Research Article

Pethidine in Hand and Forearm Surgeries under Intravenous Regional Anesthesia

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Abstract

Background: Intravenous regional anesthesia (IVRA) is used for short duration hand and forearm surgeries with possible acute postoperative pain. This research compares using pethidine with lidocaine to the conventional use of lidocaine only in IVRA as regards postoperative analgesia and the incidence of postoperative side effects.

Methods: In a prospective, randomized, double blind study, 60 patients undergoing hand and forearm surgeries received IVRA with lidocaine (group L, n=30) or lidocaine with pethidine 30mg (group LP, n=30). Fentanyl was used as analgesic if needed intraoperatively. In the first 6h postoperatively, analgesia was provided by fentanyl i.v with recording the time for the first dose, the total doses used and possible side effects. After 6h, the patients were asked to take diclofenac oral tablets 50mg if feeling pain.

Results: The block was adequate for all patients. The time for the first dose of fentanyl postoperatively was significantly more in group LP compared to group L (156.00±7.37 vs 58.83±5.04min respectively). The total consumption of fentanyl in the first 6h postoperatively was less in group LP compared to group L (24.67±6.29mcg vs 59.17±9.75mcg respectively). The side effects were not significantly different between the two groups. After 6h, all patients in both groups took diclofenac tablets (one tab/8h) for 24h.

Conclusion: Pethidine with lidocaine in IVRA provides postoperative analgesia upto 6h without significant increase in the incidence of side effects when compared with lidocaine alone but doesn't provide significant analgesia after 6h.

Keywords: Intravenous regional anesthesia; Pethidine; Hand and Forearm surgery

Introduction

Intravenous regional anesthesia (IVRA) is safe and effective way to provide anesthesia for the forearm and hand surgeries lasting up to 90 min. Although this technique avoids the potential complications of general anesthesia, it can result in significant tourniquet and postoperative pain [1]. Increased opioid analgesic use, longer hospital stays, poor patient outcomes, and decreased patient satisfaction scores are associated with inadequate pain management modalities during the immediate postoperative period [2]. To overcome these problems many of adjunct drugs have been used along with local anesthetic agents in IVRA.

A systemic review of all the adjuncts used in IVRA, by Choyce and Peng [3] concluded that among the opioids, pethidine has substantial postoperative benefit. Pethidine is a short acting opioid with mild side effects when given systemically.

Aim of this study is to determine the efficacy of pethidine in a dose of 30 mg as an adjunct to lidocaine in IVRA.

Materials and Methods

After taking approval from the ethics committee of Ainshams university hospitals and written informed consents from patients enrolled in the study, 60 ASA grade I and II patients posted for elective forearm and hand surgeries were selected for a prospective, randomized, double blind study. All procedures were performed at Ainshams university hospitals between January 2014 and July 2014. A power analysis was performed to determine a sufficient sample size required to establish a significant difference between the two groups based on the results of a preliminary study, using a power of 0.9. This determined that a sample size of 27 patients per group was necessary. All forearm and hand surgery patients with expected surgery time less than 90 minutes who accepted intravenous regional anesthesia for the surgery were considered for inclusion for this study. Exclusion criteria included addicts on opioids, patients on chronic use of antidepressants, patients with a neuro pathological disease, patients with allergy to lidocaine or opioids, ASA physical status 3 or 4, pregnancy, inability to give consent and patients with a renal disease.

All patients were preoperatively evaluated and visual analogue score for pain (VAS) was explained to them with 0 indicates no pain and 10 indicates the worst possible pain. Patients were premedicated with intravenous midazolam 2 mg, 10 min before the procedure. Routine monitoring included ECG, NIBP, and SpO_2. A 20 G cannula was inserted and secured in a distal vein of the arm to be operated, over the dorsum of the hand. A double-cuffed tourniquet was applied

Table 1: Demographic data and ASA class comparison.

