

2024 US-China Round Table Consensus Discussion on Perioperative Opioid Management

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Abstract

An expert panel including policy experts, society leaders, anesthesiologists, pain specialist, pharmacologist, a medicinal chemist, basic and clinical scientists, physician entrepreneurs, educators, and leaders from pharmaceutical companies from the United States and China had a round table discussion on the current issues and potential solutions related to perioperative opioid management. The inappropriate usage of opioids in the perioperative period remains an important safety concern for patients, care providers, and the general public across the world. There is a huge difference in usage practice of opioids between China and USA, therefore, to bring experts from both sides could generate new viewpoints or consensus in driving better pain control with safer usage of opioids for patients in different medical systems, which might be applicable to many countries and regions. The following topics were discussed: 1) The policy and its impact on opioid usage and crisis; 2) Education on opioid usage and management; 3) Opioid monitoring and waste management; 4) Novel opioid development; 5) Perioperative opioid usage and outcome.

All the panelists agreed that standardized terminology for opioid usage and opioid pharmacology should be developed, and we should work out reasonable and practical recommendations for a safe and effective usage and management for opioids in the perioperative period.

Introduction

On Oct 18th, 2024, an expert panel including policy experts, society leaders, anesthesiologists, pain specialist, pharmacologist, a medicinal chemist, basic and clinical scientists, physician entrepreneurs, educators, and leaders from pharmaceutical companies from USA and China gathered to have a round table discussion at the Smilow Center for Translational Research at the University of Pennsylvania to discuss the current issues and potential solutions related to perioperative opioid management. Opioids are one of the commonly used medications mainly for pain management, one of

which is in the perioperative periods. There is currently no standard or consensus on which opioid should be chosen and what the proper dose for pain management despite many proposed guidance or stewardship strategies [1-3]. The inappropriate usage of opioids in the perioperative period remains an important safety concern for patients, care providers, and the general public across the world. There is a huge difference in usage practice of opioids between China and USA, therefore, to bring experts from both sides could generate new viewpoints or consensus in driving better pain control with safer usage of opioids for patients in different medical systems, which might be applicable to many countries and regions.

The Policy and its Impact on Opioid Usage and Crisis

The opium crisis was a major national security problem in China in the 1840s, resulting two opium wars [4]. The subsequent tight regulation of opioids resulted in strict usage in the perioperative period and in pain management, with a trend of increased usage in recent years [5]. On the contrary, the US is now facing mounting issues related to opioid crisis with the death toll skyrocketing and the number of people on opioid maintenance therapy increasing substantially over the years [6,7]. Fentanyl, the most commonly used opioid during surgery, now dominates the opioid crisis in the US and other countries [8-10]. The panel agreed that while there is no direct linkage of perioperative fentanyl usage to the current fentanyl crisis in the US, the current opioid crisis in the US may be associated with the less strict control of perioperative, especially postoperative opioid usage and management. There is huge push in providing opioid free and minimizing opioids during anesthesia, and FDA and ASA are working jointly by forming a group of experts on opioid analgesic risk evaluation and mitigation strategy. Appropriate policy will play a critical role in the opioid safety. It will not only modify the behavior and decision making of pharmaceutical companies, but also the behavior of medical providers in opioid administration, prescription, and proper waste etc.

However, there is a concern about overly tight control of prescription opioid usage, which might lead to inadequate pain control for people who really needs opioid for their medical needs. Due to difficulty in obtaining opioids through legal channels, it is possible that patients who need opioids for medical reason(s) might go through non-legal pathways. One panelist proposed to collect all the reported legal cases and perform analysis for potential policy changes. Appropriate policy-making relies on quality clinical and research data. There was general agreement that research funding in this area should be increased. There

was brief discussion that anesthesiologists should play a leadership role in the management of safe usage of opioid and controlling opioid related crisis.

