Comparison of Butorphanol and Buprenorphine as an Adjunct to Local Anaesthetic Solution in Supraclavicular Brachial Plexus Block

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Abstract

Introduction: Opioids are well studied adjuncts although the evidence regarding the analgesic benefit of opioid adjuncts remain equivocal. The effectiveness of buprenorphine and butorphanol administered as adjuncts to local anaesthetic solution into brachial plexus sheath was evaluated. *Aim:* The objectives of this study are to compare between Butorphanol and Buprenorphine as an adjunct to local anaesthetic solution in supraclavicular brachial plexus block with respect to – Duration of sensory and motor block, duration of analgesia and untoward side effects. *Materials and Methods:* The study was a randomized prospective double blind and comparative study carried in 60 ASA grade I and II patients undergoing elective upper limb surgeries, aged between 18-60 years were randomly allocated into 2 groups of 30 each. All patients received 1% lignocaine plain 2mg/kg and 0.5% bupivacaine at 2mg/kg body weight. In addition, 30 patients in group A received butorphanol tartarate (30mcg/kg) while the 30 patients of group B received buprenorphine hydrochloride (3mcg/kg). Using VAS score the analgesia was evaluated every hourly for six hours, every two hours for next twelve hours and then every six hours till 48 hours. *Result:* heart rate pattern of both groups shows statistical significance at 10th to 13th hour of the study period. systolic blood pressure changes between two groups shows statistical significance between 9th to 11th and 14th, 15th, 16th, 18th, 20th and 24 hrs. diastolic blood pressure between two groups show statistical significance between 8th-12th hr and 18th, 20th and 24th hr. Statistical significance with respect to respiratory rate at 2nd to 5th hr, 14th hr, 16th hr to 20th hr, 28th hr and 48th hr. postoperative pain using visual analogue scale (VAS) between the two groups with statistical significance at 3rd, 9th, 11th-13th, 17th and 18th hr no statistical significance in terms of onset, duration of surgery, sensory and motor blockade between the two groups. Average duration of analgesia were 14.13±8.41hr and 22.18±12.13hr in groups A and B respectively, showed statistical significance. The group B showed prolonged analgesia produced by addition of buprenorphine to local anaesthetic. Side effects like nausea, vomiting and numbness were comparable in both groups without any significance. *Conclusion:* We conclude that buprenorphine as an adjunct administered with local anaesthetics into brachial plexus sheath is an efficient way to overcome the perioperative pain in upper limb surgery.

Keywords: Buprenorphine; Butorphanol; Local Anaesthetic Adjuncts; Brachial Plexus Block; Perioperative Analgesia.

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Introduction

The alleviation of pain is the main concern of anaesthesiologist and has received tremendous focus in this evolving field of medicine. Many methods, many drugs and many routes have been tried for this purpose. Fundamental to modern neural blockade is the concept that pain is a sensory warning conveyed by specific nerve fibre, amenable in principle, to modulation or interruption anywhere in the nerve's pathway.

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Pain relief after upper limb surgery can be achieved by various regional anaesthetic techniques. The supraclavicular brachial plexus is one among the most popular regional nerve blocks performed. The ease and predictable landmarks makes it a popular approach. The advantages are – It provides long lasting post operative analgesia, thereby reducing the systemic analgesic requirement; it aids in early ambulation, overcoming the disadvantages of general anaesthesia.

The limitations of local anaesthetics are – slower onset of action, shorter duration of action and prolonged motor and sensory blockade. Different adjuncts have been tried to fill the lacunae created by the local anaesthetics. The novel approaches are – alkalinisation of local anaesthetics, carbonation, addition of opiates, calcium channel blockers (verapamil), clonidine. The existence of opioid receptors in peripheral nerve tissue has led to investigation of incorporating small doses of opioids in peripheral nerve blocks, hoping to achieve analgesia with minimal side effects. Hence pain relief using opioids admixed with local anaesthetics for peripheral nerve blocks have been tried.