		Groups		P value
		Group L	Group LP	
Sex				
Female		10(33.3%)	12(40.0%)	0.592
Male		20(66.7%)	18(60.0%)	
Age (years)				
Range		25-39	25-38	0.936
Mean±SD		33.67±3.38	33.73±3	
Weight(Kg)				
Range		58-75	58-71	0.830
Mean±SD		66.07±4.66	66.30±3.69	
Tourniquet time (min)				
Range		45-75	50-75	0.232
Mean±SD		62.17±8.58	64.67±7.42	
Surgical duration (min)				
Range		35-65	40-65	0.272
Mean±SD		52.17±8.58	54.50±7.70	

ASA class		Groups					
		Group L		Group LP		Total	
		N	%	N	%	N	%
I		18	60.0	20	66.7	38	63.3
II		12	40.0	10	33.3	22	36.7
Total		30	100.0	30	100.0	60	100.0
Chi-square	X2	0.287					
	P-value	0.592					

Table 2: Tourniquet pain within the group.

VAS	Group L			Group LP			Mann-Whitney Test	
	Range	Median	Mean Rank	Range	Median	Mean Rank	Z	P-value
15 min.	1-2	1	31.5	1-2	1	29.5	0.523	0.601
30 min.	1-3	2	31.0	1-3	2	30.0	0.246	0.806
45 min.	2-4	3	34.1	2-4	3	26.9	1.787	0.074
60 min.	2-5	3	32.2	2-4	3	28.8	0.880	0.379

Unpaired Student T-test was used to compare between the two groups in quantitative data.

The pain scores between the groups were compared using Mann-Whitney Test.

A P value of <0.05 was considered statistically significant.

Results

There were no differences among the groups in demographic data, tourniquet time, surgical duration and ASA class (Table 1). There was no difference between the groups for hemodynamics parameters (heart rate, systolic and diastolic blood pressure).

Tourniquet pain increased significantly between 30 and 45 min in both groups. The VAS scores were comparable between the groups during surgery (Table 2). Fentanyl requirement for treatment of intraoperative tourniquet pain was not significant between the groups.

Postoperatively, the time for the first dose of fentanyl consumption was significantly delayed in group LP compared to group L (156.00 ± 7.37 vs. 58.83 ± 5.04 min respectively) (Table 3), (Figure 1).

The total fentanyl consumption in the first 6h of the postoperative period (Table 3), (Figure 2) was lesser in group LP compared to group L (24.67 ± 6.29mcg vs. 59.17 ± 9.75 mcg respectively).

One patient in group L and 3 patients in group LP had tinnitus and dizziness. One patient in group L and two patients in group LP had postoperative nausea and vomiting. One patient in group LP had mild itching postoperatively but none in group L. None of the patients experienced intra or postoperative respiratory depression.

None of these side effects were statistically significant between the two groups (Table 4).

After 6 hours, all patients in both groups took diclofenac tablets (50mg tablet). There was no significant difference between the 2 groups as every patient took 3 tablets in 24 hours duration (one tablet/8 hours).

over the arm. The arm was exsanguinated by elevation and application of Esmarch bandage. The proximal cuff of the tourniquet was inflated to the pressure of 300 mm Hg. Isolation of the limb from systemic circulation was confirmed by observing the arm for the absence of distended veins and confirming the absence of radial pulse. The Esmarch bandage was removed and 40 mL of IVRA solution was injected through the venous cannula slowly over a period of 90 s.

The patients were randomly divided into two groups of 30 each, by closed envelope technique. They received either 40 mL of 0.5% lidocaine (group L) or 40 mL of 0.5% lidocaine along with pethidine 30 mg (group LP).

Pulse rate, blood pressure, and SpO_2 were recorded every 5 min. Intraoperative tourniquet pain was assessed every 15 min using the VAS score. During intraoperative period, for tourniquet pain (VAS > 3) 25 mcg of fentanyl was given intravenously. After deflation of cuff, pain was assessed using VAS scale at 0, 15, 30, 60, 120, 180, 240 and 360 min. For early postoperative pain up to 6 h, for VAS > 3, bolus dose of fentanyl 25 mcg was given intravenously. The time for the first analgesic consumption and the total dose of fentanyl consumed were noted.

