

艾司氯胺酮在非气管插管全麻手术中的应用进展

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摘要

随着无痛舒适化医疗理念的不断推广, 全身麻醉已广泛应用于无痛诊疗、围术期舒适管理以及疼痛管理等多个领域, 以提升患者的整体医疗体验。非插管全麻手术是一种在全身麻醉下进行, 但不需要使用气管插管来维持呼吸道通畅的手术方式, 它避免了传统气管插管可能引发的并发症, 如喉痉挛、气道损伤及术后咽喉疼痛等, 提高了患者的术后舒适度, 但非插管全身麻醉也存在可能发生呼吸和循环抑制的局限性, 因此寻找到合适的药物和麻醉方案尤为重要。艾司氯胺酮(Esketamine)是由氯胺酮中分离的一种高亲和性的N-甲基-D-天冬氨酸(NMDA)受体非竞争性抑制剂, 广泛应用于麻醉诱导与维持、急慢性疼痛管理、精神疾病以及急危重症的治疗等领域。艾司氯胺酮具有强效的镇静和镇痛作用, 并且其代谢清除迅速, 对呼吸和循环系统的影响较小, 是非插管全麻手术的理想麻醉药物选择。然而, 由于其可能引发神经精神类不良反应, 其临床使用中的剂量与应用策略仍需进一步探讨和研究。基于上述背景, 本文综述了艾司氯胺酮的药理学特性, 并对其在非插管全身麻醉手术中的优势与局限性进行了深入分析, 以期临床实践提供参考。

关键词

艾司氯胺酮, 非气管插管全麻, 麻醉药物, 麻醉方案, 不良反应, 疼痛管理

Application Progress of Esketamine in Non-Endotracheal Intubation General Anesthesia Surgery

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Abstract

With the continuous promotion of the concept of painless and comfortable medical treatment, general anesthesia has been widely used in many fields such as painless diagnosis and treatment, perioperative comfort management and pain management to improve the overall medical experience of patients. Non-intubated general anesthesia surgery is a surgical method that is performed under general anesthesia, but does not require the use of tracheal intubation to maintain airway patency. It avoids complications that may be caused by traditional tracheal intubation, such as laryngospasm, airway injury and postoperative sore throat, and improves the postoperative comfort of patients. However, non-intubated general anesthesia also has the limitation of respiratory and circulatory depression, so it is particularly important to find the appropriate drug and anesthesia program. Esketamine is a high-affinity non-competitive inhibitor of N-methyl-D-aspartate (NMDA) receptor isolated from ketamine, which is widely used in the fields of anesthesia induction and maintenance, acute and chronic pain management, mental diseases, and treatment of acute and severe diseases. Esketamine has a strong sedative and analgesic effect, and its metabolic clearance is rapid, with little effect on the respiratory and circulatory systems, which is an ideal anesthetic drug choice for non-intubation general anesthesia surgery. However, since it may cause neuropsychiatric adverse reactions, its dosage and application strategy in clinical use still need to be further explored and studied. Based on the above background, this article reviews the pharmacological characteristics of esketamine, and analyzes its advantages and limitations in non-intubated general anesthesia surgery, in order to provide reference for clinical practice.

Keywords

Esketamine, Non-Endotracheal Intubation General Anesthesia, Anesthetic Drugs, Anesthetic Protocols, Adverse Reactions, Pain Management

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1. 艾司氯胺酮的药代动力学和药效学特征

艾司氯胺酮为氯胺酮的 S-对映体, 是一种高亲和性的 NMDA 受体非竞争性抑制药, 镇痛效果是氯胺酮的 2~2.5 倍[1] [2]。小剂量就可以发挥镇静和镇痛效果。艾司氯胺酮主要通过非竞争性阻断 NMDA 受体实现麻醉和镇痛作用[3], 还可与阿片受体结合, 进一步增强其镇痛效果[4]。艾司氯胺酮的快速抗抑郁效果与其对 GluN2A 亚基的调节有关, 通过增强海马区兴奋性神经元的自主兴奋性, 实现抗抑郁作用[5]-[8]。此外, 投射到 PFC 的腹侧 CA1 神经元似乎也是其抗抑郁作用的关键靶点[3] [9]。艾司氯胺酮的神经系统不良反应呈剂量依赖性, 与其促进黑质纹状体中多巴胺的释放有关[10], 多项研究证明小剂量艾司氯胺酮静脉应用不增加神经精神症状的发生率[9] [11]。