Buprenorphine, a semi-synthetic thebaine congener is thirty to thirty five times more potent than morphine. It has a longer duration of action due to high affinity to μ receptor. Butorphanol, a synthetic opioid analgesic is five to eight times more potent than morphine. It has comparatively lesser incidence of systemic side effects. Therefore, a comparative study with buprenorphine and butorphanol as adjuncts to local anaesthetics in brachial plexus block through supraclavicular approach for upper limb surgery is desired to improve the onset, quality and duration of analgesia.

Materials and Methods

A prospective, randomised, comparative study consisting of 60 patients undergoing upper limb surgery lasting more than thirty minutes were included in the study. The elective surgical interventions were internal fixation of bones with plates and screws, excision of bone cysts, reconstructive and other surgeries involving upper limb.30 patients in group A (Butorphanol) and 30 patients in group B (Buprenorphine) is undertaken to study the change in pattern of haemodynamics, pain score by VAS, duration of analgesia, duration of sensory and motor blockade and side effects.

Inclusion Criteria

Patients with ASA I and II physical status, within the age group of 18-60 years, of both sexes undergoing elective surgeries were included in the study.

Exclusion Criteria

Patients with age <16 and >60 years; patients with coagulopathy or on anti-coagulants, peripheral neuropathy; patients who had received opioid in the past twelve hours; patients with history of substance abuse; local cutaneous infections; pregnant patients; patients with allergy to local anaesthetics, butorphanol and buprenorphine; ASA class III and IV patients; patients undergoing emergency surgical procedures were excluded from the study.

Preoperative Preparation

The study protocol was approved by the hospital ethical committee. All the patients underwent thorough preanaesthetic evaluation on the day prior to surgery. All systems were examined including airway and the surface anatomy where the block was going to be given. The anaesthetic procedure to be carried out was explained. They were informed about development of paraesthesia. Patients were reassured to alleviate their anxieties. A written informed consent was taken. They were educated regarding the visual analogue scale. All the patients were fasted overnight. All of them received oral diazepam 10mg and tablet ranitidine 150mg night before surgery.

Basic laboratory investigations were conducted including haemogram, urine analysis and whenever needed chest x-ray, electrocardiogram, blood sugar.

Method of collection of data – Supraclavicular brachial plexus block was carried out as an elective procedure on the patients undergoing upper limb surgery. Sixty patients were randomly allocated into 2 groups (group A, n=30 and group B, n=30) in double blind fashion. All drug solutions were prepared by an anaesthesiologist not involved in administration of anaesthesia, patient care and data collection.

Group A (n=30): Received brachial plexus block with 1% lignocaine plain at the dose of 2mg/kg body weight and 0.5% bupivacaine 2mg/kg along with inj. Butorphanol 0.03mg/kg to the solution.

Group B (n=30): Received brachial plexus block with 1% lignocaine plain at the dose of 2mg/kg body weight and 0.5% bupivacaine 2mg/kg along with inj. Buprenorphine 3mcg/kg to the solution.

All the necessary equipments and drugs needed for administration of general anaesthesia and for resuscitation were kept ready in order to manage in case of failed block or toxic reactions occurring during the procedure. Block was performed using a standard protocol.

The effect of anaesthetics on the following parameters were observed –

1. The time of onset for sensory blockade: defined as time between injection and total abolition of pinprick response, was evaluated in four nerve areas (radial, ulnar, median and musculocutaneous) at every 3 minutes until 45 minutes after the injection. The block was judged to be failed if anaesthesia was not present in 2 or more peripheral nerve distribution and such patients were excluded from the study.

2. The duration of sensory blockade: defined as the time between onset of action and return of pinprick response, was assessed every 30 minutes in at least 3 major nerve territory.