Postoperative nausea and vomiting, itching, tinnitus, dizziness and respiratory depression (respiratory rate <10/min or SpO_2 < 90%) were noted.

After 6 hours, all patients in both groups were asked to take diclofenac tablets (50mg tab) (one tab/8h) for the coming 24 hours if feeling pain.

Statistical presentation and analysis of data was conducted, using the mean, standard deviation, unpaired student t-test, Mann-Whitney and chi-square by SPSS V17.

Table 3: Time for the first dose of fentanyl consumption and the amount of fentanyl used in the first 6h postoperatively.

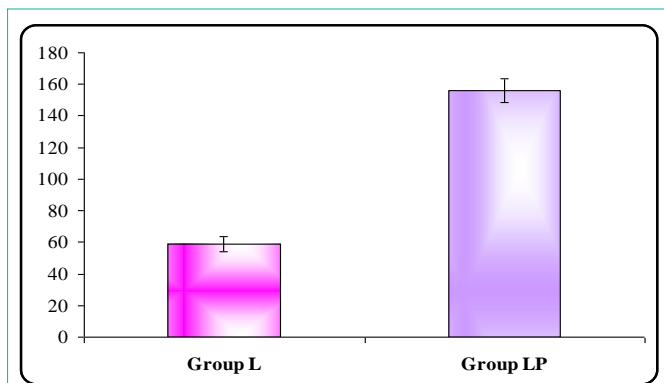| Groups	Time for the first analgesic postoperatively (min)					
	Range			Mean	± SD	P-value
Group L	50	-	70	58.83	± 5.04	<0.001*
Group LP	140	-	170	156.00	± 7.37	
Groups	Fentanyl used in the first 6h postoperatively (mcg)					
	Range			Mean	± SD	P-value
Group L	40	-	75	59.17	± 9.75	<0.001*
Group LP	10	-	35	24.67	± 6.29	

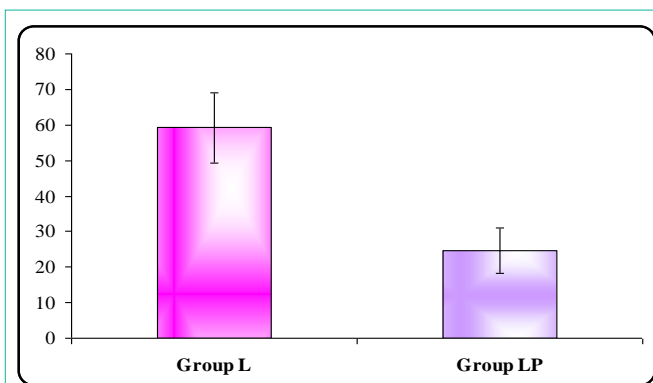**Figure 1:** Time for the first dose of fentanyl consumption in minutes*.

Figure 2: Doses of fentanyl used in first 6h in mcg*.
*: statistically significant.

Table 4: Side effects profile.

	Groups				Chi-square	
	Group L		Group LP			
	N	%	N	%	X2	P-value
Tinnitus and dizziness	1	3.3	3	10.0	1.071	0.301
Postoperative nausea and vomiting	1	3.3	2	6.7	0.351	0.554
Postoperative itching	0	0.0	1	3.3	1.017	0.313

Discussion

Numerous studies have recommended the preemptive treatment of postoperative pain as the modality of choice to decrease the time to the first opioid use, decrease the hospital stays, improve the patients' outcomes, and increase the patients' satisfaction [2, 4, 5]. Postoperative pain control should be started intraoperatively [6].

Intravenous regional anesthesia (IVRA) is a technique involving the administration of a local anesthetic into a region where the venous return is mechanically impeded [7].

It is easily learned and requires minimal personnel. IVRA was introduced in 1908 by the German surgeon August Gustav Bier, hence the more common term "Bier block" for this technique. Although used commonly when it was first introduced, Bier block fell in popularity before being reintroduced by Holmes in 1963 [8].

