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Assessing the Tolerability and Safety of Oliceridine, a Biased Opioid, for Acute Pain Management: A Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 May 2024 and was last updated on 21 May 2024.

INTRODUCTION

Review question / Objective This study aims to deliver a systematic review and meta-analysis to scrutinize the tolerability and safety of oliceridine in acute painpatients.A comprehensive search was carried out in quintessential databases (like PubMed, Embase, and Cochrane Library) for pertinent studies published until July 31, 2023. We included Randomized Controlled Trials (RCTs) that compared oliceridine with other interventions in acute pain management. Utilizing the RevMan 5.4 software, data on nausea, vomiting, sedation, dizziness, pruritus, and hypoxemia were assembled and evaluated.

Condition being studied The management of acute pain is a crucial facet in patient care, underlining the ongoing need for effective and safe analgesics. In particular, postoperative contexts demand medical practitioners to constantly explore treatments that can offer optimal pain alleviation, simultaneously reducing potential side effects. Morphine —a widely utilized mu-opioid receptor agonist— often acts as the first line of treatment. Regardless of its powerful analgesic properties, the drug is notorious for fostering a host of adverse effects including nausea, vomiting, sedation, dizziness, pruritus, and hypoxemia. Given these substantial drawbacks, researchers continue the search for substitute analgesics that can offer a better safety and tolerability profile.
A promising contender is oliceridine, a peculiar G-protein path-selective mu-opioid receptor agonist, which is being hailed as a potential alternative. Oliceridine is a novel opioid developed for the management of moderate to severe acute pain. It's a biased agonist, meaning it's designed to selectively activate certain intracellular signals of

the opioid receptor to produce analgesic effects, while avoiding the activation of those signals responsible for adverse reactions and side effects. Irrespective of these promising advancements and potential benefits of oliceridine, robust, reliable, and comparative data outcomes are required to substantiate its clinical utility.

Despite several individual studies investigating the safety and effectiveness of oliceridine, the findings are yet to converge into a consensus.While some studies praise oliceridine for its significant pain relief attributes, others emphasize the occurrence of unwanted side effects, thereby muddying the waters. This divergence calls for a systematic and comprehensive review of the current evidence to assess the benefits associated with oliceridine and potential risks in the domain of acute pain management.

In this light, our study utilizes a systematic review and meta-analysis to scrutinize available Randomized Controlled Trials (RCTs) concerning the safety and tolerability of oliceridine . Our meta-analysis pivots its focus on a host of specific adverse effects including nausea, vomiting, sedation, dizziness, pruritus, and hypoxemia . It is our hope that by amalgamating the available evidence, we can offer a clearer perspective on the safety and tolerability profile of oliceridine, potentially paving a fresh course for acute pain management.

METHODS

Participant or population The studies had to provide data on potential side effects including nausea, vomiting, sedation, dizziness, pruritus, or hypoxemia. We also limited our focus to studies conducted on adult human subjects (18 years and above).

Intervention The data curation process was carried out by two researchers who worked independently, sifting through search results, reviewing titles, abstracts, and disregarding duplicates. Differences of opinion regarding which research to include were settled by reaching consensus. Following an in-depth review of full-text potential studies, we compiled data utilizing a standardized data extraction format. This encompassed author details, year of publication, study design, sample size, patient characteristics, details regarding the dosage of oliceridine and morphine administered, duration of treatment, and outcomes central to tolerability and safety, specifically addressing side effects like nausea, vomiting, sedation, dizziness, pruritus, and hypoxemia.

Comparator Quantitative analysis of the data was carried out utilizing the Review Manager (RevMan 5.4) software. Relative risk (RR) assessment alongside 95% confidence intervals (CI) was employed to investigate dichotomous data. We determined potential heterogeneity in the studies by quantifying the with the I2 statistic. Should the I2 statistic exceed 50%, we construed this as substantial heterogeneity.

Study designs to be included Our research methodology entailed a systematic exploration of three pertinent databases, namely: PubMed, Embase, and the Cochrane Library, through July 31, 2023. We aimed to uncover randomized controlled trials (RCTs) that evaluated the tolerability and safety of oliceridine in acute pain management. To achieve this, a versatile range of search terms was used in varying permutations. These included "oliceridine", "tolerability", "safety", "randomized controlled trial", "acute pain management", and terms indicative of potential side effects such as "nausea", "vomiting", "sedation", "dizziness".

Eligibility criteria We also limited our focus to studies conducted on adult human subjects (18 years and above). Exclusion criteria saw the removal of case reports, observational studies, reviews, animal studies, or investigations involving pediatric or adolescent subjects from our consideration.

Information sources PubMed, Embase, and the Cochrane Library.

Main outcome(s) The preliminary search discovered 429 potential studies. Having gone through a careful screening process, a total of 7 RCTs met our inclusion benchmarks. Five distinct publications analyzed postoperative nausea and vomiting (PONV). According to our meta-analysis findings, patients assigned to the oliceridine group experienced a notably lower PONV rate compared to the morphine group (RR = 0.55, 95% CI 0.41-0.74, P < 0.0001), (RR = 0.36, 95% CI 0.28-0.47, P < 0.00001). Data from 4 documents examined sedation and dizziness. Our findings demonstrate that oliceridine recipients had a significant decline in the incidence of both sedation and dizziness (RR = 0.64, 95% CI 0.45-0.91, P = 0.01), (RR = 0.71, 95% CI 0.57-0.88, P = 0.002). Moreover, the oliceridine group recorded a lower incident of hypoxemia showcasing a favorable safety profile (RR = 0.52, 95% CI 0.41-0.65, P <0.00001).

Quality assessment / Risk of bias analysis Two researchers independently evaluated potential bias risks within the RCTs by employing the Cochrane Collaboration's tool. We scrutinized diverse bias domains including selection bias, performance bias, detection bias, attrition bias, as well as reporting bias and other possible sources of bias. Each bias domain was subsequently categorized as either being of high, unclear, or low bias.

Strategy of data synthesis Quantitative analysis of the data was carried out utilizing the Review Manager (RevMan 5.4) software. Relative risk (RR) assessment alongside 95% confidence intervals (CI) was employed to investigate dichotomous data. We determined potential heterogeneity in the studies by quantifying the with the I2 statistic. Should the I2 statistic exceed 50%, we construed this as substantial heterogeneity. In such instances, we applied a random-effects model, or else, we utilized a fixed-effects model. Statistical significance was attributed to a p-value of less than 0.05.

Subgroup analysis We executed a subgroup analysis on the basis of oliceridine dosage in contrast with morphine： 0.1 mg group; 0.35 mg group； 0.5 mg group.

Sensitivity analysis According to the characteristics, distribution, and scale of the experiment, you can choose to use the fixed effects model or the random effects model in the analysis model.

Country(ies) involved China.

Keywords oliceridine, acute pain management, meta-analysis, tolerability, safety.

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