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Comparative Study between Continuous Wound Infusion Using Bupivacaine and Bupivacaine with Dexmedetomidine on Postoperative Analgesia after Inguinal Hernia Repair

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Abstract: Background: A single dose of local anesthetic injection is vulnerable to wear off for several minutes or hours depending on the medication and dose used. The purpose of this research is to evaluate the effectiveness of adding dexmedetomidine to bupivacaine wound infusion on postoperative pain and the analgesics required in repair of open inguinal hernia (OIH). **Materials and Methods:** A double-blind randomized controlled study was done on 75 patients aged 18 to 60, both sexes, scheduled for repair of primary OIH. Patients have been randomly distributed in 3 groups (25 in each) received 2 mL / h of continuous wound infusion; Group I (Control Group): 48 mL of normal saline; group II: 48 mL of bupivacaine 0.25%; and group III: 48 mL (bupivacaine 0.25%, and dexmedetomidine 0.8-1 µg / kg). **Results:** Heart rate showed significant increase in group I compared to group II and III at ½ and 1h postoperatively and in group I compared to group III at 3h postoperatively. Mean arterial blood pressure showed insignificant difference at all times of recording postoperatively. Visual analogue scale showed significant increase in group I compared to group III at ½ h postoperatively, in group I compared to group II and III at 1, 3, 6 and 12h postoperatively. The postoperative consumption of pethidine in group I showed significant increase compared to group II and in group II when compared to group III. There was insignificant difference in postoperative adverse effects. **Conclusion:** Addition of dexmedetomidine to bupivacaine in continuous wound infusion technique after open inguinal hernia significantly reduced postoperative pain and demand for rescue analgesics, as compared to that in the group received bupivacaine alone with insignificant side effects.
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Keywords: Continuous wound infusion, bupivacaine, dexmedetomidine, postoperative analgesia, inguinal hernia repair.

1. Introduction:

During the post-operative period, pain management remains a major concern. Pain affects many systems, involving cardiac, respiratory and metabolic systems and can therefore affect surgical results. [1, 2]

Surgery almost invariably causes tissue damage that leads to pain. It is well-known that inappropriate pain relief has a delayed mobilization related complications, psychological distress and anxiety. [3]

Despite major advances in surgical procedures that minimize structural disruption and interrelated incisional pain. Patient readmission after outpatient operation is most commonly due to post-discharge pain. [4, 5]

Epidural analgesics and intravenous opioid analgesics are the most frequently employed analgesic strategies for pain relief by patient-controlled delivery systems. Epidural anesthesia is unfortunately more complex procedure with potential risks. [6]

Opioids are best effective medications for both acute and chronic pain, but their widespread use is hindered by side effects such as respiratory exhaustion, nausea, constipation, dependence and tolerance. [7, 8]

A single dose of local anesthetic (LA) injection is vulnerable to wear off for several minutes or hours depending on the medication and dose used. [9]

Dexmedetomidine is a selective α2-adrenoceptor agonist that is used as a sedative or anesthetic adjuvant. Past experiments have shown that dexmedetomidine has a synergistic relationship with LA. [10]

The purpose of this research is to evaluate the effectiveness of adding dexmedetomidine to bupivacaine wound infusion on postoperative pain and the analgesics required in repair of open inguinal hernia (OIH).

2. Subjects and Methods:

This double-blind randomized controlled study was performed on 75 patients aged 18 to 60 years, both sexes, which are scheduled for the elective primary OIH repair, following the acceptance of the Tanta Faculty of Medicine Ethics Committee (number 2227/12/13). A code number for each patient was used, names and addresses symbols stored in a separate register, we mask the identities of patients when we use the study and only used the findings for scientific purposes.

Exclusion conditions included: history of cardiac disease, impaired renal or hepatic function, coagulation problems, α-methyldopa-treated hypertensive patients, clonidine or β adrenergic antagonist, opioid or non-opioid analgesics within the last 72hours.

