Spring 5-2024

Evaluating the efficacy of perioperative methadone in cardiac surgery

Brock Thornton

Introduction to the Problem

Cardiac surgery includes multiple highly invasive and extensive procedures. Despite perioperative administration of opioid medications, cardiac surgery is associated with moderate to severe pain in up to 75% of patients (Bolton et al., 2019; Choinière et al., 2014; Wang et al., 2021). More than 33% of cardiac surgery patients experience chronic pain in the first six months after surgery, and 17% of patients experience chronic pain two years after surgery; this begins with uncontrolled acute postoperative pain (Lobova, Roll, & Roll, 2022). A central Illinois hospital expressed interest in the efficacy of perioperative methadone administration in cardiac surgery patients compared to traditional pharmacologic methods for controlling perioperative pain.

Literature Review

Methadone is an agonist at mu, kappa, and delta opioid receptors in the brain and spinal cord, leading to spinal and supraspinal analgesia (Lai et al., 2022). It is also a potent N-methyl-D-aspartate (NMDA) receptor antagonist in the CNS, preventing the enhancement of pain signal transmission and chronic pain (Lai et al., 2022; Kreutzwiser & Tawfic, 2020; Murphy et al., 2020). It is also unique in inhibiting serotonin and norepinephrine reuptake in the brain, modulating pain (Lai et al., 2022).

Methadone is highly lipophilic with a long duration of action. It is primarily administered via oral (PO) or intravenous (IV) routes. Both PO and IV methadone yield effective pharmacologic activity, with an average bioavailability of 80% and an average volume of distribution of 4L/kg (Eap, Buclin, & Baumann, 2002). Methadone stored in adipose tissue is slowly released into the plasma as hepatic metabolism occurs. The redistribution results in a biphasic half-life and a prolonged yet variable duration of action of six to 12 hours (Lai et al., 2022). However, when higher doses of methadone (~20mg) are administered among surgical

patients, the long elimination half-life of 24 to 36 hours appears to parallel the duration of clinical effects (Murphy & Szokol, 2019). The multi-analgesic effects of methadone depend on the dose administered, the frequency of administration, and individual variations in the rate of metabolism (Machado et al., 2018).

Methadone may cause euphoria, sedation, respiratory depression, miosis, bradycardia, nausea, and physical dependence (Lai et al., 2022). The most significant adverse effects of methadone administration are respiratory depression, QT prolongation, and the risk of physical dependence (Lai et al., 2022). However, the administration of a single dose of methadone does not appear to present a greater risk of respiratory depression, ventricular dysrhythmias due to QT prolongation, or physical dependence compared to other opioids among surgical patients (Lai et al., 2022; Murphy & Szokol, 2019).

A systematic review by Lobova et al. (2022) evaluated three double-blinded randomized controlled trials and one retrospective analysis published between 2011 and 2020. The review determined that methadone 0.1 to 0.3 mg/kg IV prior to surgical incision among cardiac surgery patients improved postoperative analgesia compared to morphine and fentanyl administration, with no differences in the risk of adverse effects from methadone administration versus traditional analgesics. Decreased postoperative opioid requirements, along with higher levels of patient satisfaction at 24, 48, and 72 hours postoperatively among patients who received methadone were also noted ($P<0.00001$) (Lobova et al., 2022; Machado et al., 2019). Among patients undergoing spinal, bariatric, cardiac, and ambulatory procedures, a single dose of methadone 0.1 to 0.3mg/kg IV decreased total opioid consumption and improved analgesia in the first 24 postoperative hours compared to intraoperative fentanyl ($P<0.001$) and hydromorphone

($P<0.0001$) (Lobova et al., 2022; Machado et al., 2019; Komen et al., 2019; Murphy et al., 2015; Murphy et al., 2015; Udelsmann et al., 2011).

Project Methods

This Quality Improvement project included a pre-and post-test design to educate cardiac anesthesia team members on perioperative methadone administration. The researcher met with a convenience sample of cardiovascular anesthesia team members (five certified registered nurse anesthetists and one anesthesiologist) and hosted an educational session to discuss recent literature on the selected topic. The presenter utilized PowerPoint to outline information on the pharmacology, appropriate dosing, side effects, and safety and efficacy of methadone administration among cardiac surgery patients. Two Qualtrics surveys were administered to determine knowledge gained and assess provider buy-in for developing perioperative methadone protocols. The educational session was held at the designated medical facility on August 11, 2023. Questions and open discussion occurred after the completion of the presentation.

The project was submitted to the Institutional Review Board (IRB) at Southern Illinois University Edwardsville prior to implementation. As a non-experimental design without human subjects, it was deemed a Quality Improvement Project and therefore exempt from IRB approval. The project presented minimal to no risk to human subjects. Participation in the evidence dissemination and survey was voluntary and without consequence.

Evaluation

The average total pre-test score among the four providers was 45.8%, while each post-test score was 100%. Seventy-five percent of providers strongly agreed that methadone may improve perioperative analgesia among cardiac surgery patients. One hundred percent of providers agreed or strongly agreed that they would consider the administration of perioperative methadone as a component of an ERAS protocol. CRNAs were able to determine the

pharmacologic overview of methadone, describe the pain theory associated with methadone, and determine the most common contraindication for the use of methadone, appropriate analgesic dosing, and common medical reasoning regarding the avoidance of methadone.

Impact on Practice

Project implementation increased provider knowledge of pharmacokinetics, pharmacodynamics, appropriate administration, contraindications, and clinical use of methadone. Although a protocol could not be developed based on literature gaps, increased provider knowledge may expand their willingness to seek out research opportunities and consider the future use of methadone in professional practice. When further research becomes available, methadone protocols in cardiac surgery may be developed. Based on the available literature, administering methadone in cardiac surgery decreases total opioid consumption, improves perioperative analgesia, decreases the risk of chronic pain, and improves patient outcomes.

Conclusions

The two primary goals of the doctoral project implementation were met. The primary researcher was able to determine baseline knowledge among providers and evaluate their willingness to change if methadone is included in a cardiac ERAS protocol in the future. The researcher received positive feedback from clinical attendees. Pre-test and post-test scores show increased knowledge gained through project implementation. In the future, this knowledge may be used to improve clinical outcomes among cardiac surgery patients.

Author Contact Information

Brock Thornton BSN, RN, SRNA

brthorn@siue.edu