Most experiences with Bier block have been in the operating rooms, where it is considered a safe and effective alternative to general anesthesia in selected cases involving the upper and lower limbs. Bier block can also be used in the emergency department to provide rapid and complete anesthesia, as well as muscle relaxation and a bloodless operating field [9-12]. Many local anesthetics were used in IVRA but the most common one is lidocaine. Lidocaine, which has been in clinical use for over 60 years, is one of the most widely used local anesthetics and is useful for treating ventricular arrhythmias. The mechanism of action of lidocaine has been intensively investigated, yet there remain important unresolved questions. Although there is evidence that lidocaine can interact with multiple targets, lidocaine's primary clinically relevant target is believed to be voltage-gated sodium channels. Voltage-gated sodium channels play a critical role in the generation and propagation of action potentials in neurons and muscle cells. Lidocaine inhibition of voltage-gated sodium currents involves complex voltage and use dependence that is thought to be crucial for many of the therapeutic effects. Toxicity ranges from mild CNS manifestations like numbness and tingling up to severe

symptoms like tremors and convulsions [13].

Pethidine as one of the opioids exerts its analgesic effects by acting as an agonist at the μ-opioid receptor [14].

Pethidine has structural similarities to atropine and other tropane alkaloids and may have some of their effects and side effects [15]. In addition to these opioidergic and anticholinergic effects, it has local anesthetic activity related to its interactions with sodium ion channels. Pethidine also has stimulant effects mediated by its inhibition of the dopamine transporter (DAT) and norepinephrine transporter (NET). It has also been associated with cases of serotonin syndrome suggesting some interaction with serotonergic neurons, but the relationship has not been definitively demonstrated. It is more lipid-soluble than morphine, resulting in a faster onset of action. Its duration of clinical effect is 120–150 minutes, although it is typically administered at 4 to 6 hour intervals. The severe side effects unique to pethidine among opioids (serotonin syndrome, seizures, delirium, dysphoria and tremor) are primarily or entirely due to the action of its metabolite, norpethidine which accumulates in renal failure [16].

The peripheral action of opioids could be mediated by either the peripheral opioid receptors or by the local anesthetic action of their own [17]. Many opioids (morphine, pethidine, fentanyl, tramadol, sufentanil and alfentanil) have been used as adjuncts in IVRA previously. Among these opioids, only pethidine in a dose above 30 mg has substantial postoperative benefits but at the expense of post deflation side effects [3]. It was noticed in this study that the addition of pethidine (30 mg dose) as adjunct to lidocaine in (IVRA) did not increase the tourniquet tolerance when compared to the lidocaine group because there was no significant difference in the intraoperative fentanyl consumption and intraoperative VAS scores for the tourniquet pain between the two groups. In both groups the tourniquet pain increased significantly between 30 and 45 min period. This is in correlation with the other studies which suggested that under regional anesthesia, tourniquet pain usually appears about 45 min after inflation and becomes more intense with time [18]. The analgesic consumption for treatment of early postoperative pain was significantly less in group LP compared to group L. The time for the first analgesic requirement was delayed in group LP compared to group L. This signifies that pethidine at a dose 30 mg provides significant postoperative analgesia which goes with a study done by Desai and Santhosh [19].

There were no significant changes in pulse rate, blood pressure and Spo2 between the two groups. The analgesic consumption was not significantly different between 6 and 24 h period after the surgery. Therefore, the addition of pethidine is unlikely to provide significant analgesia beyond 6 hours.

Although in a Scott Reuben's study [20] there was high incidence of side effects in pethidine group, there was no significant difference in the incidence of side effects between the two groups in this study.

All of the 60 patients had successful block. Thus, the success rate was 100%.

In conclusion, the addition of pethidine at a dose 30 mg as adjunct to lidocaine in IVRA provides significantly better postoperative analgesia in the first 6h. However its efficacy in postoperative analgesia is limited beyond 6h. The addition of pethidine does not increase the tourniquet tolerance or the incidence of side effects.

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