Dear editor,

Thank you for carefully reviewing our manuscript "Advances in the clinical application of oxycodone in the perioperative period". We have revised our manuscript and answered the reviewers' comments point-by-point.
If any further questions or recommendations, please do not hesitate to contact us.

Reviewer #1:
This is a short but detailed review of the current literature on the important subject of the clinical application of oxycodone. The authors present an easily understandable walk-through of the subject. However, the manuscript still needs some editing before it is suitable for publication. The text needs to be read and corrected concerning the English language. The title clearly explains the topic of the review paper The abstract is not detailed enough to get a complete understanding of the review's aim, results, and conclusions. It needs to be prolonged. The manuscript writing needs to be improved in some places. Here are some specific comments: Page 4: "It is an opioid μ and κ receptor agonist, a class of potent opioid analgesics". The sentence is unclear Page 7: "Oxycodone reduced opioid-induced constipation and prevented gastrointestinal adverse effects in chronic pain management, but had little effect on analgesic efficacy" – it is unclear what is meant with analgesic efficacy. And it might be easier to read, if you started the sentence with "The study by… showed that…" Page 11: "The analgesic strength is better than that of each single drug" – which drugs? it is easier to understand if you write the specific drugs again. Page 13: "The analgesic effect of morphine is mainly mediated by μ-receptors, and the analgesic effect of oxycodone is mainly mediated by κ-receptors". It would help if you had a reference to this statement. Some references state that oxycodone's analgesic effect is mediated mainly by μ-receptors, e.g. see the review "Kinnunen, M., Piirainen, P., Kokki, H. et al. Updated Clinical Pharmacokinetics and Pharmacodynamics of Oxycodone. Clin Pharmacokinet 58, 705–725 (2019). https://doi.org/10.1007/s40262-018-00731-3" Page 13: "The results showed that. The analgesic effect of morphine in combination with an oxycodone controlled-release formulation was also significantly enhanced in patients with cancer pain, and patient subjective satisfaction and quality of life were significantly improved." – Typo with an extra "." Page 15: "Some literature reports[52], that fentanyl doses greater than 5 μg/kg to completely block the sympathetic response ." – unclear writing

Resopnse: Thank you for your time and effort to review our manuscript, and your suggestions are really helpful for us. We have revised the relevant content in the resubmitted manuscript based on your comments.

Reviewer #2: The title of this review clearly explain the potential role of oxycodone in clinical application. The abstract is too concise and does not adequately define the

role played by oxycodone in analgesia and anesthesia. The abstract should be expanded. The keywords are precise and appropriate. The review is relevant for the precise selection of topics concerning the use of oxycodone and morphine in all the aspects of pain relief. The paper completely explain that all the literature regarding the clinical use of oxycodone and morphine was reviewed based on relevant publications.

Resopnse: Thank you for your careful review. We have fully expanded the abstract and emphasized in the abstract section that oxycodone is a potent dual-opioid analgesic that can be used in the clinical work.