

无阿片麻醉及其在骨科手术中的研究现状

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摘 要

随着加速康复外科学理念(ERAS)的提出及多模式镇痛的发展, 无阿片麻醉在非阿片类药物和技术的进步下得到进一步完善。骨科手术患者作为急性疼痛和慢性疼痛的高危人群, 减少阿片类药物的使用可显著降低相关风险, 促进患者预后。然而目前学界对围术期完全避免使用阿片类药物尚存争议。本文从无阿片麻醉的相关理论基础及其在骨科手术中的实施方案、有效性、安全性、局限性等方面进行综述, 为临床应用和开展进一步研究提供参考。

关键词

无阿片麻醉, 骨科手术, 多模式镇痛

Current Research Status of Opioid-Free Anesthesia in Orthopedic Surgery

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Abstract

With the introduction of the Accelerated Recovery Surgery Concept (ERAS) and the development of multimodal analgesia, opioid-free anesthesia has been further refined by advances in non-opioid medications and techniques. As orthopedic surgical patients are at high risk for both acute and chronic pain, reducing the use of opioids can significantly reduce the associated risks and promote patient prognosis. However, the complete avoidance of opioids in the perioperative period is currently controversial in the academic community. This article reviews the relevant theoretical basis of opioid-free anesthesia and its implementation protocols, effectiveness, safety, and limitations in

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orthopedic surgery to provide reference for clinical application and conducting further research.

Keywords

Opioid-Free Anesthesia, Orthopedic Surgery, Multimodal Analgesia

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1. 引言

骨科手术包括骨折、关节损伤(如髌、膝关节置换)、脊柱疾病(如椎间盘突出)等,人口老龄化加剧了关节退行性变的需求,运动普及、意外事故及微创手术、人工关节等发展提高了手术量;骨科手术创伤大,疼痛剧烈,若控制不佳,急性疼痛可能转为慢性,导致康复延迟,甚至功能丧失[1]-[3]。阿片类药物是围术期疼痛管理的重要组成部分,虽然能够提供足够的镇痛,但经常引起镇静、呼吸抑制和恶心呕吐等不良反应,无阿片麻醉(OFA)旨在通过多模式镇痛技术在围术期避免使用阿片类药物而实现术中麻醉与术后疼痛的控制,减少或消除阿片类药物的副作用,通过精准镇痛优化患者康复[4][5]。骨科手术需早期活动以预防血栓和肌肉萎缩,OFA通过有效的靶向镇痛,促进患者术后活动和功能锻炼,契合加速康复外科理念。本文就OFA在骨科手术中研究现状重点展开阐述。

2. OFA 常用药物与技术

OFA是一种多模式的麻醉管理方法,结合了多种作用于不同伤害通路的非阿片类药物或技术。药物包括基础麻醉药物:右美托咪定作为选择性的 α 受体激动剂,从脊髓和脊髓上区通过下行疼痛抑制通路释放去甲肾上腺素,抑制背角初级传入神经元的神经传递,提供镇静镇痛作用,及减少术中应激反应[6];低剂量(0.3~0.5 mg/kg)的氯胺酮通过激活单胺能下行疼痛抑制通路和对N-甲基-天冬氨酸(NMDA)受体的拮抗来缓解疼痛[7][8];静脉输注利多卡因可减少炎症反应,减少阿片类药物的需求及相关不良事件的发生率,提高术后恢复质量[9]。吸入麻醉药可联合其他非阿片类药物维持麻醉深度同时加强镇痛强度。其次为辅助性镇痛药物:非甾体类抗炎药(NSAIDs)如酮咯酸或帕瑞昔布,抑制环氧化酶(COX)导致前列腺素合成减少,进而减轻炎性疼痛[10];对乙酰氨基酚可能作为间接COX抑制剂或通过调节大麻系统发挥镇痛作用[11];糖皮质激素如地塞米松兼具抗炎和止吐作用,当进行局部阻滞时,全身和周围使用地塞米松均可改善阻滞的质量和持续时间[12][13];神经阻滞剂如加巴喷丁和普瑞巴林是中枢神经系统的电压门控钙通道拮抗剂,减少神经兴奋性递质的释放,进而抑制神经病理性疼痛[14]。多种药物的联合使用可以抑制损伤神经纤维的冲动和伤害性刺激的传递,并可能在术后前24小时内加强镇痛作用,同时减少术后早期阿片类药物的消耗[15]。OFA通过结合多种非阿片类药物应用于多种手术类型,不同的手术类型可能需要不同的药物组合和剂量调整;患者的个体差异大,不同的患者也需寻求最优的无阿片类药物组合,如有消化道出血的患者,禁用NSAIDs;老年患者在右美托咪定的使用剂量上也应斟酌。无阿片麻醉药物组合作为一种有前景的麻醉方案,探索并优化其不同手术类型中的应用效果,促进骨科患者术后的长期恢复。

