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Comparison of Dexmedetomidine And Fentanyl As Adjuvant for Wound Infiltration To Bupivacaine for Postoperative Pain Relief After Abdominal Hysterectomy

[1*]Neha Kadyan , [2]M L Khatri
SGT University, Gurugram
*Corresponding Author: *Neha Kadyan*

Abstract
Introduction: *Several methods have been proposed to alleviate pain after hysterectomy. Local infiltration of the surgical wound is one of the important components of multimodal analgesia for post-operative pain relief. This study determines the post-operative analgesic effect of addition of dexmedetomidine and fentanyl to bupivacaine for local infiltration of the surgical wound.*
Methods: *40 patients with ASA class of I or II scheduled for abdominal hysterectomy were recruited for the study. The patients were randomly assigned to Group A` (control group) where patients received wound infiltration with 30 mL 0.25% bupivacaine and 25μg of fentanyl, and Group B, where patients received wound infiltration with 1.0 μg/kg dexmedetomidine diluted in 30 mL 0.25% bupivacaine. The primary objective of the study was to assess post-operative pain scores. Post-operative quality of analgesia was assessed by VAS (0-10) for 24 h and when VAS > 4 rescue analgesic was administered. Total dose of rescue analgesic and side effects were noted. They were also asked for satisfaction regarding the pain relief intervention.*
Results: *The time of administration of first rescue analgesic was significantly higher in group B (10.52±5.54 h) as compared to group A (3.275±1.8 h). Mean VAS was significantly lower in group B as compared to group A. The total dosage of rescue analgesic was more in group A as compared to group B patients.*
Conclusion: *Addition of dexmedetomidine to bupivacaine significantly prolonged the time to first rescue analgesic requirement and the total consumption of rescue analgesic in 24 h as compared to fentanyl added to bupivacaine.*
Keywords: *general anesthesia, dexmedetomidine, fentanyl, bupivacaine, wound infiltration.*

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I. Introduction

Abdominal hysterectomy is associated with moderate to severe postoperative pain. To shorten the length of hospital stay and reduce the adverse effects of opioid agents, several methods of analgesia that have opioid-sparing effects are frequently used to reduce postoperative morbidity. Pain after abdominal surgeries leads to restricted breathing effort and inability to adequately cough out secretion[1] which leads to a decrease in functional residual capacity, early airway closure, segmental or lobar collapse, retention of secretions leading to bronchopneumonia.[2]It was found that combination of local anesthetic with opioid for wound infiltration in a patient reduces opioids consumption, minimizes opioid adverse reactions, reduces nursing work, decreases resting pain, pain on motion, and thus allows better patient mobility.[3] Dexmedetomidine also has been used as an adjunct to local anaesthetics for various nerve blocks.[4]Thus, present study was designed to compare the analgesic efficacy of fentanyl and dexmedetomidine as adjuvant to bupivacaine for local wound infiltration.

II. Materials And Methods

After obtaining approval from the institutional ethical committee and informed written consent from the patients, 40 patients, aged30–60 years ASA physical status I–II patients scheduled for abdominal hysterectomy via a Pfannenstiel incision.

Patients with severe cardiovascular or liver disease, those who received opioids as premedication, and those with known allergic response to local anesthetics were excluded from the study.

The study was conducted as a randomized double-blind study using two solutions:

a. Solution containing added fentanyl 25μg to 30ml of 0.25% bupivacaine
b. Solution containing added dexmedetomidine (1μg/kg) to 30 ml of 0.25% bupivacaine

Coding of the solutions was done by a senior anesthetist and the person administering the drug was unaware of its constituents. In this prospective, randomized, double-blind, controlled study, after obtaining approval from the Ethics Committee of our hospital and written informed consent from all patients, we studied 40 American Society of Anesthesiologists (ASA) physical status I–II patients scheduled for abdominal hysterectomy via a Pfannenstiel incision. The exclusion criteria were as follows: patients with second- or third-degree heart block, allergy to any study drug, renal insufficiency, hepatic insufficiency, psychiatric diseases. Patients were randomized by sealed envelope method. In the operation room, the study solution (prepared by the second anesthesiologist in a sterile condition and in the same volume) was injected by the same surgeon who was blinded to the study solution. The person who prepared the study solution did not participate in data collection.

