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" *Assessment of the Impact of Two Dexmedetomidine Dosages Added with Bupivacaine in Ultrasound-Guided Transversus Abdominis Plane Block for Postoperative Analgesia Following Inguinal Hernia Repair: A Randomized double-blind Study*"

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ABSTRACT:

Background: Open surgery for inguinal hernia is a frequently executed technique that may result in significant postoperative pain. The transversus abdominis plane (TAP) block is extensively employed as a component of a multimodal analgesic strategy to manage this discomfort. This study aimed to assess the effectiveness of two dosages of dexmedetomidine (0.5 µg/kg and 1 µg/kg) combined with isobaric bupivacaine in transversus abdominis plane blocks for analgesia after unilateral inguinal hernia surgery.

Methods: One hundred individuals slated for elective spinal anesthesia-based unilateral inguinal hernia surgeries participated in this study. Two groups of fifty participants each were randomly assigned. Group D1 was given a TAP block that included 0.5 µg/kg of dexmedetomidine and bupivacaine, while Group D2 had the same block but with an increased dosage of 1 µg/kg of dexmedetomidine.

Results: The results indicated a substantial decrease in Visual Analogue Scale (VAS) pain scores for Group D2 relative to Group D1, both at rest and during movement, at the 6- and 12-hour intervals. Moreover, patients in Group D2 necessitated reduced postoperative analgesics, encompassing both paracetamol and ketorolac, and exhibited an extended duration prior to requiring the initial dosage of analgesics in comparison to Group D1.

Conclusion: The combination therapy of 1 µg/kg dexmedetomidine with isobaric bupivacaine demonstrated enhanced analgesic efficacy relative to 0.5 µg/kg, evidenced by prolonged TAP block duration, diminished postoperative VAS scores during both movement and rest, and decreased analgesic requirements. The advantages were observed without any adverse effects, save from an increased incidence of bradycardia in the 1 µg/kg group.

Key words: TAP block, Dexmedetomidine, inguinal hernioplasty.

Introduction:

One of the most frequently performed surgical procedures worldwide is the repair of an open inguinal hernia, with a postoperative pain severity of moderate to severe affecting over 60% of patients [(1)].

Post-surgical analgesia frequently employs a multifaceted approach, incorporating oral pharmacotherapy and regional anesthetic procedures. Opioids are a conventional option for postoperative pain management; nevertheless, their administration is linked to adverse effects such as nausea, vomiting, sleepiness, pruritus, and respiratory depression, which may impede the recovery process. Non-opioid alternatives, however, can improve patient rehabilitation and overall outcomes. The Transversus Abdominis Plane (TAP) block efficiently reduces early postoperative discomfort and decreases narcotic usage, which is a significant advantage for patients undergoing inguinal hernia repair. To alleviate pain in the abdominal wall muscles, peritoneum, and skin, this treatment involves administering a local anesthetic into the space between the transversus abdominis and internal oblique muscles. [(2)]

These local anesthetics affect the T7–T11 intercostal nerves, as well as the subcostal (T12), ilioinguinal, and iliohypogastric (L1–L2) nerves [(3)]. Ultrasound guidance improves the precision of the TAP block, which can be executed using many procedures, including posterior, subcostal, lateral, and oblique subcostal approaches. Meta-analytical evidence suggests that the posterior TAP block may yield prolonged analgesia relative to the lateral technique [(4)].

Adjunctive drugs employed in single-shot peripheral nerve blocks (PNB), including NSAIDs, α2 agonists, dexamethasone, and midazolam, aim to prolong the duration of local anesthetics while mitigating dosage-dependent side effects. [(5)]

The sympatholytic activity is caused by dexmedetomidine, an α2 adrenergic receptor agonist that selectively inhibits the release of noradrenaline at both the central and peripheral sympathetic nerve terminals. Its moderate analgesic effects, soothing effects, and low toxicity profile make it a desirable substance [(6)]. Studies indicate that incorporating dexmedetomidine with bupivacaine in a TAP block may prolong its analgesic duration; however, the optimal dosage of dexmedetomidine for this use remains undetermined. [(7,8,9)]

The purpose of this study was to evaluate the analgesic efficacy of two doses of dexmedetomidine, administered at 1 µg/kg and 0.5 µg/kg, in conjunction with isobaric bupivacaine in a TAP block for the purpose of reducing post-operative pain after inguinal hernia repair surgery.

