Comparative study of ketorolac versus butorphanol as an adjuvant in Intravenous regional anaesthesia (IVRA)

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Abstract

Background: Intravenous regional anaesthesia (IVRA) is simple, effective technique for upper limb orthopaedic surgeries specifically in developing countries like India because of cost-effectiveness. IVRA is also called Bier’s block after the name of its inventor August Bier. Aim: Present study was carried out to evaluate the effects of adding either butorphanol or ketorolac to lignocaine during Bier’s block. Materials and Methods: In a prospective randomized double blind study, 60 patients of age group 18-65 years of either sex with weight range of 65-70 kg of ASA grade I-III were randomly allocated into two groups of 30 each. Group I received butorphanol 1mg added to 3mg/kg lignocaine and group II received ketorolac 30 mg added to 3mg/kg lignocaine. Sensory and motor block onset, regression time, intraoperative and postoperative VAS score, duration of analgesia, total analgesic consumption in first 24 hr and side effects were noted. Statistical analysis of data was based on chi square test and post hoc test. Results: Demographic profile in both the groups was same. Duration of analgesia was significantly prolonged in group II (10.8 ±6.42) as compared to group I (3.02±1.52). In both the groups, patients remained haemodynamically stable and side effects and complications were also comparable. Conclusion: Ketorolac with lignocaine in IVRA provides prolonged post-operative analgesia as compared to butorphanol and lesser number of patients require rescue analgesia intraoperatively as well as postoperatively without any significant side effects.

Keywords: Intravenous regional anaesthesia, Butorphanol, Ketorolac, Post-operative Pain.

Introduction

IVRA was first described by German surgeon August Bier in 1908 for short operative surgeries on hand and forearm surgeries [1]. It gained popularity when lidocaine was used in 1960s [2]. It is simple to administer, cost effective, reliable [3] and doesn’t alter normal metabolic processes of the body. It avoids the hazards associated with general anaesthesia in patients with severe systemic diseases. However, there are some limitations of IVRA too which include slow onset in action, local anaesthetic toxicity in case of early tourniquet release, poor muscle relaxation, tourniquet pain and shorter post-operative analgesia [4]. To improve the efficacy of IVRA various adjuvants has been added like fentanyl, tramadol, clonidine, dexamethasone, NSAIDS like ketorolac acetyl-salicylate, and muscle relaxants [5, 6]. Ketorolac is a nonsteroidal anti-inflammatory drug (NSAID) in the family of heterocyclic acetic acid derivatives used as analgesic which acts by inhibiting the synthesis of prostaglandins by competitive blocking of enzyme cyclooxygenase (COX). Ketorolac is a nonselective COX inhibitor [7]. Studies investigating the addition of ketorolac to local anaesthetic in IVRA have demonstrated the reduced tourniquet pain and improved post-operative pain relief [8]. Butorphanol is an agonist-antagonist opioid that resembles pentazocine. Butorphanol has, low affinity for mu receptors to produce antagonism, moderate affinity for kappa receptors to produce analgesia and anti shivering effects, minimal affinity for sigma receptors so the incidence of dysphoria is low [9].
The aim of the present study was to evaluate the effects of adding either butorphanol or ketorolac to lignocaine for intravenous regional anaesthesia (Bier’s block). The two groups were compared with respect to hemodynamic changes, onset and regression of sensory and motor blockage, intra-operative and post-operative analgesic requirements, side effects and complications.

**Material and Methods**

After approval from the hospital ethical committee and obtaining written informed consent, a prospective, randomized double blind study was done on 60 patients of age group 18-65 years of either sex with weight range of 65-70 kg of ASA grade I, II, III were divided randomly into two groups of 30 each. Lignocaine used was without any preservative.

**Group I:** Butorphanol 1 mg added to 3 mg/kg lignocaine 0.5% diluted up to 40 ml with normal saline.

**Group II:** Ketorolac 30 mg added to 3 mg/kg lignocaine 0.5% diluted up to 40 ml with normal saline.

Pre-anaesthetic check up was done before surgery and after confirming fasting status patients were taken up for surgery. Patients with coagulation disorders like sickle cell disease, Raynaud’s disease, history of any drug allergy and patients who refused to enter the study were excluded from the study. A randomization list was generated and identical syringes containing each drug were prepared by personnel blinded to study. No sedative premedication was given on the day of surgery.

Baseline vitals such as non invasive blood pressure, ECG, pulse rate, oxygen saturation were monitored. Intravenous line was secured on non operative hand for giving injection of drugs and crystalloid infusion. The operative arm was exsanguinated with esmarch bandage. After applying double pneumatic tourniquet the proximal cuff was inflated to 250 mm Hg. Circulatory isolation of the arm was verified by inspection and absence of radial pulse. Then patients were injected with one of the study drug. After injection sensory block was assessed by pin prick performed by 25G short bevelled needle at every 30 seconds interval in sensory distribution of median, ulnar and radial nerves of hand.