技术层面包括局部和区域麻醉技术,局部和区域麻醉是在切口周围或沿着疼痛传导路径注射局部麻醉剂以阻断信号到达大脑[16]。随着超声技术的发展,周围神经阻滞和平面筋膜阻滞对手术相关区域进行

靶向麻醉,降低了对全身麻醉药物的需求,减轻对循环、认知功能的干扰[17][18];椎管内麻醉通过阻断脊神经传导实现麻醉,主要包括硬膜外阻滞、蛛网膜下腔阻滞、腰硬联合麻醉及骶管阻滞[19];局部浸润麻醉通常由外科医生进行,在手术创面或创口附近及关节内注射局部麻醉药,提供术中及术后的镇痛[20]。非药物干预包括冷敷或热敷、经皮电神经刺激(TENS)和针灸[21]。通过多模式、多靶点策略,根据患者病情及手术类型个体化选择无阿片麻醉技术,有助于安全有效的替代传统的阿片麻醉方案。

3. OFA 在骨科手术中的应用现状

通过检索 PubMed、Embase、Cochrane Library、Web of Science、知网、维普等数据库,共获取了 24 篇已发表的相关研究,其中 6 项研究因病例报告或年代久远被排除,其余 18 项被纳入讨论。研究涉及多个国家,国内开展的相关研究仅 2 项[22][23],手术类型分别为髋关节置换术和脊柱后路内镜手术。约半数的研究中有右美托咪定或氯胺酮的使用,对乙酰氨基酚、酮咯酸等作为辅助性镇痛药。大部分研究报告了术后镇痛方案,同时将阿片类药物作为重度疼痛的补救性措施。

在两项髋关节置换的研究中,均单用右美托咪定作为 OFA 方案,与传统阿片组形成对照。其中 Clement 等[24] ($n = 40$)术前静脉滴注右美托咪定 $1 \mu\text{g}\cdot\text{kg}^{-1}$,持续 30 min,然后联合异丙酚 $2\sim 3 \text{ mg}\cdot\text{kg}^{-1}$ 和氯胺酮 $0.4 \text{ mg}\cdot\text{kg}^{-1}$ 进行诱导麻醉,根据术中需求,可予 $0.4 \mu\text{g}\cdot\text{kg}^{-1}$ 右美托咪定持续输注 30 min 进行补救性镇痛。Brendan 等[25]在麻醉诱导前 20 min 泵注 $0.7 \mu\text{g}\cdot\text{kg}^{-1}$ 右美托咪定,诱导后以 $1.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ 的速度持续泵注至外科医师切皮,然后每 10~15 min 减量 $0.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$,关闭切口前 30 min 停止输注。在一项前瞻性随机对照试验中[26],针对行脊柱侧弯术的青少年患者,OFA 组($n = 33$)采用氯胺酮联合右美托咪定的方案,氯胺酮 $0.5 \text{ mg}\cdot\text{kg}^{-1}$ 联合异丙酚 $5 \text{ mg}\cdot\text{kg}^{-1}$ 进行麻醉诱导,随后氯胺酮以 $0.15 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ 的速度持续输注,右美托咪定在患者俯卧位后开始给药,10 min 以内推注 $1 \mu\text{g}\cdot\text{kg}^{-1}$,随后以 $0.04 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ 的速度连续输注。

区域神经阻滞技术通过在特定神经或神经丛周围注射局部麻醉药,阻断神经信号的传导,从而达到镇痛或麻醉的效果。已有文献证实,区域麻醉可以完全阻断伤害性刺激的传入,在骨科手术中是减少或避免术中和术后阿片类药物的最佳技术[27]。目前在骨科手术的 OFA 相关研究中,常用的区域神经阻滞技术包括膝关节股神经阻滞[28]-[30]、收肌管阻滞[29][31][32];肩关节臂丛神经阻滞[33][34];髋关节囊周神经阻滞(PENG) [3] [35];踝关节隐神经和坐骨神经阻滞[36]、胫后和腓肠神经阻滞[37]等,其中,在一项前瞻性随机对照研究中[38],对照组和试验组均采用了神经阻滞技术作为多模式镇痛的一部分;还有研究[39]在行髋关节置换术的患者中联合应用腰麻和椎旁阻滞或竖脊肌平面阻滞作为 OFA 方案;另外在一项回顾性队列研究中[40],将锁骨上臂丛神经阻滞应用在小儿肘部骨折手术中。此外,三项研究应用了椎管内麻醉,其中两项[41][42]以布比卡因腰麻联合局部浸润镇痛,另一项[22]以 2%利多卡因 7.5 ml 与 1%罗哌卡因 7.5 ml 行硬膜外阻滞,联合异丙酚 $2 \text{ mg}\cdot\text{kg}^{-1}$ 、罗库溴铵 $0.6 \text{ mg}\cdot\text{kg}^{-1}$ 、艾司洛尔 $1.5 \text{ mg}\cdot\text{kg}^{-1}$ 进行麻醉诱导。根据不同的手术类型选择不同的神经阻滞方案以达到最优镇痛效果,如脊柱手术可选择躯干神经阻滞(椎旁神经阻滞);上肢手术可选择臂丛神经阻滞,又根据手术的具体部位有肌间沟、锁骨上、腋路三种不同阻滞入路可供选择;下肢手术可采用股神经阻滞、坐骨神经阻滞、股外侧皮神经阻滞、收肌管阻滞、髂筋膜阻滞等。在临床实践中,膝关节置换术中单髁置换的患者可以采用收肌管神经阻滞联合股外侧皮神经阻滞,在提供足够镇痛的同时最大程度减少阻滞技术对股四头肌肌力的影响。

