

Original Article

Intravenous Acetaminophen Effect on Postoperative Narcotic Analgesic Demand after Elective Cesarean Section

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Abstract

Background: Opioid analgesics are the mainstay of the treatment of postoperative pain. Appropriate monitoring of patients receiving opioid analgesics is essential to detect those with side effects such as respiratory depression. The discovery of Acetaminophen as a COX-3 variant may represent a primary central mechanism by which acetaminophen decrease pain. The aim of this study was to assess the effect of intravenous acetaminophen on morphine requirement in post-operation pain after elective cesarean section.

Materials and Methods: In a randomized clinical trial, patients' candidate for elective cesarean section. In experiment group, intravenous acetaminophen (1000 mg/6 hour) was administered and normal saline to control group. Visual analogue scale (VAS) was measured at 1, 3, 6, 12, and 24 hours post-operation. Besides, Morphine dose requirement were measured during next 24 hours.

Results: 83 patients were enrolled in the study; which 44 patients assigned in placebo group and 39 in Acetaminophen. Mean Age of placebo group was 29.64 ± 5.55 and Acetaminophen was 30.33 ± 5.50 which was not significantly different ($p=0.568$). Only at 1 and 3 hours, there was a significant difference between two groups of study. Total dose of morphine requirement was 5.73 ± 2.78 mg/24 h in placebo group and 3.64 ± 2.42 in Acetaminophen group which was significantly different ($p=0.001$).

Conclusion: Intravenous Acetaminophen could decrease post cesarean pain and decrease post operation total morphine requirement particularly at first 3 hours post operation.

Keywords: acetaminophen, postoperative, narcotic, analgesia

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Introduction

Widespread recognition of need for management of acute post-operative pain by clinicians, has led to the development of a various guidelines for management of acute pain. Uncontrolled post-operative pain may produce a range of detrimental acute and chronic effects. The attenuation of post-operative pain may

decrease complications and facilitate recovery during the immediate post-operative period¹. It has been assumed that sufficient pain relief will improve the surgical outcome with reduced morbidity, need for hospitalization and convalescence, and there is a common consensus that optimal pain relief is a prerequisite for early postoperative recovery. Opioid analgesics are the mainstay of the treatment of

postoperative pain. These agents generally exert their analgesic effects through μ -receptors in the CNS². An advantage of opioid analgesics is that there is no analgesic ceiling. However, the incidence of respiratory depression from opioids is an imminent threat to patients. Appropriate monitoring of patients receiving opioid analgesics is essential to detect those with side effects such as respiratory depression thus, decreasing dose is desirable.

The discovery of Acetaminophen as a COX-3 variant may represent a primary central mechanism by which acetaminophen decrease pain³. Acetaminophen is categorized as B class for pregnancy. Intravenous (IV) acetaminophen has the potential to reduce postoperative narcotic analgesic requirement but this has not been reported in obstetric surgeries⁴. The aim of this study was to assess the effect of intravenous acetaminophen on morphine requirement in post-operation pain after elective cesarean section.

Methods

Patient Selection: The study was reviewed and approved by the University Review Board and hospital ethics committee. Information about trial was given comprehensively both orally and in written form to the patients. All patients gave their written informed consents prior to their inclusion in the study according to University Hospital Ethics Board Committee.

In a randomized clinical trial, patients' candidate for elective Cesarean section, ASA class 1, 2 were admitted to the study. Exclusion criteria were allergy to the acetaminophen, drug addiction, and pre-eclampsy. Patients were randomly assigned to one of groups based on accidental numbers.

Spinal Anesthesia: Spinal anesthesia was performed using Bupivacain 0.5% 2.8 cc (14mg) (Astra Zenca, Sweden) and a G25 spinal needle. Level of anesthesia was fixed at L3-4 and surgery was performed. No other drugs were administered to the patients. After end of surgery patients were transferred to recovery. Patient control analgesia (PCA) pump containing 15 mg of morphine were attached for post operation analgesia (0.7 mg/h) for all patients.