Materials and methods:

Study design and participants

Participants in this randomized, double-blind trial at the Egyptian Liver Hospital were Scheduled for unilateral inguinal hernioplasty under spinal anesthesia between 15 January 2024 and 15 November 2024. The Institutional Review Board (IRB) has given its approval (CT2023-010) and registration of clinicaltrials.gov (ID: NCT06703229). Following the guidelines laid out by the Declaration of Helsinki, the study was carried out. Written informed permission was obtained from all individuals.

The inclusion criteria comprised patients aged 18 to 60 years, of both genders, with ASA physical status I or II, scheduled for elective unilateral inguinal hernioplasty under spinal anesthesia. Exclusion criteria comprised patient refusal, BMI $\geq$ 40 kg/m², incapacity to engage in pain assessment, contraindications to spinal anesthesia (e.g., coagulopathy, skin infection), and allergy to the research medications.

Randomization and masking

One hundred patients participated in this randomized double-blind trial; using sealed envelope and computer-generated randomization, they were split evenly into two groups of fifty. The first group, D1, had a TAP block that included 0.5 µg/kg of dexmedetomidine and isobaric bupivacaine, while the second group, D2, received the same block but with 1 µg/kg of dexmedetomidine. An independent researcher formulated the study drugs. The anesthesiologist unsealed the envelopes just before the injection, while the data collector remained unaware of the research details.

Procedure

Before surgery, patients received information about spinal anesthesia, the TAP block, and the application of the visual analogue scale (VAS) for pain evaluation in the preoperative context. Upon entering the operation room, an 18-gauge intravenous catheter was placed, and 500 mL of acetated Ringer's solution was infused. A standard monitoring apparatus, comprising pulse oximetry, electrocardiography, and noninvasive blood pressure assessment, was utilized. Spinal anesthesia was subsequently administered under aseptic conditions at the L3-L4 or L4-L5 intervertebral area via a 25-gauge needle, involving the administration of 15 mg of hyperbaric bupivacaine 0.5% (3 mL) and 20 mcg of fentanyl. Surgery began upon reaching a sensory level of T6.

After skin closure and dressing application, a unilateral posterior TAP block was administered by an anesthesiologist, uninvolved in data collection or injectate preparation, utilizing ultrasound guidance while the

patient was supine. In the D1 group, patients were administered 20 mL of 0.375% isobaric bupivacaine with 0.5 mcg/kg of dexmedetomidine. Patients in the D2 group received 20 mL of 0.375% isobaric bupivacaine with 1 µg/kg of dexmedetomidine.

The patient was positioned supine, and the side for the block was elevated slightly by placing a cushion under the hip. A curved array transducer (2-5 MHz, SonoAceR3®□, Samsung Madison) was placed transversely between the costal border and the iliac crest along the anterior axillary line. The transducer was subsequently repositioned laterally to examine the external oblique, internal oblique, and transversus abdominis muscles. Modifications were implemented to elucidate the posterior features of these three muscles. A 22-gauge spinal needle was placed from medial to lateral in relation to the probe. Following the confirmation of negative aspiration, 20 mL of the injectate was administered under direct ultrasound guidance into the fascial plane between the internal oblique and transversus abdominis muscles, producing a hypoechoic separation.[10].

