践指南的认可[29]。关节置换术指南中的主要建议有：(1) 与给予安慰剂相比，所有 TXA 给药途径(静脉、口服和局部)均有效减少失血量和输血需求；(2) TXA 的剂量不影响结果，1 g TXA 静脉给药为中位剂量；(3) 未观察到多次给予 TXA 的额外益处；(4) 切皮前使用 TXA 可在防止失血方面提供最大益处；(5) 使用 TXA 未观察到静脉或动脉血栓栓塞事件风险增加。TXA 在减少术中失血、增加术后血红蛋白和减少红细胞输注需求方面的有效性已被证实[30]。把使用 TXA 作为患者血液管理(PBM)措施的组成部分得到了大力提倡，一些医疗中心的择期患者 TXA 使用率高达 95% [31]。最近，在髋关节翻修术中开始使用静脉注射 TXA。髋关节翻修术通常伴随着组织广泛损伤和手术时间较长，会导致术中和术后计算出的失血增加[32]。Yamasaki [33]发现，在关节置换术后的 2 小时内，出血时间最长，之后引流量逐渐减少。虽然 TXA 广泛用于减少初次髋关节置换术中的失血和输血需求[34]，但对于在髋关节翻修术中使用 TXA 的疗效和安全性了解甚少。

3.2. 安全性

正如几个小型试验所证明的，TXA 在各种骨科手术中能有效减少失血量，但目前还缺乏能充分评估 TXA 安全性的合适的、大型的、随机的试验。由于不良事件(如血栓形成、心肌梗死、中风和癫痫)的发生率非常低，只有更大规模的随机研究才能提供对实际风险的前瞻性、无偏倚的评估。另一种替代方法是比较大型系统评价研究中不良事件的发生率[35]。这些试验的结果未证明有与骨科手术中 TXA 相关的

不良事件的证据。最近的一项大型回顾性分析评估了 8 年期间 26,808 名有冠状动脉疾病史或冠状动脉支架植入术后的高危患者行关节置换术后的情况。在这其中接受了 TXA 的患者, 没有观察到形成静脉血栓或心肌梗死的风险增加[36]。然而, 在缺乏大型的、前瞻性、随机对照试验的情况下, 对血栓形成高风险患者(例如, 近期冠状动脉支架植入、近期中风或高凝状态患者)必须权衡血栓形成的潜在风险与最大限度减少失血的益处。关于癫痫风险, 骨科手术中使用的 TXA 剂量(10~20 mg/kg)似乎与癫痫风险增加无关[37]。

3.3. 使用方法

药代动力学研究已确定: 骨科手术中的最佳血清 TXA 浓度为 $> 10 \mu\text{g/mL}$ [38]。经口服、局部或静脉等不同方法给药, 可通过不同的药代动力学特征达到治疗水平[39] [40]。当前证据表明, 当评估使用不同途径的 TXA 给药用于大型关节置换术的效果, 发现不同途径的 TXA 给药在减少失血、输血需求或血栓并发症发生率方面的结果没有差异[41] [42]。单次或分次静脉注射总量为 10~20 mg/kg TXA 仍是最常见的给药剂量和方法之一[29] [31]。一项分析表明, 在减少失血量和输血需求方面, 静脉注射和关节内使用 TXA 相结合优于单独静脉注射 TXA [39]。研究[43] [44]报道 TXA 给药方式主要为单次静脉滴注或二次间隔静脉滴注, 二次给药间隔时间为 3 h。单次给药剂量为 15~20 mg/kg 或总量 1 g; 二次间隔给药剂量为每次 10~20 mg/kg 或每次总量 1 g。研究表明, TXA 局部应用能够提高局部药物浓度, 减少全身吸收[45]。1 项 meta 分析[46]报道 TXA 2~3 g 局部应用可以有效减少出血、降低输血率。目前, 有关 TXA 的局部应用尚无统一标准, 特别是对于术后是否放置引流管及引流管夹闭后何时开放仍存在争议, 各报道中术后引流管夹闭时间为 30 min~2 h 不等。因此, TXA 在髋关节置换术中局部应用的具体方法及术后引流管夹闭时间有待进一步研究。研究报道, TXA 在髋关节置换术围术期静脉滴注联合局部应用相比单纯静脉滴注或局部应用能更有效减少出血、降低输血率[47]。具体方法为髋关节置换术切开皮肤前 5~10 min TXA 15~20 mg/kg 静脉滴注完毕, 同时关闭切口前以总量 1~2 g TXA 局部应用。

4. 展望

综上所述, 氨甲环酸(TXA)在髋关节翻修术中的应用已经得到广泛研究。目前的研究表明, TXA 可以显著减少手术过程中的出血量和输血需求, 同时并不增加手术并发症的风险。一些研究还发现, 更早地应用 TXA 可以获得更好的止血效果。此外, 有众多研究表现出 TXA 可预防 PJI 或术区感染[48] [49]。然而, 目前的研究还存在一些限制, 例如样本量小和研究设计的差异等。因此, 为了进一步验证 TXA 在髋关节翻修术中的应用价值, 需要进行更多高质量、大规模、多中心、随机对照的临床研究来验证氨甲环酸的应用价值研究。总体而言, 以氨甲环酸作为止血药物在髋关节置换/翻修术中的应用显示出良好的止血效果和安全性, 但还需要进一步的研究来确定最佳应用时间和剂量, 以更好地指导临床实践。

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