Acetaminophen Administration: In experiment group, intravenous acetaminophen (1000 mg/6 hour)

was administered and normal saline to control group. Visual analogue scale (VAS) was measured at 1, 3, 6, 12, and 24 hours post operation. Besides, Morphine dose requirement were measured during next 24 hours. Morphine (2 mg) as rescue analgesic were administered if VAS>3 was detected. Mean of VAS score were compare between two groups of study. The mean of rescue Morphine was also compared between two groups of study.

Data recording: Hemodynamic status including mean arterial pressure (MAP), heart rate, pulse oxymetry oxygen saturation, respiratory rate was measured at mentioned time points. Other adverse effects including nausea and vomiting were also recorded if patients had any. Respiratory depression was noted if RR<10 for more than 1 minute or RR<8 for 30 seconds or SPO2<92 when awakened or SPO2<90 at sleep.

Results

In this study, 83 patients were enrolled in the study; which 44 patients assigned in placebo group and 39 in Acetaminophen. From those, 9 patients were exited from the study due to PCA malfunction. Mean Age of placebo group was 29.64±5.55 and Acetaminophen was 30.33±5.50 which was not significantly different (P=0.568). Other characteristics are also depicted in Table 1.

Pain score using VAS score was measured at time points of 1, 3, 6,12, and 24 hours post-operative which is depicted at Table 2. Only at 1 and 3 hours there was a significant difference between two groups of study.

Total dose of morphine requirement was 5.73±2.78 mg/24 h in placebo group and 3.64±2.42 in Acetaminophen group which was significantly different (P=0.001) (Table 3).

The nausea and vomiting (NV) were compared between two groups of study. Three patients in placebo group and 5 patients in Acetaminophen group had NV which was not significantly different between

Table 1: Characteristics of patients in two groups of study.

	Acetaminophen	Placebo	P value
Age	26.5±6.8	25.4±7.3	0.23
Weight	73.4±14.5	75.6±14.2	0.33
BMI	26.4±4.6	26.9±6.3	0.26

Table 2: Comparison of VAS score between placebo and Acetaminophen at time points.

	VAS1	VAS3	VAS6	VAS12	VAS24
Placebo	3.59±2.82	5.14±1.39	3.59±1.19	2.09±1.43	0.73±0.72
Acetaminophen	1.13±1.47	4.44±1.74	3.31±1.36	2.00±1.28	0.90±0.78
P value	0.0001	0.045	0.314	0.762	0.309

Table 3: Comparison of Morphine rescue analgesic at different time points.

	Morphine 1	Morphine 3	Morphine 6	Morphine 12	Morphine 24
Placebo	1.59±1.7	2.64±1.2	1.23±3.00	0.36±1.08	0
Acetaminophen	0.26 ±0.47	2.0±1.54	1.13±1.10	0.26±1.08	0
P value	0.001	0.032	0.703	0.615	NA

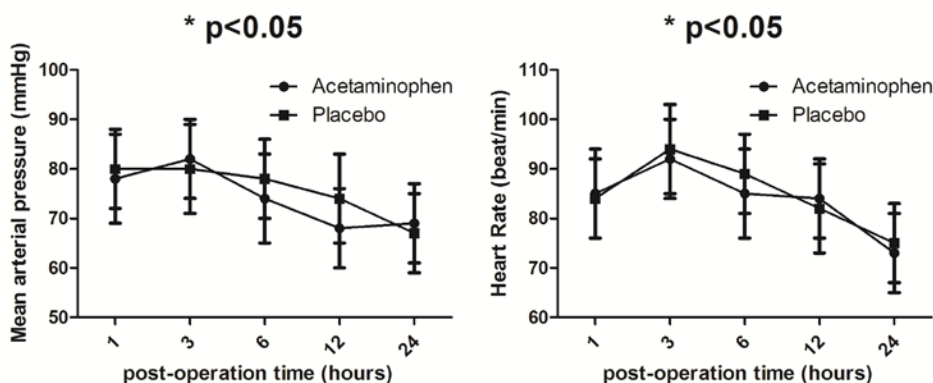


Figure 1. Comparison of heart rate and mean arterial blood pressure between Acetaminophen and placebo group

two groups of patients (P=0.29). MAP was not significantly different between two groups at any time points. Heart rate was also not significantly different at any time points (Figure1).