In the operation room, standard monitoring was established. Heart rates, non-invasive blood pressures, and peripheral oxygen saturations were recorded. The hysterectomy was performed under general anesthesia, induced with propofol 2–3 mg/kg intravenous (IV) and 2 mcg kg−1 fentanyl and 0.6 mg kg−1 rocuronium bromide. Anaesthesia was maintained with isoflurane and 60% nitrous oxide in oxygen. Ringer Lactate was infused at a rate 5–10 mL kg−1 h−1. In case of the heart rate being under 40 beats min−1, 0.5 mg atropine sulfate was administered to the patients. All patients received 3 mg ondansetron at the beginning of the surgery. If the mean arterial blood pressure was less than 60 mm Hg, it was planned to administer mephentermine 3–6 mg boluses IV. At the end of the surgery, residual neuromuscular block was reversed with neostigmine and atropine sulfate. Tracheal extubation was performed according to the standard criteria for extubation. Post-operative analgesia was provided with tramadol 1.5 mg/kg IV every 8 h.

At the end of the surgery in group A patients, the wound was infiltrated intradermally with 30ml of bupivacaine 0.25% + 25µg fentanyl and in group B infiltration was done with30 ml of bupivacaine 0.25% + dexmedetomidine (1 µg/kg). The trial preparations were blinded and numbered. The infiltration technique was standardized. Post-operative pain was assessed by a blinded investigator using a 0-10 point Visual Analogue Scale (0-no pain, 10-unbearable pain). VAS > 4 was taken to indicate significant pain and used as a cut off point for rescue analgesia with tramadol 50 mg IV. Both the groups were compared for duration of analgesia (time from wound infiltration to time of administration of first analgesic) and total consumption of supplemental analgesic in 24 h. Signs of opioid side effects like drowsiness, nausea, vomiting, and pruritus were noted. Urinary retention was not evaluated as all the patients were catheterized. Assuming the increase in duration of analgesia to be 8-10h[3,4] a sample size ≥ 7 would give the study a power of 90% with type I error 0.05. So we conducted this study with 20 patients in each group. A comparison of the mean levels of all variables between two groups was made by the unpaired *t* test. Differences were considered statistically significant if $P < 0.05$.

Rescue Analgesia

The patient was given Inj. Tramadol 50 mg iv on complaint of pain. The time of first request of analgesia was recorded. The total narcotic requirement in mg in the first 24 h was calculated and used for statistical purpose.

III. Results

The study groups were comparable in terms of age, weight, gender, and duration of surgery. Mean VAS scores were significantly lower in group B as compared to group A [Figure 1]. In group A, 10% patients required rescue analgesic within 0-6 h, 40% in 6-12 h, 45% in 12-18 h, and 50% of patients in 18-24 h. In group B, 5% patients required analgesia within 0-6 h, 5% in 6-12 h, and 15% in 18-24 hours [Figure 2]. Addition of dexmedetomidine enhanced the duration of analgesia in group B and the total dose of rescue analgesic used was significantly higher in group A patients [Table 1]. None of the patients had any opioid-related side effects like nausea, vomiting, pruritus, and drowsiness.

