
The use of continuous intravenous multimodal analgesia fentanyl-ketorolac in patients with caesarean section

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Abstract

Pain after caesarean section should be addressed so that patients feel comfortable and can be mobilized immediately. There are two classes of analgesics that can be used to reduce pain, namely class of opioids and nonsteroidal antiinflammation drug (NSAID). One class of opioids frequently used is fentanyl, whereas the NSAID class using ketorolac. Fentanyl is an opioid analgesic which are lipophilic, so it has several advantages compared to morphine. Ketorolac began to be widely used as an analgesic because of the nature of strong analgesic. This study was compare the use of multimodal analgesia techniques using a continuous intravenous fentanyl-ketorolac and ketorolac bolus intermittent. Subjects consisted of 40 post cesarean section were divided into 2 groups. Group multimodal were 20 people with a multimodal analgesic continuous use, and 20 people with intermittent single drug ketorolac as ketorolac group. Giving analgesics began shortly after the surgery is completed. Both groups were then seen when started to feel pain using a visual analog scale (VAS), and the addition of analgesics if necessary. Results showed 18 patients (90%) with multimodal analgesia had no pain since the completion of the operation up to 24 hours postoperatively (VAS 0-3), 2 patients (10%) need additional bolus intravenous ketorolac at 10 hours postoperatively (VAS 5). A total of 20 patients (100%) with ketorolac group requires 2 times ketorolac injection during 24 hours postoperatively. This study showed that multimodal analgesia technique using fentanyl-ketorolac is superior in reducing post cesarean section pain compared with single drug ketorolac.

Keywords

Multimodal analgesia, fentanyl, ketorolac, caesarean section

1. Introducing

Pain is an unpleasant feeling that arises as a result of tissue damage or potentially causing tissue damage. If acute pain is not treated properly, it can lead to chronic pain, prolong hospitalization, thus increasing hospital costs, and ultimately reduce the satisfaction and comfort of patients (Garimella, and Cellini, 2013). The World Health Organization states that pain is a human right that should be eliminated or reduced. Caesarean section surgery is a major operation that causes moderate to severe pain in more than half of patients who should be treated carefully (Hadi and Hanid, 2011). Postoperative pain caesarean section can cause patient discomfort, patient mobilization

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process becomes longer, thereby increasing the risk of thromboembolism, and can also affect the condition of the mother to immediately take care of the baby.

Pain is complex and multifactorial phenomenon and need multimodal therapy (Joshi, 2005). Relieving drugs commonly used are opioid (Gadsden, et al, 2005), or NSAIDs such as ketorolac, which is proven to reduce pain and dose of opioid if use singly (Lowder et al, 2003). The use either fraction opioid analgesics or NSAIDs, can not effectively relieve pain without causing side effects such as nausea, vomiting, sedation, or bleeding (Jin and Chung, 2001). Fentanyl is a synthetic opioid class that works by binding to receptors of the central nervous system and peripheral tissues, as well as have the effect of modulation nociceptor. Compared with morphine, fentanyl has a faster onset of action, is more potent and has a half-life faster, but has the side effect of respiratory depression, so its use is very limited and needs to be more carefully (Garimella, and Cellini, 2013). Ketorolac is a NSAIDs analgesic that can be injected intravenously, works by blocking the production of prostaglandins by inhibiting the enzyme cyclooxygenase (COX-1) and can reduce opioid use between 25-45%. Side effect of ketorolac use is risk of bleeding (Oliveira et al, 2012).

Some studies suggest the use of a combination of opioid and NSAID analgesic drugs with good results, but have not found the optimal combination. Peng and Sandler (1999) suggest a dose of fentanyl 1-2 mg/kg/h, while in the hospital Arundel (2011) uses a dose of 10 ug/hour. In the case of post-operative pain, the addition of drugs known as NSAIDs in intravenous morphine, was found to have good results (Curatolo and Svetcic, 2002). Adding morphine to ketorolac has reduced the side effect and dose dependent of opioid (Cepeda et al, 2005). This study wanted to find out whether the use of a combination of ketorolac and fentanyl in continuous doses can reduce pain better than single use of ketorolac.

