

Acetaminophen versus Fentanyl for Post-Operative Pain after Lower Limb Surgery: A Randomized Controlled Trial

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ABSTRACT

BACKGROUND: Opioids for pain management are associated with a number of adverse effects and consequently their use should be avoided. The aim of this study was to compare the analgesic effect of acetaminophen and fentanyl in the management of postoperative pain in patients following intra-medullary nail fixation.

METHODS: 114 male patients between the ages of 25 and 50 years who underwent intra-medullary nail fixation in Poursina university hospital of Rasht between 2012 and 2013 enrolled in this double-blind randomized controlled trial study. The trial registration was IRCT 2012122611898N1. After completion of the surgery, patients were taken to the recovery room and were randomly allocated to one of the two groups. One group received intravenous acetaminophen, 1000 mg in 150 mL normal saline in 15 min every 6 hours for 24 hours.

Another group received fentanyl as patient controlled analgesia, for 24 hours. Patients were evaluated by visual analogue score (VAS) and pain relief rating (PR) at 0, 15, 30 and 45 minutes, 1, 2, 3, 4 and 5 hours after elimination of intraoperative analgesic effect.

RESULTS: Of 103 patients, 47 were randomized to receive fentanyl and 56 were randomized to receive acetaminophen. The mean age of subjects was 38.7 ± 1.1 . The VAS scores were significantly higher ($p < 0.05$) in patients randomized to receive fentanyl at 30 minutes, 45 minutes, 1 hour, 3 and 4 hours.

CONCLUSION: Intravenous acetaminophen is an effective analgesic agent and may be preferable to fentanyl for postoperative pain management in orthopedic setting.

Keywords: Acetaminophen; Fentanyl; Orthopedics, Postoperative Pain

INTRODUCTION

Postoperative pain relief is important for several reasons. Pain is not only associated with patient discomfort, but can also result in thromboembolic and pulmonary complications, prolonged hospitalization, poor quality of life, mental and physical stress, increase in health care cost and may progress to chronic pain [1, 2].

A number of analgesics are available for using during postoperative period including local anesthetics, acetaminophen, nonsteroidal anti-inflammatory drugs, and rescue oral opioids[3, 4]. Intravenous (IV) acetaminophen received United States Food and Drug Administration approval in November 2010 for the management of mild-to-moderate pain, management of moderate-to-severe pain with adjunctive opioid

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analgesics[5].

However, there is controversy about the best treatment for post-operative pain. Jonathan et al reported IV Acetaminophen as a preferred postoperative analgesic in joint replacement because of its safety and efficacy[6]. While, Merivirta et al demonstrated that Fentanyl patch is a safe and easy option to manage postoperative pain after arthroscopic shoulder surgery [7].

The aim of this study was to compare the analgesic effect of acetaminophen and fentanyl in the management of postoperative pain in patients following intra-medullary nail fixation.

METHODS

Ethics: Ethical approval of this study was provided by the Institutional Review Board and the Ethical Committee of the research deputy of Guilan University of Medical Sciences, Rasht, Iran with protocol number IRCT 2012122611898N1.

This double-blind randomized controlled trial study was performed on male patients with American Society of Anesthesiologists physical status I or II, aged 25-50 years who underwent the intra-medullary nail fixation for non-segmental and non-comminuted fibula and tibia fractures at Poursina university hospital of Rasht between September 2012 and March 2013.

Patients who had history of allergy to acetaminophen or fentanyl, had contraindications to acetaminophen or opioids use, had severe pain (VAS ≥ 3), GCS ≤ 13 , renal disease (serum creatinine >1.5 mg/dL), liver disease (liver enzymes > 1.5 normal), chronic lung disease, hemorrhagic conditions, coagulation abnormalities and history of addiction to opioids or alcohol, were excluded [8, 9].

Informed consent was obtained from each subject. Subjects were identified only by number. Then the demographic data was asked. The patients were transported to PACU (Post Anesthesia Care Unit). All consenting patients underwent spinal anesthesia in a sitting position.

The number of patients was calculated on the basis of a comparison of propacetamol and ketorolac by using a parallel design with $\alpha=0.05$ and $\beta=0.1$ for pain scores. In order to conduct randomization, 114 medical packets, consisting of A and B groups were prepared, mixed and then given to the nurse of PACU. The average time of surgery was about 1 hour. After completion of surgery and recovery from anesthesia, patients were divided by random allocation into two groups; one received fentanyl

in patient controlled analgesia (PCA) and another received IV acetaminophen; 1000 mg of acetaminophen every 6 h for 24 h.

According to double blinding, neither the anesthesiologist nor the patient knew allocation of which packet included pharmaceutical component.

Pain intensity was evaluated with a 10-cm visual analogue scale (VAS) from 0=no pain to 10=worst possible pain at 0, 15, 30 and 45 minutes, 1, 2, 3, 4 and 5 hours after surgery. The last evaluation was by the pain relief rating (PR) (0=poor, 1=fair, 2=good, 3=excellent). For the patients with VAS >3 , morphine was administered (0.1 mg/kg). The patients were evaluated for 24 h and if they needed to control analgesia tightly, 5 mg morphine was administered.

Incremental doses of naloxone (0.1 mg) were to be used for any patient whose respiratory rate per minute was 8 or lesser. 24 hours post-operation, the patients were monitored for any adverse effects such as respiratory or cardiac complications. For the statistical analysis the software SPSS 19.0 was used. Quantitative data was analyzed with ANOVA, post-hoc, regression and categorical data was analyzed with Chi-square and Fischer exact test. Statistical significance was accepted at the level of $P < 0.05$. If the type of data was ordinal in nature, the nonparametric tests and Mann Whitney U test were used.