Motor function was assessed by flexion and extension of wrist and fingers of the patients. After achieving sensory and motor block the distal tourniquet was inflated to 250 mm Hg then proximal tourniquet was deflated and operation was started. After tourniquet application tourniquet pain was assessed at 10 min intervals by visual analogue scale 0 = no pain and 10 = worst pain. [10] If at any given time, VAS >3 then Inj butorphanol 0.5 mg was given and requirement for rescue analgesic doses was recorded.

The tourniquet was not deflated before 30 min and not inflated more than 90 min of duration. After the completion of surgery, the tourniquet deflation was done by cyclic deflation-inflation technique. Sensory and motor block recovery time was noted.

Postoperatively VAS score was measured for surgical pain every hourly after tourniquet deflation until 4 hours than 4 hourly till 24 hours. Rescue analgesia in terms of inj diclofenac 75 mg IM was given if VAS > 3. Total numbers of rescue analgesic required during 24 hours were recorded. Intraoperative as well as postoperative complications if any were noted. Statistical analysis was performed with IBM SPSS 21.0 version. Study population group was calculated based on previous studies, p-value, confidence interval and other variables taking Power of study as 90%.

**Results**

**Table 1: Patient Demographics**

| Variable               | Group I n = 30 | Group II n = 30 | ‘p’ value | Significance |
|------------------------|----------------|-----------------|-----------|--------------|
| Age (years)            | 38.73 ± 13.3   | 41.67 ± 16.6    | 0.062     | NS           |
| Sex                    | Male 24, Female 6 | Male 23, Female 7 | 1.00      | NS           |
| Weight (kg)            | 67.00 ± 5.6    | 68.80 ± 5.1     | 0.30      | NS           |
| Duration of Surgery (minutes) | 40.57 ± 7.96 | 41.63 ± 7.2 | 1.00 | NS |
Table 2: Baseline parameters

| Parameters     | Group I          | Group II         | ‘p’ value | Significance |
|----------------|------------------|------------------|-----------|--------------|
| PR (rate/min)  | 80.47 ± 4.41     | 82.53 ± 4.58     | 0.84      | NS           |
| SBP (mmHg)     | 131.73 ± 7.13    | 132.33 ± 7.52    | 0.51      | NS           |
| DBP (mmHg)     | 86.80 ± 3.39     | 84.87 ± 3.63     | 0.89      | NS           |
| SpO₂ (%)       | 99.87 ± 0.33     | 98.89 ± 0.35     | 0.35      | NS           |

Table 3: sensory & motor block parameters

| Parameters                  | Group I (n = 30) | Group II (n = 30) | ‘p’ value | Significance |
|-----------------------------|------------------|-------------------|-----------|--------------|
| Onset of sensory block (min)| 3.08±1.21        | 3.58±1.25         | 0.67      | NS           |
| Onset of motor block(min)   | 7.64±1.60        | 8.01±1.20         | 0.36      | NS           |
| Sensory block recovery(min) | 4.59±1.33        | 4.18±1.21         | 0.56      | NS           |
| Motor block recovery(min)   | 8.12±0.45        | 7.31±0.66         | 0.66      | NS           |

Table 4 Intra operative VAS score at different time interval

| Time interval | Group I Mean | S.D. | Group II Mean | S.D. | ‘p’ value |
|---------------|-------------|------|---------------|------|-----------|
| 0 min         | 0           | 0    | 0             | 0    | -         |
| 10 min        | 0           | 0    | 0             | 0    | -         |
| 20 min        | 0.20        | 0.45 | 0.27          | 0.45 | 1.00 (NS) |
| 30 min        | 1.33        | 0.66 | 1.47          | 0.93 | 0.96 (NS) |
| 40 min        | 1.75        | 0.67 | 1.79          | 0.72 | 0.97 (NS) |
| 50 min        | 2.44        | 0.71 | 2.38          | 0.72 | 0.96 (NS) |

P > 0.05; NS (not significant)