A medical and surgical history has been assessed for each patient and a clinical examination has been performed. Routine laboratory investigations included a complete blood picture, prothrombin time and activity, and liver and renal function tests.

An intravenous (IV) line with 18 G cannula was established. Heart Rate Monitoring (HR) of 5 leads ECG, non-invasive blood pressure and pulse oximetry of the peripheral oxygen saturation (SpO_2). Fluid crystalloid has been delivered.

Anesthesia was started with morphine 1 µg / kg and propofol 2 mg / kg after a preoxygenation of 100% O_2 for 3-5 minutes. Ventilation was continued through an appropriate size laryngeal mask and facilitated atracurium 0.5 mg / kg with a end tidal CO_2 between 32 and 35 mmHg. The maintenance of anesthesia was obtained by 1.5–2 percent isoflurane with oxygen and 0.1 mg / kg atracurium as increments.

A multi-orifice epidural catheter was inserted between the mesh and external oblique aponeurosis after the operative repair of the inguinal hernia and before the wound was closed, brought out through a separate stab wound laterally and then connected to a pump electrical device to be withdrawn after 24 hours.

Following skin closure, the pump was activated immediately and placed in a carry pouch for ease of ambulation. Patients were then transferred to post anesthetic care unit.

Individuals were divided equally in three groups (each of 25 individuals). Randomization was done by sealed envelope technique. Group I: Control group (C): received continuous wound infusion postoperatively 2mL/h from 48mL normal saline. Group II: Bupivacaine group (B): received continuous wound infusion postoperatively with 2 mL/h 0.25% bupivacaine from 48 mL solution prepared by adding 24 mL 0.5% bupivacaine to 24 mL normal saline. Group III: Bupivacaine Dexmedetomidine group (BD): received continuous wound infusion postoperatively with 2 mL/h from 48 mL solution which contains 0.25% bupivacaine and 0.8-1 µg/kg dexmedetomidine prepared by adding 8 mL dexmedetomidine (1600µg) and 24 mL 0.5% bupivacaine to 16 mL normal saline.

Patients were evaluated at 0.5, 1, 3, 6, 12 and 24 h after removal of laryngeal mask with the following measurements: mean arterial blood pressure (MAP), HR, visual analogue pain scale (VAS). Rescue analgesia (IV Pethidine 10mg) was given when VAS was ≥4 and could be repeated after 10-15 minutes with maximum dose 30 mg/h.

Adverse events (postoperative nausea and vomiting, sedation, toxicity or infection 10 days after the operation) were recorded.

Statistical analysis:

Statistical analysis was conducted by SPSS v20 (IBM ©, Chicago, IL, USA). Quantitative variables have been provided as a mean and standard deviation (SD) and were compared by ANOVA (F) test with post hoc test if significant. Qualitative variables were provided as numbers and percentages and compared with the Chi-square (X^2) test. Statistical significance was at P value <0.05.

3. Results

There was no significance difference in demographic data (age, weight and height) among the three groups [Table (1)].

As regards HR, there was insignificant difference at pre-induction, 6, 12 and 24h postoperatively among the three groups. At ½ and 1h postoperatively, the mean value of heart rate in group I shows significant increase when compared to group II and group III. At 3h postoperatively, the mean value of heart rate in group I shows significant increase when compared to group III. [Figure (1)]

As regards MAP, there was insignificant difference at all times of recording postoperatively among the three groups. [Figure (2)]

At ½ h postoperatively, the mean value of pain score in group I showed significant increase when compared to group III. At 1, 3, 6 and 12h postoperatively, the mean value of pain score in group I showed significant increase when compared to group II and group III. There was also significant increase in pain score in group II when compared to group III. At 24h postoperatively, the mean value of pain score in group I showed significant increase when compared to

group II and group III, but there was insignificant increase in pain score in group II when compared to group III. [Table (2)]

The postoperative consumption of pethidine in group I showed significant increase when compared to group II and in group II when compared to group III. [Table (3)]

There was insignificant difference in postoperative adverse effects in the three groups. [Table (4)]