Patients were relocated to the Post Anesthesia Care Unit (PACU), where postoperative pain was assessed via the Visual Analogue Scale (VAS) at rest and during movement (hip flexion) at 1, 6, 12, and 24 hours post-surgery. Patients with a VAS score of ≥ 4 were administered 30 mg of ketorolac (1 ampoule) and 1 g of paracetamol (1 vial), with supplementary doses provided every 6 hours as required. If pain continued for 1 hour following the final administration of ketorolac and paracetamol, and the VAS score was > 4, 2 mg boluses of morphine were administered. The duration until the initial analgesic request and the aggregate use of paracetamol vials, ketorolac ampoules, and morphine throughout the first 24 hours were documented.

Postoperative complications occurring during the first 24 hours were documented, including vomiting (treated with 10 mg of intravenous metoclopramide) and bradycardia (defined as a heart rate <50 beats per minute, handled with intravenous atropine in 0.01 mg/kg increments), hypotension (defined as a >20% decrease in mean arterial pressure from baseline, addressed with intravenous fluids and/or ephedrine 0.1 mg/kg), and pruritus, as reported by the patient at any time.

The principal outcome assessed was the duration until the initial request for analgesia post-surgery. The secondary outcomes encompassed the total quantity of analgesics administered (ketorolac, paracetamol, and morphine) within the initial 24 hours. Pain levels, measured using the Visual Analogue Scale (VAS), were evaluated at rest and during movement at many intervals following surgery (1, 6, 12, and 24 hours). The study also observed postoperative complications, such as emesis, hypotension, bradycardia, and pruritus.

Sample size justification

Data used to determine the sample size came from research by Madangopal et al., [11]. The time until the first need for analgesics acted as the base line. A minimum of 43 patients per group is required for each trial to meet the 90% power and 5% significance levels. To guarantee a small margin of error, one hundred patients were included, with fifty in each group.

Statistical analysis

The data were analyzed using SPSS, version 24 for Windows, which stands for the Statistical Package for the Social Sciences. At first, we used the one-sample Kolmogorov-Smirnov test to see if the data was normal. Frequencies and percentages were used to display data for categorical variables. Fisher's exact test was used when the anticipated frequency in any cell was below 5. Chi-square tested categorical variables. Continuous data for regularly distributed variables is expressed as mean ± SD, while non-normally distributed variables are stated as median (range). The Mann-Whitney U test was utilized for non-parametric data analysis, whilst independent t-tests were used for parametric group comparisons. We regarded a p-value of less than 0.05 to be statistically significant. There is more evidence to reject the null hypothesis when the p-value decreases.

Results:

This prospective, randomized, double-blind trial included 100 participants, aged 18 to 60 years, all of whom were slated for elective inguinal hernioplasty under spinal anesthesia. The study design conformed to the CONSORT principles, as depicted in Figure 1. Recruitment concluded upon reaching the predetermined sample size established through power calculations.