2. Material and Method

This prospective study was approved by the institutional ethics in teaching hospitals Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta. The subject of this research is patients who underwent caesarean section at teaching hospital Asri Medical Center (AMC) and PKU Gamping Yogyakarta, and has agreed to participate in the study. A total of 40 patients with a body weight between 40-70 kg, 20-45 years old who underwent caesarean section with ASA 1 and 2 status with spinal anaesthesia since June-August 2016, were included in this study. Exclusion criteria included drug addiction, allergies to opioids and ketorolac, a history of bleeding, and the use of anticoagulant drugs two weeks before surgery.

Subject were divided into two groups, namely the fentanyl and ketorolac group. In fentanyl group, the subjects were given a multimodal analgesic fentanyl-ketorolac, while ketorolac group were given ketorolac intravenous during 20 hour after caesarean section as they feel pain (VAS score>5). Before surgery, all subjects received instruction of the operation and the treatment that will be given to treat postoperative caesarean section pain. All subjects received a spinal regional anaesthesia with a needle no. 25, and the drugs used are spinal bupivacaine 12.5 mg.

After the operation is completed, all subjects were given a single dose of ketorolac 30 mg bolus intravenous, followed by administration of a combination of fentanyl analgesia-ketorolac continuously 20 hours on the subject fentanyl group. On the subject of ketorolac group, bolus administered every subject began to feel the pain and the VAS over 5. All group were given ketorolac 30 mg bolus intravenous immediately after the operation ended. Dose of fentanyl group is 200 ug of fentanyl plus ketorolac 60 mg, dissolved in aqua up to a volume of 100 ml, than fill in syrinx pump (syrinxject), and supplied continuously at a rate of 5 cc / hour, while ketorolac group doses is 30 mg intravenous. Continuous fentanyl doses given 10 ug / h, and continuous dose of

ketorolac 0.6 mg / hr. All groups of subjects then recorded how many people who require additional analgesic ketorolac. Collected data is then counted as percentage number of subjects who require ketorolac within 20 hours after surgery.

3. Result and Discussion

Forty subjects who participated in this study, were divided into 20 groups of fentanyl, and 20 others are ketorolac group. Age and weight of the data presented in Table 1. In the group of fentanyl, a total of two subjects require additional ketorolac at the 10th hour after surgery because of the pain by VAS score of 5, while all subjects in the group of intravenous ketorolac require an additional two times for 20 hours with VAS score >5. (Table 2).

Table 1. Average of age and body weight

Group	Age (years)	Body Weight (Kg)
Fentanyl	26,5	58
Ketorolac	26	57

Table 2. Amount of subject who need additional ketorolac after 20 hour

Group	Amount (%)
Fentanyl	2 (10%)
Ketorolac	20 (100%)

NSAIDs such as ketorolac, works by blocking the synthesis of prostaglandins by inhibiting the action of the enzyme cyclooxygenase (COX) type I and type II. Decrease in prostaglandin synthesis thereby reducing the production of chemical mediators accompanying acute inflammatory response. Several studies have mentioned that NSAIDs also decrease response to pain centers in the spinal nervous system (White, 2005). Opioid analgesics, such as fentanyl, acts as an agonist in the peripheral and central opioid receptors. Although the analgesic property is efficient, it has side effects such as respiratory depression (Ramsay, 2000) but respiratory depression is extremely rare in the use of continuous intravenous (Peng and Sandler, 1999).

The results showed that administration of a combination analgesic fentanyl and ketorolac continuously can reduce pain in the majority of subject compared with subject who received a single dose of ketorolac only. There were no side effects of nausea and vomiting in both groups. Additional ketorolac in the ketorolac group and fentanyl group showed patients feel pain (VAS score > 5). Ding et al. (1993) suggest that in patients with postoperative gynecological, ketorolac administration singly with a dose of 30 mg intravenously, could not reduce early postoperative pain compared to administration of a combination of ketorolac and fentanyl. Etches et al (1995) demonstrated that ketorolac supplied continuously, can reduce postoperative pain and reduce the dose of morphine given in patients with post-operative hip and knee arthroplasty. In the post-ESWL patients, the use of ketorolac 60 mg iv equally effective for reducing pain and fewer side effects when compared with the 100 ug fentanyl, but with minimal side effects (Yang et al, 2002).

4. Conclusion

In this study, administration of a combination of fentanyl-ketorolac continuously can reduce pain better than ketorolac bolus intravenous alone, with minimal side effect. Further research will be needed the most optimal dose and minimal side effects by administering a combination of fentanyl-ketorolac continuously in patients post caesarean section.

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