多模式镇痛中已广泛应用非阿片类技术,这些技术已经被证明能够提升患者的治疗效果[43]。但针灸作为多模式镇痛的一部分,仅在一项队列研究中[44]以耳电刺激形式应用,此结果不具有普遍适用性,需进一步研究评估该技术在骨科手术中的可行性。

4. OFA 在骨科手术中的有效性及安全性

在急性疼痛控制方面, 有研究[45]表明, 在择期骨科手术中 OFA 与传统阿片麻醉的术后急性疼痛评分(VAS 或 NRS)无显著差异; Soffin 等[46]报告的回顾性研究中, 36 例行脊柱手术的患者, 与基于阿片类药物的方案相比, OFA 方案术后 NRS 评分相似(1.6 ± 0.69 vs 1.0 ± 0.46 , $P > 0.05$)。在一项纳入了 23 项研究的 Meta 分析[47]中显示, OFA 组与传统阿片组术后 2 小时的静息平均疼痛评分相当(3.4 vs 3.6 , $P = 0.38$), 术后 12 小时及 24 小时静息疼痛评分也无差异(均 $P > 0.05$)。McCarthy 等[41]在膝关节置换术的研究中得出结论, 术后 24 小时静息和运动时 VAS 评分, OFA 组均低于阿片对照组($P < 0.05$)。但是对于需要早期下床活动的患者, OFA 可能因区域阻滞作用消退引起反跳痛而导致动态疼痛控制欠佳, 不过目前缺少相关研究证实该假设。

OFA 通过阻断中枢敏化机制可能降低慢性术后疼痛(CPSP)风险, 如氯胺酮作为 NMDA 受体的拮抗剂已被证明可减轻中枢敏化和痛觉过敏, 从而降低术后阿片类药物耐受性, 进而有预防慢性疼痛的潜力[48][49]。Szamburski 等[50]报道了 219 名骨科手术后的患者, 有 63 名(29%)在术后 3 个月出现了 CPSP, 通过单变量分析, 证明区域麻醉类型及急性疼痛水平与 CPSP 风险增加相关。

在术后不良事件方面, OFA 可以显著降低各类患者术后恶心呕吐(PONY)的发生率, 尤其在 PONY 高风险患者(如女性、非吸烟者)中的效果更显著[51]-[53]; 同时可以避免阿片类药物引起的呼吸抑制风险(尤其合并睡眠呼吸暂停的患者)及降低老年患者术后谵妄的发生率; 通过减少阿片类药物相关的副作用, 促进术后早期康复及缩短住院时间[42]。

OFA 替代药物的安全性体现在, 右美托咪定可根据术中疼痛管理的需求调整泵注剂量以确保其用药的安全性[54]; 亚麻醉剂量($0.3 \sim 0.5$ mg/kg)的氯胺酮联合苯二氮卓类药物可减少幻觉发生率; 此外, 在超声引导下行区域神经阻滞操作, 可大大降低该技术风险; 用于骨科区域麻醉技术的罗哌卡因等局部麻醉药心脏毒性低、毒性阈值高、血药浓度控制良好, 安全可控[55]-[57]。

OFA 在骨科手术中的有效性体现在, OFA 在术中与术后展现出不劣于传统阿片麻醉方案的急性镇痛效果; 同时通过减少阿片类药物的使用, 可以显著降低患者术后 PONY、呼吸抑制、皮肤瘙痒等不良事件的发生率, 契合 ERAS 目标; 此外, 术中使用右美托咪定、氯胺酮和利多卡因等药物组合, 可以提供良好的血流动力学稳定性; OFA 对于特殊患者群体, 如肥胖患者、阿片药物滥用者, 在术后恢复方面表现出优势。OFA 方案的可行性依赖于多模式镇痛技术的成熟与区域阻滞的精准实施, 随着目前超声等影像技术的发展, 区域阻滞技术具有更高的安全性及可行性。尽管可能存在动态疼痛控制不佳及非阿片药物配伍禁忌等局限性, 但通过优化方案设计及患者个体化选择, OFA 有望成为骨科围术期管理的优选策略。