Table (1): Patient characteristics in the three groups

		Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	ANOVA	
					F	P value
Age (year)	**Range**	20-55	18-52	19-56	0.302	0.740
	Mean ± SD	36.48±10.7	34.84±11.	37.28±12.		
Weight (kg)	**Range**	55-82	59-84	54-86	0.072	0.931
	Mean ± SD	72.60±6.95	72.84±6.61	72.08±8.14		
Height (cm)	**Range**	161-179	156-182	155-183	0.120	0.887
	Mean ± SD	170.68±5.57	170.76±7.02	171.52±7.32		

Table (2): Postoperative visual analogue scale (VAS) of the three groups.

Time	VAS									ANOVA				
	Group I (n = 25)			Group II (n = 25)			Group III (n = 25)							
	Mean	±	SD	Mean	±	SD	Mean	±	SD	F	P-value	P1	P2	P3
½h	4.64	±	0.76	4.16	±	0.85	3.64	±	0.64	11.014	<0.001*	0.069	<0.001*	0.045*
1h	4.12	±	0.60	3.40	±	0.58	2.76	±	0.66	27.453	<0.001*	<0.001*	<0.001*	0.004*
3h	3.60	±	0.50	2.76	±	0.66	2.20	±	0.41	43.471	<0.001*	<0.001*	<0.001*	0.001*
6h	2.76	±	0.52	2.32	±	0.75	1.56	±	0.58	20.576	<0.001*	<0.001*	<0.001*	0.001*
12h	1.96	±	0.35	1.32	±	0.63	0.80	±	0.50	33.026	<0.001*	<0.001*	<0.001*	0.001*
24h	1.40	±	0.65	0.76	±	0.63	0.44	±	0.51	16.096	<0.001*	0.001*	<0.001*	0.159

* P <0.05 denotes statistical significance, P1: comparison between group I and group II, P2: comparison between group I and group III, P3: comparison between group II and group III

Table (3): Postoperative consumption of rescue analgesic (Pethidine) in the three groups.

Dose	Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	ANOVA or chi-square				
				Test value	P-value	P1	P2	P3
Total pethidine consumption (mg)	87.60±20.82	42.50±23.14	23.33±11.75	F=56.33	<0.001*	<0.001*	<0.001*	0.018*
Patients requiring pethidine	25(100%)	19(76%)	15(60%)	X2=12.076	0.002*			

Data are expressed in mean ± SD or number (percentage) * P <0.05 denotes statistical significance, P1: comparison between group I and group II, P2: comparison between group I and group III, P3: comparison between group II and group III

Table (4): Adverse effects in the three groups.

	Group I (n = 25)		Group II (n = 25)		Group III (n = 25)		Chi-square	
	N	%	N	%	N	%	X2	P-value
Nausea	6	24%	5	20%	3	12%	1.230	0.540
Vomiting	3	12%	1	4%	1	4%	1.714	0.424
Sedation	-	0%	-	0%	-	0%	-	-
Neurotoxicity or Cardiotoxicity	-	0%	-	0%	-	0%	-	-
Local inflammation or infection	2	8%	-	0%	1	4%	2.083	0.352