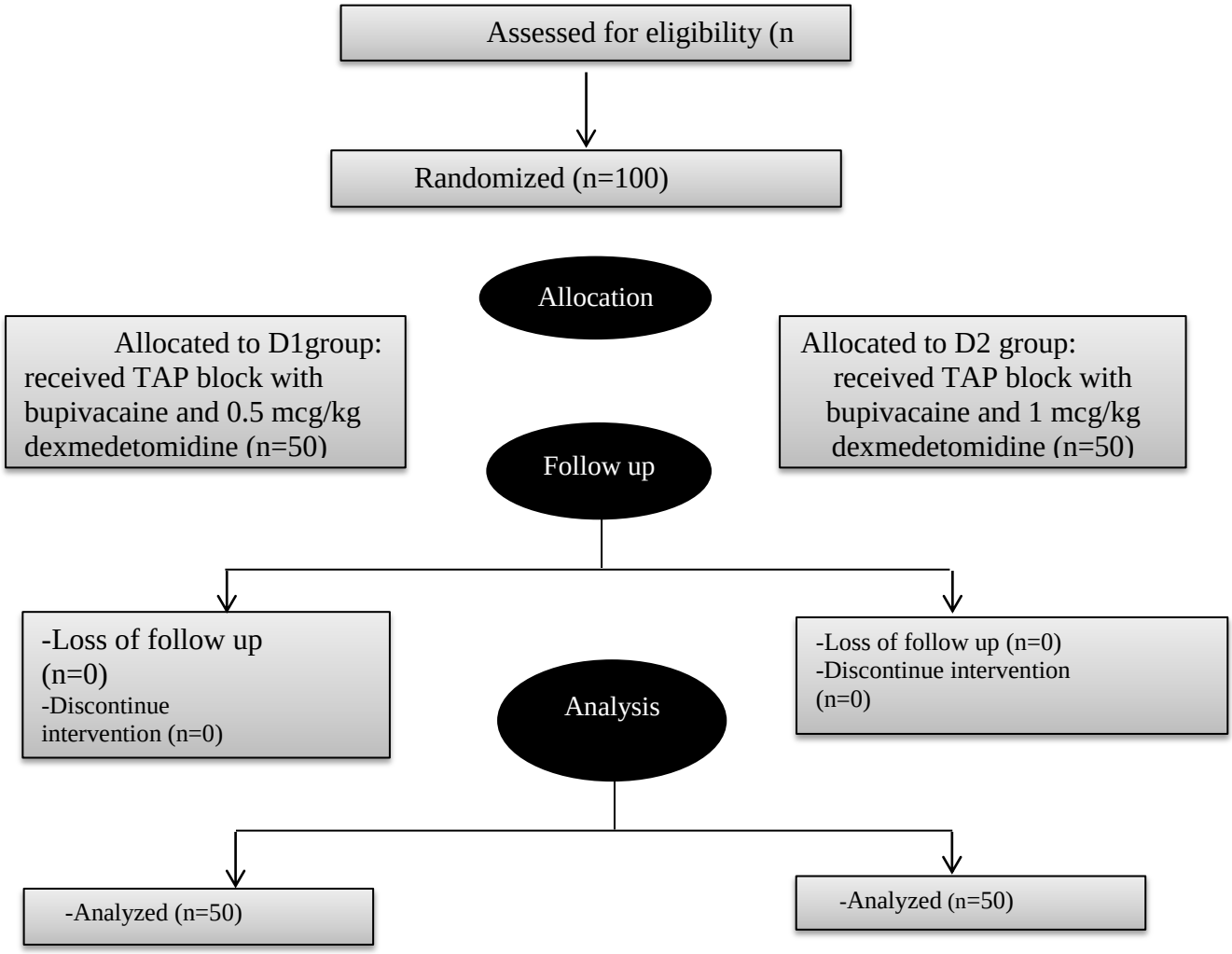

Figure (1): CONSORT (Consolidated Standards of Reporting Trials) 2010 flow diagram illustrating the sequential phases of the trial. Transversus Abdominis Plane (TAP)

No notable disparities were detected between the two groups either patient characteristics or the duration of the surgical process (see Table 1, Figure 2). Group D2 exhibited a significant decrease in the quantity for postoperative analgesia (including paracetamol and ketorolac) and an extension in the interval before the initial request for analgesics, in contrast to group D1 (see Table 2, Figure 3). Furthermore, morphine was unnecessary within the initial 24 hours post-surgery in both groups.

The postoperative Visual Analogue Scale (VAS) scores (refer to Table 3, Figure 4) after 6 and 12 hours were markedly reduced in group D2, both at rest and during movement, in comparison to group D1. No notable changes were seen between the two groups concerning pruritus or postoperative hypotension (refer to Table 4, Figure 5). Nonetheless, group D2 had a significantly elevated incidence of bradycardia (refer to Table 4, Figure 5). Additionally, two patients in group D1 exhibited postoperative vomiting (refer to Table 4, Figure 5).