艾司氯胺酮在肝脏中快速分解[12], 代谢产物主要通过肾脏排泄。与氯胺酮相比, 艾司氯胺酮的代谢和消除速度更快, 短期麻醉后的恢复时间(9 min vs. 13 min, $P < 0.05$)和定向恢复时间(11.5 min vs. 17 min, $P < 0.05$)更短[13]。

2. 艾司氯胺酮在非插管全麻手术中的应用现状

随着无痛舒适化医疗理念的不断推广, 全身麻醉已广泛应用于无痛诊疗、围术期舒适管理以及疼痛

管理等多个领域,以提升患者的整体医疗体验[14][15]。非插管全麻手术是一种在全身麻醉下进行,但不需要使用气管插管来维持呼吸道通畅的手术方式[16],它避免了传统气管插管可能引发的并发症,如喉痉挛、气道损伤及术后咽喉疼痛等,提高了患者的术后舒适度,但非插管全身麻醉也存在可能发生呼吸和循环抑制的局限性,因此寻找到合适的药物和麻醉方案尤为重要。艾司氯胺酮(Esketamine)是由氯胺酮中分离的一种高亲和性的 N-甲基-D-天冬氨酸(NMDA)受体非竞争性抑制剂,广泛应用于麻醉诱导与维持、急慢性疼痛管理、精神疾病以及急危重症的治疗等领域[17][18]。艾司氯胺酮具有强效的镇静和镇痛作用,并且其代谢清除迅速,对呼吸和循环系统的影响较小,有研究发现其还能显著降低呼吸、循环抑制的发生率[19][20],是非插管全麻手术的理想麻醉药物选择,在非插管手术中具有广泛的应用前景。然而,由于其可能引发神经精神类不良反应[21],其临床使用中的剂量与应用策略仍需进一步探讨和研究。

2.1. 艾司氯胺酮在胃肠镜中的应用

普通胃肠镜检查会产生众多不良反应如恶心、呕吐和窒息,还可能触发低血压、心动过缓、头晕等自主神经反应[22][23]。在无痛胃肠镜检查中,丙泊酚作为常用的镇静剂,具有起效快、恢复快的优点,但其缺乏镇痛作用,有较明显的注射痛,且可能引发呼吸抑制、血流动力学不稳定等不良反应[4][24][25]。艾司氯胺酮的联合使用可以减少丙泊酚相关不良事件的发生。目前,已经有很多研究探索了艾司氯胺酮与丙泊酚在无痛胃肠镜联合应用的安全性和有效性[26][27]。一项研究显示,在无痛胃肠镜检查中,采用 0.1 $\mu\text{g/kg}$ 的舒芬太尼与 0.5 mg/kg 的丙泊酚进行诱导镇静后,给予 0.15 mg/kg 的艾司氯胺酮可显著降低患者氧饱和度下降及低血压的复合事件和单独事件的发生率,同时减少丙泊酚的用量,且未增加相关的不良反应[4]。另一项研究亦得出相似结论,0.2 mg/kg 的艾司氯胺酮与丙泊酚联合使用,不仅降低了丙泊酚的用量,还缩短了诱导时间,减少了咳嗽和体动的发生率,并未显著增加麻醉相关的不良事件[28]。艾司氯胺酮的预处理在降低丙泊酚注射疼痛方面的效果与利多卡因相当,但与利多卡因相比,艾司氯胺酮能够为患者提供更为稳定的循环状态[26]。一项荟萃分析表明,在胃镜检查中,丙泊酚联合 0.25 mg/kg 的艾司氯胺酮被认为是最佳剂量[27]。在接受无痛胃镜检查的患者中,单次给予 0.5 mg/kg 的艾司氯胺酮通常被认为是安全且耐受的[21]。