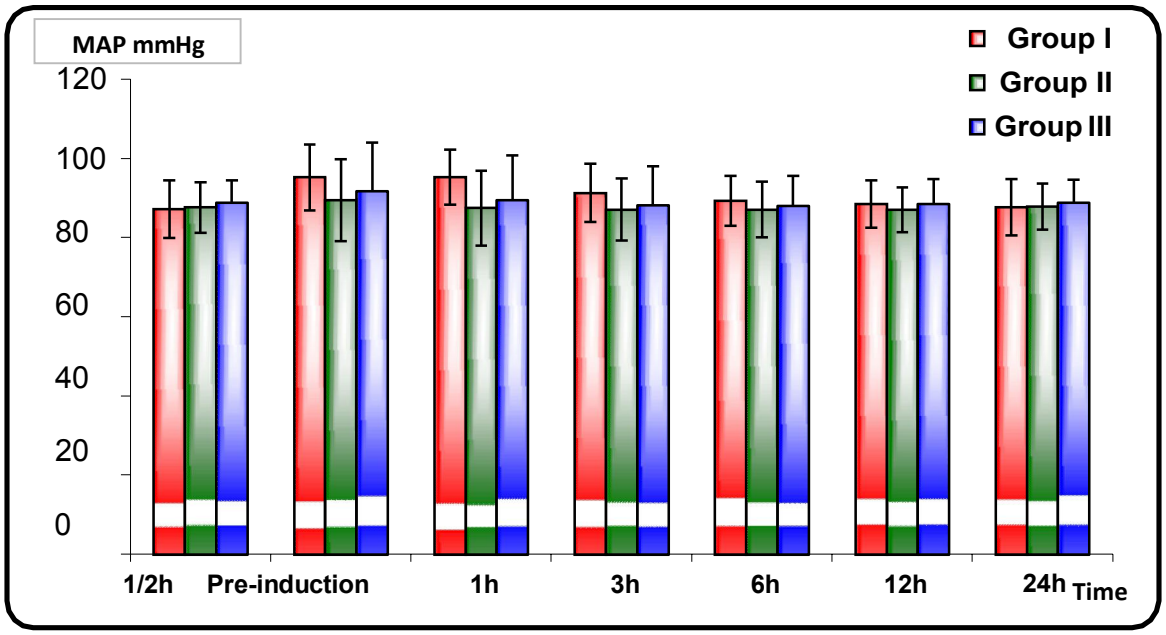

Figure (1): Postoperative mean arterial blood pressure (MAP) of the three groups.

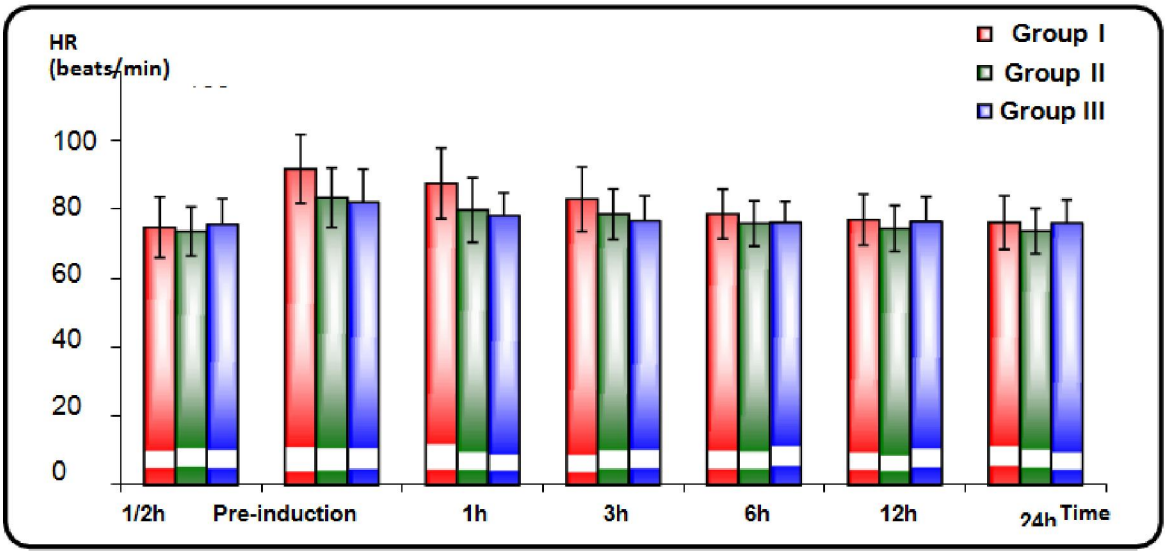

Figure (2): Postoperative heart rate (HR) in the three groups

4. Discussion

In response to a growing postoperative demand for early discharge, attempts have also increased to create anesthetic agents with more efficient recovery profiles and to reduce immediate postoperative symptoms (nausea, emesis, dizziness, exhaustion and headache). In addition to the acute postoperative complications, the treatment of postoperative pain remains an important issue to patient tolerance and an essential challenge for anesthesiologists and surgeons. [4]

The use of LA (continually pumped into the wound site with a pump) increases the analgesia, treats discomfort immediately and prevents systemic analgesics' side effects. [9]

The main findings of the study revealed that there is evidence of a significant decrease in post-operative pain and the demand for rescue analgesics by adding dexmedetomidine to bupivacaine in compare to bupivacaine alone with no significant increase in secondary effects.