Discussion:

This randomized double-blind research demonstrated that the incorporation of 1 mcg/kg of dexmedetomidine with bupivacaine in the posterior TAP block for inguinal hernioplasty markedly enhanced postoperative analgesia relative to the 0.5 mcg/kg dosage. The increased dosage of dexmedetomidine led to an extended duration of analgesia (prolonging the interval until the initial analgesic request), diminished the total requirement for analgesics (paracetamol and ketorolac), and resulted in decreased postoperative VAS scores. The postoperative adverse effects were basically similar across the two groups; however, the incidence of bradycardia was significantly elevated in the group administered 1 mcg/kg of dexmedetomidine.

Multiple studies demonstrate that the incorporation of dexmedetomidine with bupivacaine in transversus abdominis plane (TAP) blocks enhances postoperative analgesia and local anesthesia, without significant adverse effects. [7, 8, 9, 12] Nevertheless, a study conducted by Ozalp et al. [13] revealed no advantage in incorporating dexmedetomidine with ropivacaine in interscalene blocks. Ding et al. [14] similarly found that the addition of dexmedetomidine to ropivacaine in TAP blocks after gastrectomy did not result in any significant enhancement in the length or quality of the block.

Consistent with our findings, Almarakbi and Kaki [15] revealed that patients administered 0.25% bupivacaine in conjunction with 0.5 mcg/kg of dexmedetomidine exhibited a markedly prolonged duration until the initial request for analgesia (470 vs. 280 minutes, $P < 0.001$) and utilized less morphine in the first 24 hours (19 vs. 29 mg, $P < 0.001$) compared to those receiving bupivacaine alone in bilateral TAP blocks for abdominal hysterectomy. Talebi et al. [7] noted that incorporating 1 mcg/kg of dexmedetomidine into bupivacaine for TAP blocks during elective open inguinal herniorrhaphy under spinal anesthesia led to diminished postoperative pain management requirements and an extended analgesic duration (surpassing 8 hours) in contrast to the 0.5 mcg/kg dosage.

Consistent with our findings, Ghobara et al. [16] performed research comparing two cohorts of 30 women who underwent bilateral ultrasound-guided TAP blocks after cesarean delivery. Group 1 was administered 20 mL of 0.25% bupivacaine mixed with 2 mL of saline, whereas group 2 received the identical bupivacaine formulation supplemented with 1 µg/kg of dexmedetomidine diluted in 2 mL of saline. A considerable disparity in VAS values was seen between the two groups, with group 2 indicating markedly lower pain scores from 10 to 24 hours postoperatively. According to Madangopal et al., [11] compared to the group that received 0.25 µg/kg dexmedetomidine, the one that received 0.5 µg/kg dexmedetomidine in TAP blocks for elective unilateral inguinal hernia repair had significantly lower VAS scores from 2 to 6 hours post-surgery.

The findings of our study align with those of Varshney et al. [8], who examined the application of levobupivacaine in conjunction with 1.0 µg/kg dexmedetomidine in TAP blocks for patients undergoing cesarean sections. Their research revealed markedly improved patient satisfaction and substantially reduced VAS scores, both at rest and during movement, at 6, 12, and 24 hours post-surgery, in comparison to patients who got only levobupivacaine.

Conversely, Qin et al. [17] discovered that the addition of 1.0 µg/kg of dexmedetomidine to ropivacaine during laparoscopic gynecological procedures resulted in a markedly increased incidence of bradycardia and a higher utilization of atropine, particularly in comparison to the lower doses of 0.25 µg/kg and 0.5 µg/kg ($P < 0.05$).

The exact mechanism by which dexmedetomidine enhances the efficacy of the local anesthetic remains unclear. Firstly, it is believed that the action takes place at the peripheral level. By reducing the local anesthetic's systemic absorption at the injection site, it may extend analgesia through its local vasoconstrictive activity **[18, 19].** Dexmedetomidine is believed to prolong the sensory block rather than the motor block, in contrast to clonidine. This differential sensory motor impact may arise from a greater inhibitory influence on C and Aδ nerve fibers compared to motor neurons **[20, 21].** Dexmedetomidine can sustain the hyperpolarized condition of cells, impede subsequent action potentials by blocking potassium channels, preserve cellular depolarization, and enhance sodium channel inhibition, hence amplifying the efficacy of local anesthetics **[22]**.

