Comment on "Effectiveness and Safety of Hydromorphone Compared to Morphine for Postoperative Analgesia: A Systematic Review and Meta-analysis"

To the Editor:

The study "Effectiveness and Safety of Hydromorphone Compared to Morphine for Postoperative Analgesia: A Systematic Review and Meta-analysis" authored by Li Y et al (1) and published in *Pain Physician* in 2024, examines the clinical effects of hydromorphone in comparison to morphine for postoperative pain relief. Their findings indicate no significant differences in postoperative analgesic effects or the occurrence of severe sedation, nausea, or vomiting within 24 hours post-surgery between hydromorphone and morphine. However, the incidence of pruritus was lower with hydromorphone within 24 hours postoperatively. This revelation holds significant implications for clinical practice, especially in minimizing postoperative complications and enhancing pain management. While we acknowledge the merits of this study, we propose the following three suggestions for consideration:

Detailed Subgroup Analysis

The authors have accounted for variations in drug dosage, administration routes, and follow-up times, but significant heterogeneity in these factors was evident. This could influence the interpretation and generalizability of the results. We propose that future studies should incorporate a comprehensive subgroup analysis, considering parameters such as different dosages, patient age and gender, disease severity, and comorbidities (2-5). Further, designing subgroup analyses focusing on specific patient groups (e.g., those with renal insufficiency or those undergoing different types of surgery) could help understand the benefits of hydromorphone in these specific populations (6,7).

Diversification of Data Sources

The authors analyzed 8 randomized controlled trials, encompassing a total of 833 patients. However, these trial populations were somewhat homogeneous. Future research should consider multi-center collaborations and design larger-scale randomized controlled trials to gather data from a more diverse patient population (8). Examining differences in drug metabolism and clinical responses across diverse populations will improve our understanding of the specific effects of hydromorphone and morphine in different ethnic groups. Integrating more clinical practice data and patient-reported outcomes could also mitigate the sample size limitations and regional biases present in the current trials.

Investigation of Long-Term Outcomes and Mechanistic Studies

The authors concentrated on postoperative analgesic effects and adverse reactions within 48 hours, but did not assess long-term outcomes, such as addiction, the risk of chronic pain, and quality of life. Hence, we recommend that future studies should include follow-up periods of 6 months to one year to evaluate the impact of hydromorphone versus morphine on addiction, tolerance, and long-term quality of life (9).

In summary, the suggestions provided aim to enhance the rigor and comprehensiveness of the study's findings. We sincerely hope that the authors will consider these recommendations in their future research, which could include comprehensive subgroup analyses, diversified data sources, and continued exploration of long-term outcomes and mechanisms, ultimately increasing our understanding of the clinical effects and safety of hydromorphone.

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