3. The duration of analgesia: defined as the time between the onset of action and the onset of pain, was the time when the patients received the first dose of analgesic. Supplemental analgesia was given in the form of intramuscular inj. Diclofenac sodium 50mg to 75mg, when visual analogue scale was more than 4.

4. The duration of motor blockade: was assessed every 30 minutes till the return of complete muscle power in at least 2 major nerve distribution.

During surgery, pulse rate, non-invasive blood pressure and peripheraloxygen saturation through pulse oximetry were monitored.

Post-operative assessment: Patients would be evaluated postoperatively, every hourly for first six hours, second hourly for next twelve hours, for the following parameters – intensity of pain, motor and sensory recovery. Patients were also monitored for the side effects of opioids including nausea, vomiting, drowsiness, pruritis and urinary retention. The intensity of pain was assessed using visual analogue scale (VAS) score. This scale consists of a 100mm line on which the patients represented the degree of pain he/she was experiencing by placing a point somewhere between "no pain" ("0") and the worst pain ever experienced ("100"). The supplemental analgesia was given in the form of inj.Diclofenac 50-75mg IM, when VAS score was more than four.

Statistical methods – Chi-square test and Fisher Exact test has been used to find the homogeneity of sex distribution between the two groups and Student t test has been used to find the homogeneity of age and weight distribution between the two groups. Student t test (Two tailed) has been used to find significant difference of haemodynamics between the two groups and the study parameters namely – time of onset, duration of surgery, duration of motor and sensory blockade, and duration of analgesia between the two groups. Mann Whitney U test has been used to assess the significant difference of VAS score between the two groups. Chi-square and Fisher Exact test has been used to find significant difference of incidence of side effects between the two groups. The statistical software used was SPSS.12.0.1 for windows and statistica.

Results

The table 1 shows that the average age was 33.47±10.97 yrs in group A and 35.07±10.98 yrs in group B. The average weight of the patients were 60.40±8.62 kg in group A and 63.33±9.48 kg in group B respectively. Both groups had predominantly male patients, accounting to nearly 2/3 of the total study population in each group. There was no significant difference in age, weight and sex distribution.

This line chartcomparing the heart rate pattern of both groups shows statistical significance at 10th to 13th hour of the study period although they are within an acceptable clinical range (Figure 1).

In this line chart the compared systolic blood pressure changes between two groups shows statistical significance between 9th to 11th and 14th, 15th, 16th, 18th, 20th and 24 hrs. (Figure 2).

Table 1: Comparison of demographic parameters

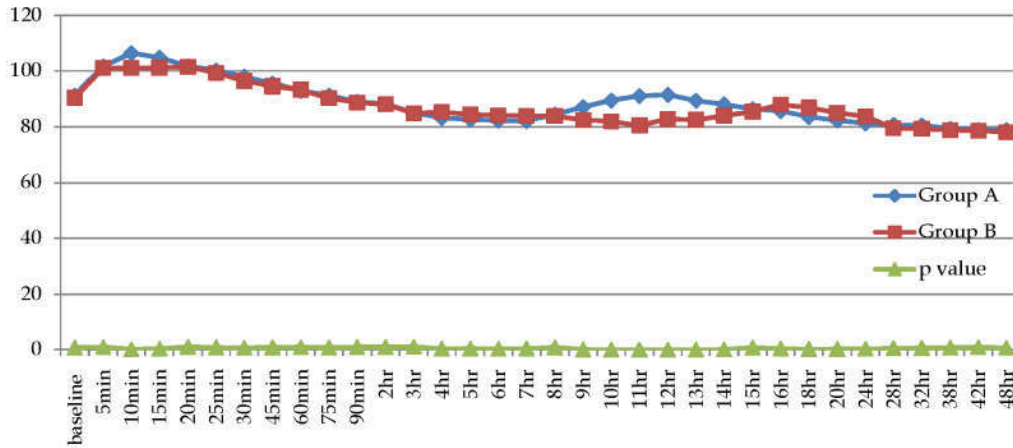| Demographic parameters	Group A (n=30)	Group B (n=30)	P value
Age in years (Mean±SD)	33.47±10.97	35.07±10.98	0.575
Weight in Kg (Mean±SD)	60.40±8.62	63.33±9.48	0.215
Sex	M:F – 20:10	M:F – 23:7	0.781
Inference	Samples are age, sex and weight matched with p>0.05		