The second hypothesized mechanism involves its effect at the spinal cord level. Upon systemic absorption or local diffusion, it binds to α2 receptors in the spinal dorsal horn, thereby reducing the production and reuptake of excitatory neurotransmitters, including substance P and glutamate. Hyperpolarized interneurons suppress the ascending spinal route associated with nociceptive feeling, resulting in analgesia **[23]**. The third hypothesized mechanism pertains to its activity at the supraspinal level. Following systemic absorption, it may disseminate to the cerebrospinal fluid and interact with α2A and α2C adrenergic receptors in the brainstem, inhibit the descending noradrenergic pathway in the medulla, or diminish sympathetic nerve impulses, so producing an analgesic action at the central level **[24]**.

Our study has limitations due to the exclusion of morbidly obese patients (BMI ≥ 40 kg/m²). The viability and efficacy of the TAP block in this cohort remain uncertain, because the degree of sensory blockade and success rate could not be evaluated due to lingering sensory blockade from spinal anesthesia.

Conclusion: The administration of 1 µg/kg dexmedetomidine in conjunction with bupivacaine yielded superior analgesic efficacy compared to the 0.5 µg/kg dosage, evidenced by an extended duration of the TAP block, diminished pain levels (VAS ratings) at rest and during movement, and a reduced requirement for

postoperative analgesics. The enhancements were realized with little adverse effects, however there was a markedly elevated occurrence of bradycardia in the 1 µg/kg cohort.

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Conflicts of interest

The authors declare that: they have no conflicts of interest.

Table (1): Demographic data among the studied groups

Demographic data	D1 group (no=50)	D2 group (no=50)	Test of significance	p value
Age (Years) **Mean ± SD**	46.10±8.15	45.88±8.15	t=0.135	0.893
Sex **Male** **Female**	 32 (64.0%) 18 (36.0%)	 28 (56.0%) 22 (44.0%)	χ^2=0.667	0.414
BMI **Mean ± SD**	32.14±4.06	31.31±3.84	t=1.05	0.295
Duration of surgery **Mean ± SD**	58.90±8.28	58.20±10.53	t=0.369	0.713

t: Independent t test, χ^2 : Chi square test

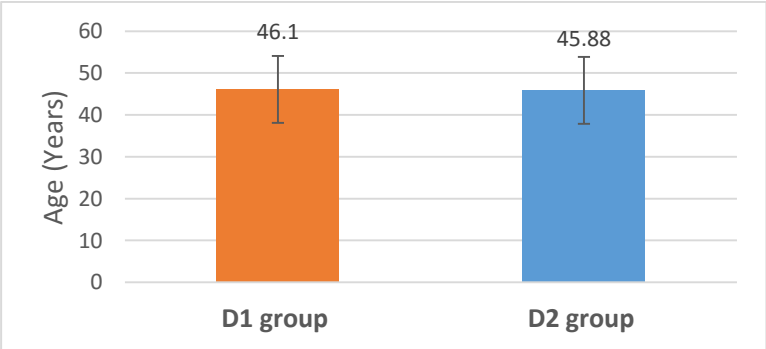

Figure (2): Age distribution among the studied groups

Table (2): Total analgesics and time to first analgesic among the studied groups

	D1 group (no=50)	D2 group (no=50)	Test of significance	p value
Total analgesic ketorolac (ampoule) Median (Min-Max)	2.0 (1.0-3.0)	1.0 (1.0-3.0)	Z=3.26	0.001*
Total analgesic paracetamol (vial) Median (Min-Max)	2.0 (1.0-3.0)	1.0 (1.0-3.0)	Z=3.26	0.001*
Time to first analgesic Mean ± SD	6.62±2.36	9.64±2.73	t=5.90	≤0.001*