Education on Opioid Usage and Management

A consensus was reached that education for safe opioid usage and management for both medical professionals and the public is needed and enhanced. For example, while the partial prescription fill programs have been officially approved and have been implemented in the US, many medical professionals and patients do not know the existence of such programs. The increased number of times of copays for each prescription is another potential reason that patients are less willing to use such programs. Education is especially needed for pediatric patients and their family members [11]. A recent educational video highlights such needs [11].

Opioid Monitoring and Waste Management

Through this expert round table meeting, the team from the US and China learned from each other about the status and opinions of perioperative opioid management in two different medical systems. Both countries are moving towards enhanced monitoring on perioperative opioid usage and management. New technologies are available or under development. In the US, the dedicated opioid waste bins are implemented in major hospitals in the US in the perioperative areas [12]. To dispose of the opioid pills into the toilet is still recommended if there is no proper opioid return program available. It is still the common practice in China to dump the opioid leftover into the trash bin or to the sink in the perioperative areas.

Novel Opioid Development

With the understanding of the molecular pharmacology of existing opioids, new opioid development is targeting engineering new molecules that can only activate G protein pathway in the mu opioid receptor without beta-arrestin pathway. It is believed that the G protein pathway is associated with potent analgesia and beta-arrestin pathway is associated with the notorious side effects including respiratory depression and addiction. With this mindset, oliceridine was developed in the US and now marketed both in the US and China. Oliceridine is considered the first new opioid that has been marketed as a biased opioid for pain management purposes [13]. New clinical trials on the effectiveness and side effect profile for oliceridine are needed to compare it with other commonly used clinical opioids to determine its superiority over other opioids. There was a discussion which opioid should be used as an appropriate control.

It is known now that dezocine is also a biased

opioid of G protein pathway in mu opioid receptor. It is currently marketed in China as a perioperative analgesic [14,15]. Dezocine is currently off market in the US, but there is growing discussion about whether it could potentially be brought back to the US market to address the current opioid crisis, and used as an alternative pain medication in the perioperative period [14-16].

Perioperative Opioid Usage and Outcome

While opioid free anesthesia can be achieved in some selective cases, the panel agreed that opioids are essential in most surgical cases. To use multi-modal pain management plan can reduce opioid usage and their associated side effects. Inappropriate opioid dosage is associated with patient outcomes in the perioperative period including sleep patterns changes due to pain, stress level, depressive moods, and postoperative delirium. One panelist talked about an ongoing pilot study and the preliminary data indicated that both too little opioid usage and too much opioid usage are associated with higher incidences of postoperative delirium. Too little or opioid free anesthesia might be associated with increased postoperative opioid usage and chronic pain with long-term opioid usage after surgery [17-19].

Joint US-China Perioperative Opioid Management Taskforce

All the panelists agreed that standardized terminology for opioid usage and opioid pharmacology should be developed, and we should work out reasonable and practical recommendations for a safe and effective usage and management for opioids in the perioperative period. At the end of this invitational meeting, we unanimously agreed to form a joint perioperative opioid management taskforce to deal with the issues of opioid safety, with the goal of developing a policy and clinical brief.

Acknowledgement

Dr. Renyu Liu acknowledges the funding support from NIH for the opioid receptor related work (1R01GM111421). Dr. Koichi Yuki acknowledges the funding support from NIH (R01GM127600). The authors also appreciate other participants and supporters who made this round table meeting possible.

Conflict of Interests Statement

Dr. Renyu Liu is the Founder of the Neurokappa Therapeutics LLC under the Penn Center for Innovation. Dr. Hanzhong Cao is the Founder and president of the Rehn Meditech, Jaingsu China.

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Citation: Liu R, Abou-Hgarbia M, Cao H, Chen X, et al. A Sino-US Round Table Consensus Discussion on Perioperative Opioid Management. *Transl Perioper Pain Med* 2024; 11(3):683-686

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Additional publication details

Journal short name: *Transl Perioper Pain Med*

Received Date: December 22, 2024

Accepted Date: December 24, 2024

Published Date: December 30, 2024