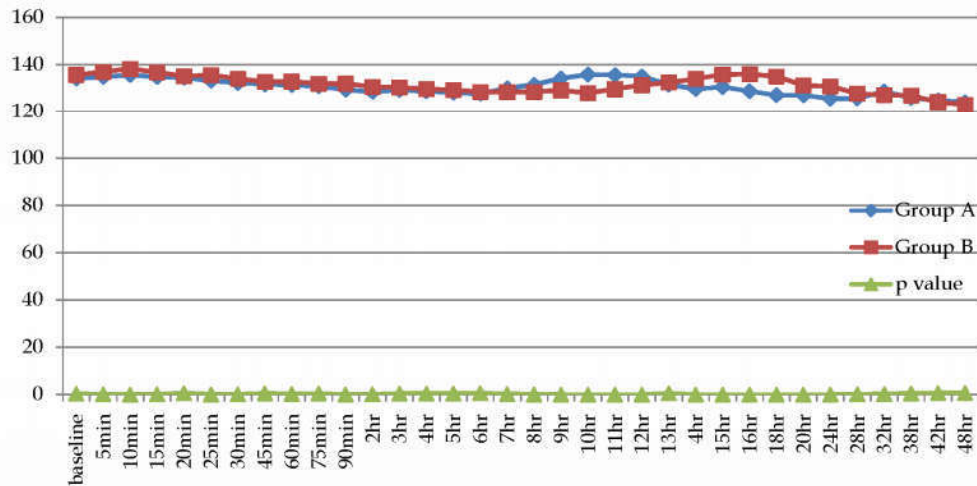**Fig. 1:** Comparison of heart rate between the two groups

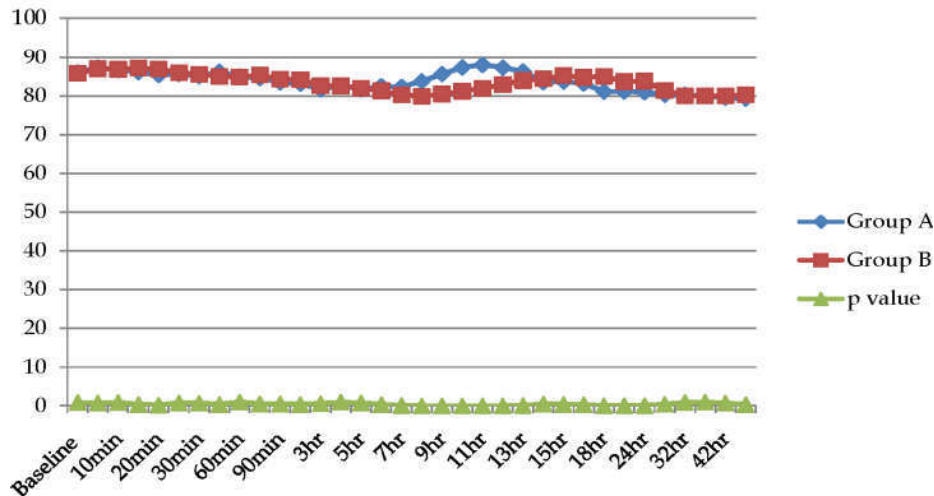**Fig. 2:** Comparison of systolic BP between the two groups

Fig. 3: Comparison of diastolic BP between the two groups

The compared diastolic blood pressure between two groups show statistical significance between 8th-12th hr and 18th, 20th and 24th hr. (Figure 3).