Z: Mann Whitney test, t: Independent t test, *significant p≤0.05

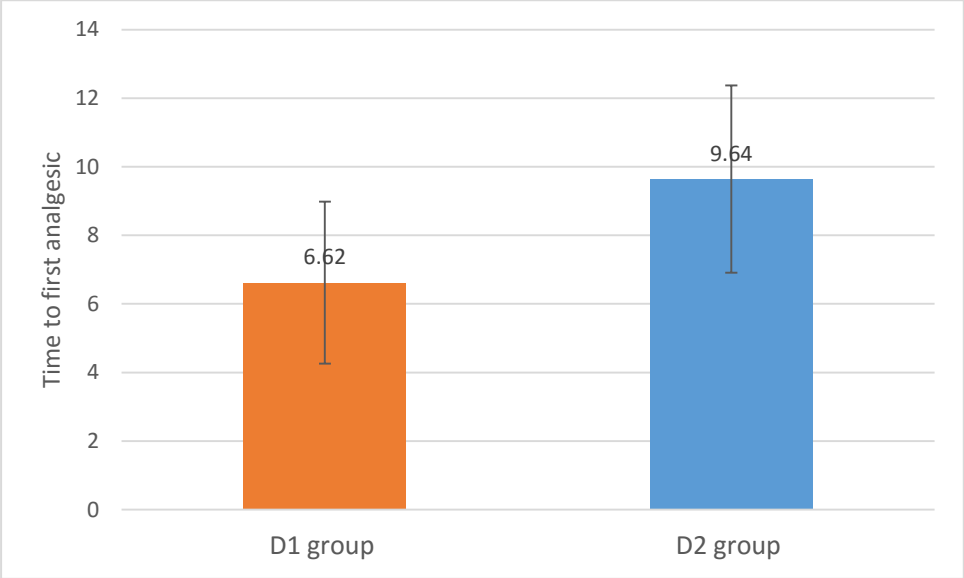

Figure (3): Time to first analgesic among the studied groups

Table (3): Visual analogue scale among the studied groups

VAS		D1 group (no=50)	D2 group (no=50)	Test of significance	p value
Vas 1 hour	R	1.0 (0.0-2.0)	1.0 (0.0-2.0)	Z=1.02	0.308
	M	2.0 (0.0-6.0)	1.0 (0.0-3.0)	Z=1.75	0.081
Vas 6 hour	R	3.0 (1.0-5.0)	1.5 (0.0-6.0)	Z=4.12	≤0.001*
	M	3.5 (2.0-7.0)	2.0 (1.0-7.0)	Z=3.65	≤0.001*
Vas 12 hour	R	3.0 (2.0-6.0)	2.0 (1.0-5.0)	Z=4.11	≤0.001*
	M	4.0 (3.0-6.0)	3.0 (1.0-6.0)	Z=3.74	≤0.001*
Vas 24 hour	R	4.0 (2.0-6.0)	4.0 (2.0-6.0)	Z=1.70	0.089
	M	5.0 (1.0-7.0)	4.0 (2.0-7.0)	Z=0.865	0.387

Data expressed as Median (Min-Max) , Z: Mann Whitney test, *significant p≤0.05, R: Rest, M: Movement