5. OFA 在骨科手术中的局限性

镇痛效能不足, 难以覆盖重度急性疼痛: 骨科手术常涉及骨骼切割、关节腔暴露或神经牵拉, 术中或术后急性疼痛剧烈且复杂, 涉及躯体痛和内脏痛的双重机制[58]。非阿片类药物如 NSAIDs、对乙酰氨基酚的镇痛效果存在剂量上限, 超量使用可能引发消化道出血或肾毒性, 即使联合区域阻滞, 对深部组织和内脏痛的疼痛覆盖仍可能不足[59][60]; 无阿片方案在抑制手术刺激引起的交感神经兴奋(如高血压、心动过速)方面效果有限, 在老年或合并症患者中可能增加心血管不良事件风险。

技术依赖性与操作复杂性: OFA 依赖多种非阿片药物的协同作用, 需精确计算剂量与给药时机, 以免发生不良药物相互作用[5]。右美托咪定作为 α -2 受体激动剂, 可能增加手术期间低血压和心动过缓的风险, 其镇静作用可能会延长术后苏醒时间, 需与麻醉深度监测紧密结合[61]。除了多模式镇痛的精细化要求, 还存在区域阻滞的失败风险, 骨科手术中区域神经阻滞技术已被证实有确切的镇痛及麻醉效果,

但阻滞技术的成功率受操作者经验和解剖变异的影响。当多部位创伤手术时,如骨盆骨折合并长骨骨折,单一区域阻滞无法阻断所有伤害性感受的传导,因而不能覆盖所有疼痛区域,此时需多导管置入联合镇痛,增加技术难度。而当操作失败或者效果欠佳,若未及时补救可能被迫转为阿片类药物方案。

术后恢复期的潜在风险:区域阻滞作用消退后,若无长效镇痛衔接,可能引发患者剧烈的反跳痛。其次可能还会存在替代药物副作用的累积,如加巴喷丁类药物引起的头晕、嗜睡,可能影响术后早期活动,延迟骨科患者康复进程[62][63];NSAIDs会抑制血小板功能可能加重术中出血,尤其联合抗凝治疗的骨科患者(如关节置换术后深静脉血栓预防)[64];氯胺酮在老年患者中幻觉、谵妄等精神副作用发生率升高等。

患者选择与个体差异的限制:患有慢性疼痛或术前服用阿片类药物的患者理论上是OFA方案受益的人口学类型,这些患者术后严重急性疼痛和术后疼痛慢性化的风险较普通患者高,对此可以通过避免术中阿片类药物来减少痛觉过敏,进而降低术后急慢性疼痛发生率和对阿片类药物的需求[65][66]。然而患者疼痛敏感度存在差异,慢性疼痛患者或阿片耐受者可能对非阿片药物反应不佳,例如在一项前瞻性研究中[67]显示,术前已存在慢性腰痛的患者接受脊柱手术后,氯胺酮干预组患者术后6个月疼痛并未优于对照组患者($P = 0.24$)。此外,特殊人群的药代动力学也是一项挑战,老年患者对右美托咪定的敏感性增加,更易导致心动过缓;肾功能不全者需避免MSAIDs,限制了药物的选择空间。

6. 讨论

OFA作为一种新兴的镇痛策略,旨在通过避免阿片类药物的使用来减少术后并发症及成瘾风险。现有的相关前瞻性RCT多集中于择期的关节置换手术,缺乏复杂创伤、肿瘤切除等高风险手术数据。完全避免阿片类药物的使用有疼痛控制不足的风险,术中镇痛不全可能通过中枢敏化机制增加术后慢性疼痛的发生率,目前尚无足够证据证明OFA在预防慢性疼痛方面优于传统方案。长期随访数据匮乏。OFA技术具有多样性,更好地理解伤害性感受可能有助于最大限度地发挥其不同背景和潜在适应症中的潜力。OFA应该在考虑特定的患者和手术情况下采用,而不是作为一种通用方法。虽然目前已有研究证实OFA在骨科手术中的可行性,但是仍存在诸多争议和局限性,对于特定类型的骨科手术,最佳的OFA方案尚未达成共识,且不同选择方案之间缺乏详细对比,未来仍需进一步的临床研究来寻求最佳方案,优化多模式方案、建立预测模型筛选OFA适用人群、完善术后过渡镇痛策略(如长效脂质体局麻药)等,克服镇痛强度、技术门槛及个体化适配等核心问题,在严格监测下平衡风险与获益。

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