In Figure 4 there is statistical significance with respect to respiratory rate at 2nd to 5th hr, 14th hr, 16th hr to 20th hr, 28th hr and 48th hr. (Figure 4).
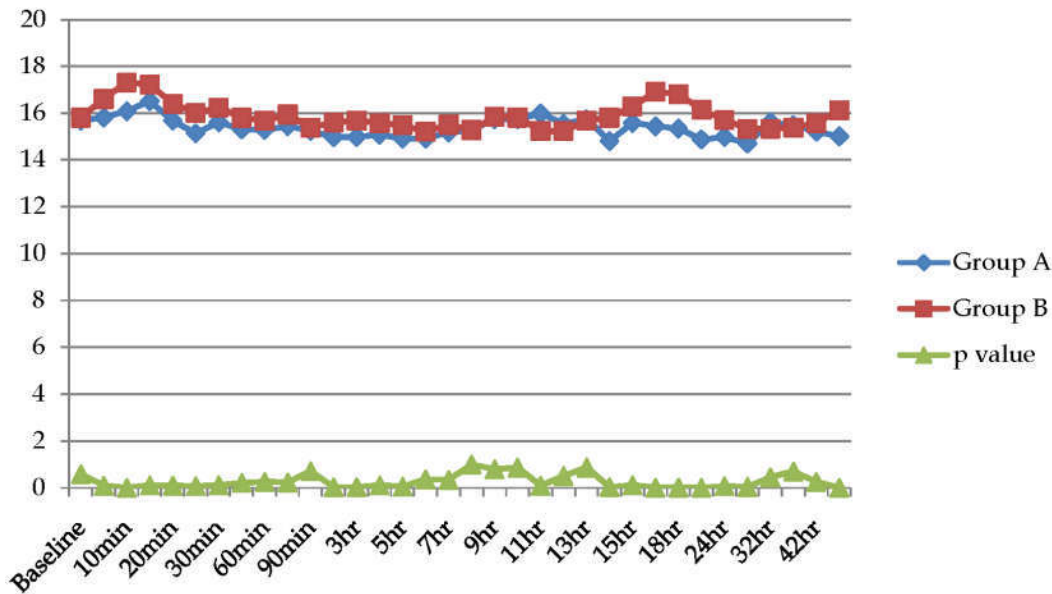
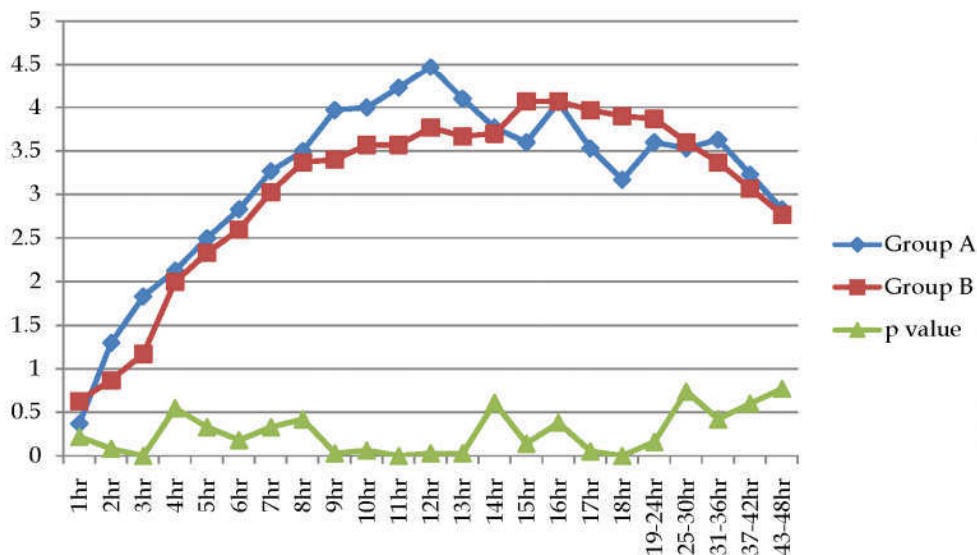**Fig. 4:** Comparison of respiratory rate between the two groups