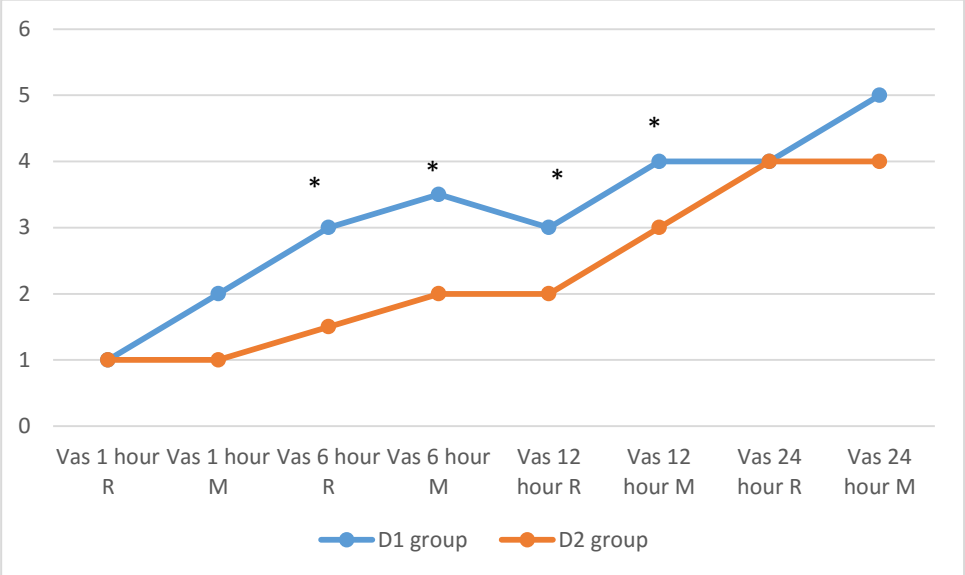

Figure (4): Visual analog scale among the studied groups

Table (4): Side effects among the studied groups

Side effects	D1 group (no=50)	D2 group (no=50)	Test of significance	p value
Hypotension				
Yes	0 (0%)	1 (2.0%)	FET	1.0
No	50 (100%)	49 (98.0%)		
Bradycardia				
Yes	0 (0%)	7 (14.0%)	χ^2=7.53	0.006*
No	50 (100%)	43 (86.0%)		
Pruritus				
Yes	1 (2.0%)	1 (2.0%)	FET	1.0
No	49 (98.0%)	49 (98.0%)		
Vomiting				
Yes	2 (4.0%)	0 (0%)	FET	0.495
No	48 (96.0%)	50 (100%)		

FET: Fisher exact test, χ^2: Chi square test, *significant p≤0.05

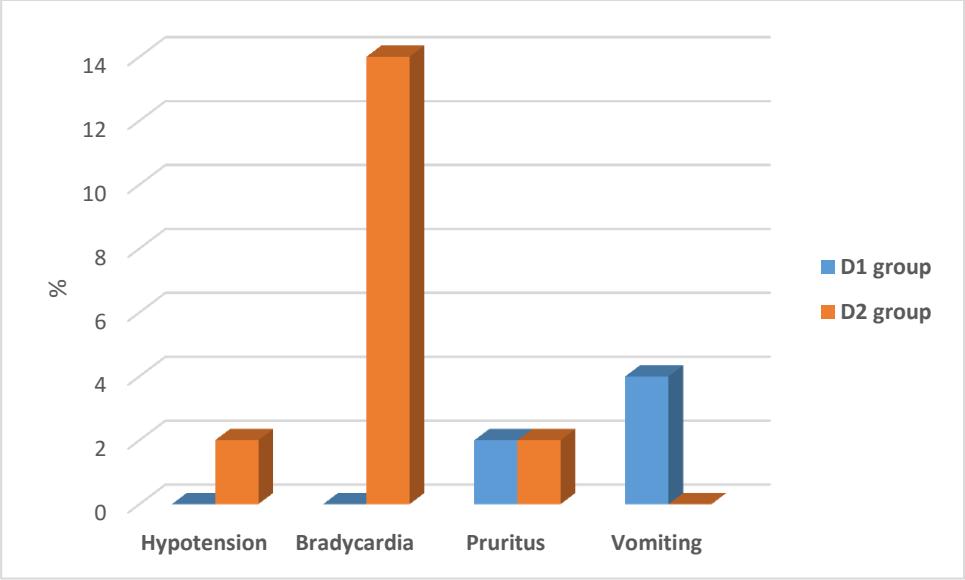

Figure (5): Side effects among the studied groups

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