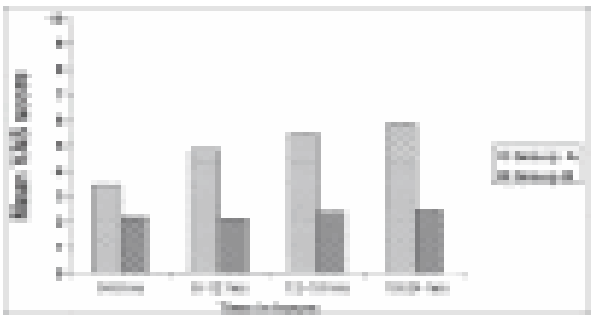

Figure 1
Comparison of mean VAS scores

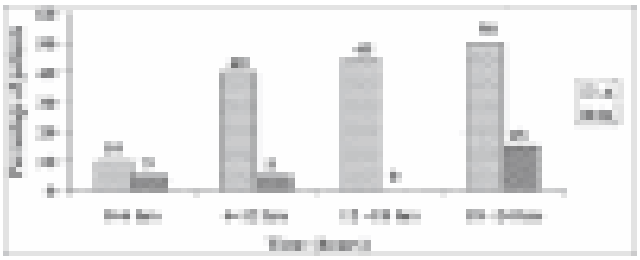

Figure 2
Rescue analgesic requirement (percentage of patients)

Table 2
Rescue analgesic requirement

	Group A	Group B
Time to first analgesic requirement (hours)	3.275 ± 1.8	10.52 ± 5.54*
Total consumption of tramadol in 24 h (mg)	72 ± 12.4	12.5± 5.38*

Table 1
Rescue analgesic requirement

The time of administration of first rescue analgesic was significantly higher in group B (10.52±5.54 h) as compared to group A (3.275±1.8 h). Mean VAS was significantly lower in group B as compared to group A. The total dosage of rescue analgesic was more in group A as compared to group B patients.

IV. Discussion

Several studies have been done for finding efficacious drugs to combat postoperative pain. Narcotics have been the main stay of postoperative pain management and morphine as the standard drug despite its various side effects. NSAIDS are also associated with gastric ulceration and bleeding complications and a concern in renal dysfunction. However, there has been renewed interest in local anesthetic wound instillation for postoperative pain control. Local anaesthetic infiltration with added adjuvants can improve the quality and duration of analgesia. The added adjuvants are epinephrine, fentanyl, ketorolac, opioids, clonidine, etc.[5] Dexmedetomidine, a potent α_2 adrenoceptor agonist, is approximately eight times more selective towards α_2 adrenoceptor than clonidine.[6]

In this study, we compared fentanyl and dexmedetomidine as adjuvant to bupivacaine for postoperative pain relief and we found significant difference in analgesic requirement in dexmedetomidine group. Various animal studies have reported potent antinociceptive effect of dexmedetomidine on peripheral administration along with its safety. Dexmedetomidine enhanced duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any evidence of histopathological damage to the nerve.[7],[8] In another study, dexmedetomidine added to ropivacaine increased the duration of sciatic nerve blockade in rats, most likely due to the blockade of hyperpolarisation-activated cation current (i.e., a direct effect on the peripheral nerve activity).[9] When dexmedetomidine and clonidine were added to lignocaine for nerve block, it enhanced the local anaesthetic action of lignocaine through peripheral α-2A adrenoceptors.[10]Peripherally, α_2-agonists produce analgesia by reducing the release of norepinephrine and causing α_2-receptor-independent inhibitor effect on nerve fibre action potential. Infiltration of dexmedetomidine in surgical wound may be useful to avoid the adverse hemodynamic effects of IV administration while still providing post-operative analgesia.[11] In the present study, patients who received dexmedetomidine in wound infiltration with bupivacaine after abdominal hysterectomy had reduced post-operative pain score and analgesics requirement when compared with the control group. This was similar to few other studies using local infiltration of dexmedetomidine for various surgeries with no delay in psychomotor recovery or increase in post-operative clinically significant adverse effect.[10],[12],[13]

In this study, we found statistically significant reduction in post-operative analgesics requirement when the patients were given post-operative wound infiltration with bupivacaine and dexmedetomidine combination. Furthermore, complications such as hypotension, sedation and bradycardia associated with IV dexmedetomidine were negligible when dexmedetomidine was given as local infiltration.

The mean duration of analgesia was higher in the dexmedetomidine bupivacaine group compared to the fentanyl bupivacaine group. Further, the mean rescue analgesic doses were significantly less in Group B as compared to Group A.

V. Conclusions

In conclusion, combination of bupivacaine and dexmedetomidine for wound infiltration in abdominal surgeries was associated with better postoperative analgesia and reduced analgesic consumption.

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