在小儿胃镜手术中,艾司氯胺酮的应用显著缩短了患儿的恢复时间,并降低了丙泊酚的消耗量(0.70 mg/kg),诱导时间和平均血氧饱和度未显示出显著变化。该研究还发现艾司氯胺酮的使用减少了患儿 59% 的不自主运动,但是显著增加了患儿出现头晕的概率,总体不良事件、呼吸抑制和呕吐的发生率无显著差异。有研究表明, $\leq 0.3 \text{ mg/kg}$ 的艾司氯胺酮能够显著减少恢复时间、丙泊酚的消耗量以及不自主运动的发生,同时增加了平均心率,而并未显著增加头晕的发生概率[29]。另有研究表示,当艾司氯胺酮与 3 mg/kg 的异丙酚联合使用时,其有效剂量(ED50)为 0.143 mg/kg 。在该剂量下,艾司氯胺酮能够在小儿患者胃镜手术中实现有效的镇静,且几乎未观察到明显的不良反应。这些结果为小儿胃镜手术的麻醉管理提供了重要的临床依据[30]。

在老年患者中,一项使用狄克逊检验法进行艾司氯胺酮计量实验的研究发现,丙泊酚联合 0.3 mg/kg 艾司氯胺酮用于接受胃镜检查的老年患者安全有效[31]。在肥胖患者的无痛胃镜检查中,小剂量艾司氯胺酮的应用也显示出显著优势。研究发现,与单用丙泊酚相比,联合使用 0.3 mg/kg 艾司氯胺酮显著降低了注射痛、低氧血症、低血压、心动过缓、窒息等不良事件的发生率[32]。

艾司氯胺酮在无痛胃肠镜手术中表现出了良好的应用前景,可以降低呼吸暂停和低血压的发生率[33],但术中应用艾司氯胺酮增加了术中高血压的概率,术前血压控制不佳的患者使用本品时应谨慎[27]。

2.2. 艾司氯胺酮在经内镜逆行性胰胆管造影术(ERCP)中的应用

内镜逆行胰胆管造影术(ERCP)是一种常见的胃肠道介入手术,通常需要对患者进行镇静。近年来,

静脉注射丙泊酚联合阿片类药物的深度镇静已成为此类手术的首选镇静方案。然而,使用高剂量丙泊酚可能导致呼吸抑制等副作用。一项研究显示,在 799 名接受丙泊酚镇静的内窥镜手术患者中,有 12.8% 的患者出现了低氧血症[34]。另一项研究则比较了 ERCP 过程中小剂量艾司氯胺酮与舒芬太尼联合丙泊酚镇静的安全性和有效性。结果表明,与舒芬太尼相比,小剂量艾司氯胺酮(150 $\mu\text{g/kg}$)显著减少了手术中所需的丙泊酚总量,且患者及医生对小剂量艾司氯胺酮的应用均表示较高的满意度,未观察到额外的不良反应[5]。

2.3. 艾司氯胺酮在妇产科短小手术中的应用

2.3.1. 宫腔镜

一项研究表明,在宫腔镜手术中,艾司氯胺酮的 95%有效药物剂量(ED95)为 0.254 mg/kg 。当以 ED95 剂量给予艾司氯胺酮并联合丙泊酚进行静脉麻醉时,能够获得令人满意的麻醉效果。与舒芬太尼和丙泊酚的麻醉方案相比,艾司氯胺酮与丙泊酚联合使用在呼吸抑制方面发生率更低,血流动力学更加稳定,且不良反应发生率较少[35]。另一项针对宫腔镜手术的研究建议,对于需要进行喉罩插管的患者,使用 2.0 mg/kg 丙泊酚联合 0.2 mg/kg 艾司氯胺酮的麻醉方案较为合适[36]。