Fig. 5: Comparison of VAS score between the two groups

Table 2: Comparison of study parameters between the two groups

Study parameter	Group A (n=30)		Group B (n=30)		P value
	Mean	SD	Mean	SD	
Time of onset (min)	20.47	3.64	19.47	4.90	0.37
Duration of surgery (min)	79.50	26.27	84.33	37.20	0.56
Duration of sensory blockade (min)	385.67	66.67	380.50	80.15	0.79
Duration of motor blockade (min)	367.40	71.43	360.00	77.87	0.70
Duration of analgesia (hrs)	14.13	8.41	22.18	12.13	0.00

The patients were assessed for postoperative pain using visual analogue scale (VAS). The above graph compares the VAS scores between the two groups with statistical significance at 3rd, 9th, 11th-13th, 17th and 18th hr of the study period. (Figure 5).

In the Table 2, there was no statistical significance in terms of onset, duration of surgery, sensory and motor blockade between the two groups. However, the average duration of analgesia were 14.13±8.41hr and 22.18±12.13hr in groups A and B respectively, showed statistical significance.

Table 3: Comparison of side effects between the two groups

Side effects	Group A (n=30)	Group B (n=30)
Nausea	3 (10.0%)	3 (10.0%)
Vomiting	2 (6.7%)	1 (3.3%)
Numbness	1 (3.3%)	1 (3.3%)
No side effects	24 (80.0%)	25 (83.3%)
Inference	Side effects are statistically similar between the two groups with p=0.739.	

The group B showed prolonged analgesia produced by addition of buprenorphine to local anaesthetic.

The observed parameters like nausea, vomiting and numbness were comparable in both groups without any significance (Table 3).

Discussion

Varieties of receptors mediate nociception in peripheral sensory nerve fibres. The knowledge of these receptors has been used in the form of various adjuncts administered along with local anaesthetics. These adjuncts may not only prolong the analgesic duration but also thought to reduce the systemic analgesic consumption as well as their side effects. To prolong perioperative analgesia various adjuncts such as opioids, clonidine, verapamil, neostigmine and tramadol have been tried. Although the role of opioid as an adjunct has been debated over a long period, it is still in regular use.

The objective of the study was to compare the analgesic efficacy between butorphanol and buprenorphine as an adjuncts to local anaesthetics in brachial plexus block.

The study was a prospective, randomized, double blind study carried out at our hospital. 60 patients belonging to ASA I and II physical status patients undergoing upper limb surgeries were included in the study. Patients were divided into 2 groups –

Group A (n=30): Received brachial plexus block with 1% lignocaine plain at the dose of 2mg/kg body weight and 0.5% bupivacaine 2mg/kg along with inj. Butorphanol 0.03mg/kg to the solution.

Group B (n=30): Received brachial plexus block with 1% lignocaine plain at the dose of 2mg/kg body weight and 0.5% bupivacaine 2mg/kg along with inj. Buprenorphine 3mcg/kg to the solution.

In our study, we observed that there was no change in the time of onset of sensory blockade between two groups. This was similar to the observation done by Eric J. Veil [1], who found no change in the onset time when morphine and buprenorphine were added to 0.5% bupivacaine into brachial plexus sheath.

However, Flecher et al. [2] had an early onset of block with fentanyl. The pH of the injected solution around the nerve would certainly influence the onset of action.

The other block characteristics like duration of sensory and motor blockade were similar in both groups.

We observed that addition of buprenorphine to local anaesthetic solution much longer acting analgesia (22.18±12.13) than produced by addition of butorphanol (14.13±8.14hrs).