This was in agreement with Mohamed et al [11] who showed that dexmedetomidine added to bupivacaine, in local wound infiltration of patients had undergone total abdominal hysterectomy, had the advantages of opioid-sparing effect, increased time of

first rescue analgesia, and decreased postoperative stress response.

Also, the prospective double blind study done by Kanazi GE et al. found that dexmedetomidine of 3 µg and clonidine 30 µg had equipotent block effects without any hemodynamic instability or sedation when investigating the impact of the application of dexmedetomidine in patients with transurethral prostate or bladder tumor on the characteristics of the bupivacaine spinal block.[12]

Gupta et al who contrasted intrathecal 5µg dexmedetomidine and 25µg fentanyl as adjuvants to 12.5 mg of hyperbaric bupivacaine in lower-abdominal surgery patients, have shown intraoperatively hemodynamic stability in patients of both groups. [13]

In contrast, Arya et al. studied the efficacy of various doses of intrathecal dexmedetomidine in 60 female patients planned for hysterectomy as an adjuvant to bupivacaine. It showed a significant drop in hemodynamics and a longer time in patients with higher dose of dexmedetomidine. [14]

In agreement, Kang showed that, in patients with inguinal herniorrhaphy in comparison with the group treated with mere ropivacaine infiltration, the addition of dexmedetomidine to ropivacaine infiltration significantly reduces postoperative pain and fentanyl intake. [10]

Al-Ghanem et al. also found that, in women experiencing vaginal re-constructive surgery, 5 µg dexmedetomidine as an additive to 10 mg bupivacaine created a prolongation of motor and sensory block in contrast with 25 µg of fentanyl as an additive. [15]

In the research, Ammar also observed that the application of dexmedetomidine to bupivacaine during ultrasonic single-injection infraclavicular plexus blockage improves sensory and motor blockage, extended analgesia and decreases sensory and motor blocks in patients who underwent upper limb surgery.[16]

Cheong et al. have observed that direct continuous wound infusion of bupivacaine 0.5 percent is as successful in postoperative pain relief during laparotomy as morphine PCA [17]

However, Rackelboom et al. observed that constant infusion of wound underneath the fascia resulted in significantly reduced rest and overall post-operative morphine intake compared with wound administration above the fascia. [18]

In contrast, Schurr et al. concluded that continuous infusion of LA with inguinal herniorrhaphy results in modest pain improvement and functional results as compared to placebo. However, the effects are limited to only the first day after the operation. [19]

In Magnano et al. also concluded that infiltration with bupivacaine followed by a 36-hour continuous subcutaneous infusion did not appear either to lower post-operative pain or to reduce ventilation times after median sternotomy [20]

Al‐Metwalli et al., which examined the effectiveness of intraarticular dexmedetomidine on postoperative analgesics during arthroscopic knee surgery and stated that there were no variations in the frequency of nausea and vomiting between the groups. [21]

Also, Brummett et al. studied perineural dexmedetomidine addition to ropivacaine and revealed that dexmedetomidine caused no significant perineural inflammation. [22]

Konakci et al., against this research, reported that dexmedetomidine has no motor or sensory effects but can harm the sheath of myelin when provided via the pathway. [23]

Conclusion

Addition of dexmedetomidine to bupivacaine in continuous wound infusion technique after open inguinal hernia significantly reduced postoperative pain and demand for rescue analgesics, as compared to that in the group received bupivacaine alone with insignificant side effects.

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