2.3.2. 宫颈锥切手术

在接受宫颈锥切术的患者中,有研究评估了舒芬太尼与丙泊酚联合镇静时添加艾司氯胺酮的效果。结果显示,在脑电双频指数(BIS)引导下进行丙泊酚靶控输注(TCI)镇静期间,联合使用艾司氯胺酮能够有效降低与镇静相关的不良事件的发生率和严重程度,如重度氧饱和度下降和呼吸暂停等。该研究表明,在此类手术中,使用 0.075 mg/kg 的艾司氯胺酮与 0.05 mcg/kg 的舒芬太尼联合应用方案是合理且有效的[37]。

2.3.3. 无痛人流手术

传统的堕胎方法常伴随显著的不适和疼痛,甚至可能导致患者死亡[38]。无痛人流手术显著减轻了手术带来的不适感,降低了患者的恐惧和紧张情绪,减少了术后不良反应的发生率。

有研究表明,单次给予艾司氯胺酮(0.25 mg/kg)能够有效降低无痛人流手术中缺氧及总体不良事件的发生率,同时减少了额外补充丙泊酚的剂量和频率。此外,艾司氯胺酮的使用对医患满意度未产生显著影响[39]。这些结果表明,艾司氯胺酮在无痛人流手术中的应用具有重要的临床价值

2.4. 艾司氯胺酮在非插管骨科手术中的应用

在一项针对经皮内镜椎间盘切除术(PELD)的研究中,研究者发现 0.1 mg/kg 和 0.2 mg/kg 的艾司氯胺酮与右美托咪定联合应用均可有效降低手术患者的疼痛视觉模拟评分(VAS 评分)。该联合用药对患者的呼吸和循环系统影响较小。然而,术后头晕和精神副作用的发生率有所增加,并未显著提高患者与术者的满意度[40]。因此,在此类手术中,艾司氯胺酮的用量仍需进一步深入研究。

2.5. 艾司氯胺酮在射频消融术的应用

在需要保持患者清醒状态的射频消融术中,研究探索了小剂量艾司氯胺酮(0.2 mg/kg)与右美托咪定联合静脉输注的麻醉效果。结果表明,艾司氯胺酮与右美托咪定的联合应用在麻醉可控性、血流动力学稳定性及苏醒时间方面均优于舒芬太尼联合右美托咪定。右美托咪定能够有效抑制艾司氯胺酮引发的交感神经兴奋和躁动,而艾司氯胺酮则能够减轻右美托咪定对心血管系统的不良影响[41]。

尽管小剂量艾司氯胺酮显示出优良的镇痛和镇静效果,但其使用可能会导致高血压患者的血压波动增加。因此,在临床应用中,特别是对术前血压控制不佳的患者,应严格监控其血压变化,以确保用药

的安全性。

3. 艾司氯胺酮的不良反应

艾司氯胺酮在临床应用中最常见的不良反应包括头晕、拟精神症状以及心血管系统反应[8]，小剂量应用时精神症状发生率较低，不过可能会轻微延迟患者的苏醒[42]。此外，艾司氯胺酮具有交感神经激活作用，能够剂量依赖性地增加心输出量，从而升高血压和心率[43]。在高血压患者中，艾司氯胺酮可能引发血压的显著波动，增加心血管事件的发生风险。因此，在临床应用中，应严格监测患者的血压和心率变化，尤其在术前血压控制不佳的患者中，应避免大剂量应用艾司氯胺酮。艾司氯胺酮有舒张支气管的作用，但其同时可能增加气道分泌物[44]。

4. 总结

艾司氯胺酮在非气管插管全麻的应用中显示出广泛的临床价值，其具有良好的镇痛、镇静效果，可以减轻阿片类和丙泊酚的呼吸抑制，并能够改善术后恢复质量。然而，其潜在的不良反应和安全性问题仍需进一步研究。未来的临床研究应关注不同手术方式和患者群体中的最佳剂量选择，并深入探讨艾司氯胺酮在围术期管理中的长期安全性和经济性，以优化其临床应用效果

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