Bazin et al. [3], had observed a similar duration of analgesia (median 20hrs). On buprenorphine administration, in a similar way, Candido et al. [4] has observed duration of analgesia produced with buprenorphine wasthree times longer than that produced by local anaesthetics alone.

Wajina et al. [5] has also found satisfactory and prolonged analgesia with butorphanol administered as continuous intrabrachial infusion. The prolonged analgesic duration [6] observed with buprenorphine may be attributed to its high affinity for μ opioid receptor and high lipid solubility, which favours easy penetration through the axonal myelin and nerve membrane.

The other factor that might have influenced the protracted analgesia of buprenorphine, was its potency. Buprenorphine in 33-35 times more potent than morphine when compared with butorphanol which is only 3.5 times more potent.

The other proposedmechanisms [7] for the opioid mediated analgesia are: It has more of a central action than peripheral action. The transport of the administered drug into extradural or subarachnoid space either by diffusion or by the centripetal axonal transport results in central action. The presence of the bidirectional axonal transport of opioid binding receptors has been already confirmed.

This thought has been questioned by Dahl et al. [8]. He compared the effects of morphine injected extradurally with that injected perifemorally. He

concluded that, if centripetal axonal transport exists it was clinically not significant. Christen et al. later confirmed that morphine concentration in CSF were similar after perifemoral or IM injection.

The expression of opioid receptors during the time of inflammation has been proposed mechanism of action. Mays et al. [9] obtained long lasting pain relief up to 24 hours , when 6mg of morphine was given in 30ml of saline into brachial plexus sheath, for chronic pain relief. But most of the studies, conducted for the postoperative pain relief, during minimal inflammation, have come with better analgesic durations. The electrophysiological study results with morphine, pethidine, fentanyl have suggested that opioids may exert non- specific action on nerves by impairing sodium and potassium conduction.

The presence of variety of receptors and the difference in the affinity of administered drug to the receptor can be alternative explanation to the longer duration of analgesia produced by buprenorphine than butorphanol. Buprenorphine has high affinity for opioid receptors whereas butorphanol is kappa agonist with moderate affinity.

Gobeaux et al. [10], in his first study observed a significant reduction in the time of onset with fentanyl 0.1mg administered into axillary sheath along with local anaesthetics. However, there wasno prolongation of analgesic duration. In his second study, he found prolonged analgesia with pethidine 100mg without any change in onset time.

They concluded that, varying results were due to greater lipid solubility of fentanyl and pethidine compared to morphine. The same fact allows greater distribution of the drug at the site of action as afferent nociceptive fibres are surrounded by a layer of myelin which presents a significant obstruction to water soluble agents.

We found no significant difference with respect to side effects like nausea, vomiting, numbness between the two groups. At the same time there was no incidence of pruritis, respiratory depression or urinary retention.

The significant changes observed with respect to haemodynamic parameters were due to variability in the onset of pain between the two groups. The early raise of heart rate and blood pressure in group A were due to analgesic wear off. The same occurred in group B in the later period. On the average the number of supplemental Diclofenac sodium injections received were two in group A, where as patient's in group B received one supplement over 48 hours.

From our study, we observed that buprenorphine may be a superior adjunct than butorphanol, when administered with local anaesthetic solutions into brachial plexus sheath for providing perioperative analgesia following upper limb surgeries.

In our study we did not have a control group and the pH of the administered solutions are not studied which are the other important factors that influence block characteristics as mentioned earlier.

Although the analgesic properties of the opioids have been studied with the establishment of peripheral opioid receptor, it awaits further studies to establish the local anaesthetic action of the opioids. This could be established by using varying drug concentrations of opioids administered alone in the regional techniques.

Conclusion

Buprenorphine (3mcg/kg body weight) is superior to butorphanol (0.03mg/kg body weight), as an adjunct to local anaesthetic solution when administered into brachial plexus sheath for perioperative analgesia during upper limb surgery.

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