Discussion

Here in this study we embarked on post cesarean analgesia by using IV Acetaminophen to decrease total dose of morphine requirements. Here we described how a multimodal approach to post-operative analgesic management which showed administration of intravenous Acetaminophen is effective in reducing the total dose of Morphine administered on post-operative pain. Cesarean is an elective operation with moderate to severe pain which high dose of opioids are not required, however, moderate dose is recommended. Using IV

Acetaminophen in our patients decrease total morphine dose and best decreased morphine rescue analgesic at 1 and 3 hours post operation. This is of utmost important due to the fact that respiratory depression is mostly observed at early post operation period.

Pain score (VAS) was significantly lower in Acetaminophen group at 1 and 3 hours post operation. This is consistent with other studies, which post cesarean pain is met at first 3 hours post operation. There is evidence that the combination of nonsteroidal antiinflammatory drugs with patient-controlled analgesia morphine offers some advantages over morphine alone^{5,6}. Other studies showed the additive impact of intravenous acetaminophen on reducing opioid use after hysterectomy⁷. In another controversial study using rectal Acetaminophen in controlling post hysterectomy pain, they showed that 1

gram of rectal Acetaminophen could not induce an appropriate serum level. IV acetaminophen did not significantly decrease postoperative opioid use in patients who underwent surgical knee procedures⁸. One group has suggested IV paracetamol to provide better post-operative pain management without considerable neonatal complications in women undergoing cesarean section⁹.

The dosing and interval of acetaminophen use is also important. It is possible that one dose of 1000 mg IV Acetaminophen is enough to reduce pain in post cesarean section. A dosage of rectal paracetamol 1000 mg four times daily is too low, and higher serum concentrations of paracetamol may cause lower serum concentrations of morphine¹⁰. One study confirms that additive analgesic effect of paracetamol can be detected in strong, but not moderate, pain after Caesarean section¹¹.

Other studies have also used Acetaminophen to decrease opioid requirement. In addition, Acetaminophen is a safe drug during lactation with no side effect on mother or infant¹²⁻¹⁴. Other studies using NSAIDs combination with Acetaminophen which were effective in decreasing total morphine dose¹⁵. In contrary, other studies showed that NSAIDs are more effective than Acetaminophen alone in decreasing total morphine dose for post-operation pain control¹⁴.

However, this study was performed on major surgeries, while NSAIDs increase risk of post operation peptic ulcer and GI bleeding in compare to Acetaminophen. Patients given a combination of diclofenac and paracetamol used 38% less morphine compared to patients given paracetamol¹⁶. Acetaminophen combined with PCA morphine induced a significant morphine-sparing effect but did not change the incidence of morphine-related adverse effects in the postoperative period¹⁷.

The perioperative period is associated with a variety of pathophysiologic responses that may be initiated or maintained by nociceptive input toward post-operative time. Uncontrolled postoperative pain may potentiate some of these pathophysiologies and increase patient morbidity. Control of acute postoperative pain may improve long-term recovery. Patients whose pain is controlled in the early

postoperative period may be able to actively participate in postoperative rehabilitation, which may improve short- and long-term recovery after surgery¹⁸. In conclusion, intravenous Acetaminophen could decrease post cesarean pain and decrease post operation total morphine requirement particularly at first 3 hours post operation.

Conclusion

In conclusion, intravenous Acetaminophen could decrease post cesarean pain and decrease post operation total morphine requirement particularly at first 3 hours post operation.

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