Table 5: Comparison of post operative VAS score

| Time interval | Group I Mean | S.D. | Group II Mean | S.D. | ‘p’ value |
|---------------|-------------|------|---------------|------|-----------|
| 0 min         | 0           | 0    | 0             | 0    | -         |
| 15 min        | 0           | 0    | 0             | 0    | -         |
| 30 min        | 0           | 0    | 0             | 0    | -         |
| 1 hr          | 1.73        | 0.72 | 1.54          | 0.6  | 0.08 (NS) |
| 2 hr          | 2.88        | 0.60 | 2.10          | 0.2  | 0.07 (NS) |
| 3 hr          | 3.63        | 0.71 | 2.63          | 0.90 | 0.05(S)   |
| 4 hr          | 1.88        | 0.71 | 3.03          | 0.90 | 0.02 (S)  |
| 8 hr          | 3.30        | 0.68 | 2.27          | 0.85 | 0.05 (S)  |
| 12 hr         | 2.67        | 0.54 | 2.68          | 0.85 | 0.05 (NS) |
| 16 hr         | 3.20        | 0.66 | 2.76          | 0.40 | 0.05 (S)  |
| 20 hr         | 2.93        | 0.78 | 3.62          | 0.72 | 0.05 (S)  |
| 24 hr         | 2.97        | 0.83 | 2.57          | 0.32 | 0.76 (NS) |

P > 0.05; NS (not significant); *p<0.05; significant

Both the groups were comparable with respect to demographic variables and baseline haemodynamic parameters as shown in table 1 and table 2. There was no significant difference among groups when compared for Mean arterial pressure (MAP), pulse rate, oxygen saturation, sedation score intraoperatively as well as post-operatively. The sensory and motor block parameters are shown.
Table-6: Comparison of analgesics in 24 hours and mean time to first analgesic

| Group                      | Group I | Group II |
|----------------------------|---------|----------|
| Patients requiring no analgesics | 6 (20%) | 10 (33%) |
| Patients requiring analgesics | No. of analgesics given | No. of analgesics given |
|                             | 1       | 2        | 3    | 1  | 2  | 3  |
|                             | 40%     | 25%      | 15%  | 35% | 25% | 7% |
| Mean time to first analgesic (hrs) | 3.02 ± 1.52 | 10.8 ± 6.42 |

Graph-1

Graph-2

Intraoperatively VAS score was comparable in both groups at 20 min, 30 min, 40 min, 50 min. (Table 4). Intraoperatively the total number of doses of rescue analgesic was comparable in both the groups. Postoperatively VAS score was significantly higher in group I at 3hr, 8hr and 16 hr than group II (Table 5 and Graph 1). The total number of inj diclofenac use was less in group II than group I. Total duration of analgesia was significantly higher in group II than group I (Table 6 and Graph 2). There were no significant side effects seen in both the groups.
As a result of damage to nerve endings due to surgical trauma patient suffers pain during postoperative period. As a result of inflammation there is release of chemical mediators like bradykinin, histamine, serotonin and substance P that causes activation of nociceptors.[11, 12] Prostaglandins make nociceptors more sensitive to the chemical mediators resulting into cutaneous hyperalgesia at the site of surgery.[12, 13] These nociceptive pathways were blocked by pre treatment with Non steroidal anti inflammatory drugs (NSAIDS) or opioids before the surgery. IVRA is a reliable and economical method of anaesthesia specifically in upper limb surgery. [14, 15]

In the present study there was no statistically significant difference among the two groups in terms of sensory block onset, sensory block recovery, motor block onset and motor block recovery time. Results of our study are comparable with the results of study done by Bansal et al [16] and Myoung J K et al. [17]

The current study signifies that addition of ketorolac to lidocaine in IVRA which significantly prolong the duration of analgesia in postoperative period as compare to butorphanol group. Based on the time for request of first dose of supplement analgesic in the post-operative period, duration of analgesia was calculated. The mean duration of analgesia was 3.12±1.42 hrs in group I and 10.8±6.42 hrs in group II. Duration of analgesia in group II was significantly higher than first group. In a study conducted by Reuben et al [18] on sixty patients mean time to first rescue analgesia was 653±501 minutes in ketorolac group. Study done by Bansal et al [16] reported that time to first analgesic requirement in butorphanol group was 169.50±99.25 minutes. The results of our study are comparable with the above studies.

During post-operative period mean doses of rescue analgesia in group I was 3.20±0.4 doses and in group II was 1.60±0.4 doses. There was statistically significantly higher rescue analgesic requirement in group I than group II. Our results are comparable with studies done by Reuben et al [17] and Bansal et al. [16]

In our study two patients in group I suffered from nausea and vomiting which were resolved with intravenous ondansetron 4mg. No other statistically significant side effects or complications were observed in our study

**Conclusion**

We conclude that duration of post-operative analgesia is better in ketorolac group as compared to butorphanol group as number of rescue analgesic doses during post-operative period were significantly higher in butorphanol group. However, there are some limitations in the present study.

Firstly, we cannot exclude a more generalised effect of systemic ketorolac and butorphanol which would be released into the circulation upon tourniquet deflation. Secondly, the result of our study could have been more precise if the sample size of the study group would have been large, but the patient willing for IVRA for forearm and hand surgeries were limited in our institution.

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