RESULTS

Of the 114 patients included in the study, 103 patients completed the study. Forty-seven patients were randomized to receive fentanyl in PCA and 56 were randomized to receive IV acetaminophen. Eleven patients were excluded from the study, 1 from the acetaminophen group and 10 from fentanyl group. Just one patient had nausea during the intervention in fentanyl group and he became symptom free with metoclopramide injection.

Analysis showed that the mean score of VAS was significantly more in the group receiving fentanyl at 30 (P=0.001) and 45 minutes (P=0.019), 1 hour (P=0.008), 3 (P=0.027) and 4 hours (P=0.001) after elimination of analgesic effect (Table 2). But there was no significant difference between age and VAS scores.

There was no significant difference between 2 groups in PR. Of 56 subjects treated with acetaminophen, 24 (42.9 %) had excellent and 32 (57.1 %) had good scores. Of 47 subjects

Table 1: The mean score of VAS at 0, 15, 30 and 45 min, 1, 2, 3, 4 and 5 h after the elimination of the analgesic effect in 2 groups

Time	Acetaminophen	Fentanyl	P value
0 min	1.08±0.34	1.25±0.82	0.203
15 min	1.07±0.25	1.17±0.76	0.775
30 min	1.01±0.13	1.38±1.03	0.001
45 min	1.12±0.38	1.61±1.42	0.019
1 h	1.64±1.06	2.38±1.60	0.008
2 h	2.78±1.34	3.27±1.81	0.224
3 h	3.76±1.23	3.12±1.89	0.027
4 h	5.48±1.68	2.74±1.53	0.001
5 h	2.01±0.82	2.31±0.95	0.144

treating with fentanyl, 25 (53.2 %) had excellent, 18 (38.3 %) had good and 4 (8.5 %) had fair scores. Chi Square test showed a significant difference between 2 groups in the administration of morphine ($P=0.001$). Thirty seven patients (66.1 %) in the IV acetaminophen and 44 patients (93.6 %) in the fentanyl group used morphine. Repeated-measure ANOVA, showed no significant interaction effect between the changes in VAS score and morphine consumption ($P=0.82$) (Fig 1).

DISCUSSION

As 30-80 % of patients have moderate-to-severe pain, management of postoperative pain is essential and the first line of treatment is the pharmacologic [10, 11]. Although the use of IV acetaminophen has become widespread for postoperative pain relief as it can be administered for all ages, IV opioid PCA is the gold standard treatment for acute pain [1, 12-14]. This study was conducted to evaluate the efficacy and effectiveness of these two groups of drugs for the management of postoperative pain.

In a recent study it was shown that fentanyl offers an easy and safe treatment option for postoperative pain after arthroscopic shoulder surgery [7]. In this study, the patients who received fentanyl had significantly lower pain intensity.

Many studies compared different analgesic agents for postoperative pain. Langlais et al showed that the pain relief seemed to last longer with the ketoprofen than with the pethidine[15]. But Kouček et al, by evaluating 40 patients, reported that the analgesic properties of acetaminophen and fentanyl were similar[16]. In another comparative study between acetaminophen and tramadol for post-operative pain management after urologic surgery, there was no superiority of acetaminophen over tramadol[17].

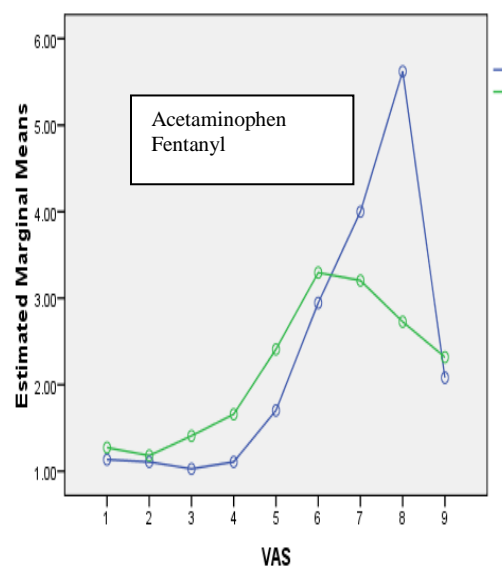
According to systematic reviews and meta-

analysis, acetaminophen has been shown to reduce opioid requirements [18, 19]. Carney et al demonstrated that patients receiving ketorolac had significantly less morphine requirements in comparison to the control group in the first 48 postoperative hours[20]. In our current study, patients randomized to receive IV acetaminophen used less morphine in comparison to the patients randomized to receive fentanyl. As fentanyl is 100 times more potent than morphine, it seems that patients should not have needed morphine as an analgesic [1][21-23]

Acetaminophen probably acts through its central analgesic effect and therefore, does not cause respiratory depression or tolerance as do opiate drugs. This drug could therefore be useful in elderly patients and during recovery from surgical procedures where the active participation of patients is required for early rehabilitation, e.g. joint mobilization [15, 24].

One of the major limitations of the study was that we could not continue evaluating VAS scores for

Figure 1: VAS alterations after morphine consumption in both acetaminophen and fentanyl groups



24 hours. A well-designed larger randomized-controlled trial is needed to validate our findings.

CONCLUSION

In conclusion, we found that IV acetaminophen was better in controlling post-operative pain than fentanyl given as PCA in orthopedic patient population. Our findings need validation in a larger study. Use of a non-opioid analgesic for post-operative pain will result not only in early mobilization and rehabilitation of patients but will also likely decrease the possibility of opioid abuse.

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