EGYPTIAN JOURNAL OF ANAESTHESIA
2022, VOL. 38, NO. 1, 373–382
https://doi.org/10.1080/11101849.2022.2092300

Effect of Epidural Dexmedetomidine vs Nalbuphine for Labor Analgesia:A randomized clinical trial

Sanaa M. El Fawal, Reem Hamdy El Kabarity, Nourhan Tarek Fouad Ahmed and Samar M. Abd El Tawab

Anesthesia, Faculty of Medicine, Ain Shams University, Cairo, Egypt

ABSTRACT

Background: The addition of dexmedetomidine or nalbuphine to epidural bupivacaine was tested to decrease labor pain in women undergoing normal delivery.

Patients and Methods: Sixty-four patients were randomly allocated into 2 groups of 32 parturients, each with consent from the parturient. Groups A and B received a bolus of 12 ml volume consisting of 11 ml of 0.25% bupivacaine and 0.5 µg/ml dexmedetomidine (1 ml volume) through the epidural catheter, then a top-up dose of 6 ml volume consisting of 5 ml of 0.25% bupivacaine and 0.5 µg/ml dexmedetomidine (1 ml volume) was given when the VAS score becomes 4 or more, and a bolus of 12 ml volume consisting of 11 ml of 0.25% bupivacaine and 10 mg nalbuphine (1 ml volume) through the epidural and a top-up dose of 5 ml of 0.25% bupivacaine and 2 mg nalbuphine (1 ml volume) were given, respectively. Assessments included the VAS score, vital data monitoring, duration of stages of labor, APGAR score, and adverse effects.

Results: Both groups had satisfactory labor analgesia, but those in the dexmedetomidine group had lower pain scores than those in the nalbuphine group, because dexmedetomidine had a faster onset than nalbuphine.

Conclusion: Epidural dexmedetomidine seems to offer some advantages over epidural nalbuphine. Thus, it can be used safely as an adjuvant to epidural bupivacaine in labor analgesia.

ARTICLE HISTORY
Received 15 April 2022
Revised 12 June 2022
Accepted 16 June 2022

KEYWORDS
Dexmedetomidine; nalbuphine; epidural analgesia; labor pain

1. Introduction

Labor pain often causes a strong stress response. Several inhalation and parenteral anesthetics, sedatives, tranquilizers, and analgesics have been used for pain relief during labor, while over the last decade, lumbar epidural analgesia has greatly increased [1].

Recently, it was concerned by most mothers and doctors that how to alleviate the pain during delivery. The ideal labor analgesia should be based on maternal and child safety and should have a fast-acting good analgesic effect and less adverse reaction [2].

Epidural anesthesia is convenient and has a less adverse reaction and obvious effect in the commonly used analgesic methods, which are widely used in the current way of analgesia [3].

Studies have confirmed the efficacy of dexmedetomidine in prolonging the duration of perineural nerve blocks. Specifically, perineural dexmedetomidine enhances sensory, motor, and analgesic block characteristics. Dexmedetomidine is a selective α_2 receptor agonist and has a sympatholytic, sedative, and opioid-sparing effect. It does not cause respiratory depression and can therefore be used as an adjuvant in certain clinical settings [4].

It has also been proved that dexmedetomidine would not increase the risk of side effects, such as nausea, headache, vomiting, shivering, and hypotension [5].

Nalbuphine is a synthetic agonist-antagonist opioid that has the characteristics of Mu-antagonist and Kappa-agonist activities. Nalbuphine has gained parenteral analgesia for intraoperative, postoperative, and obstetrical uses [6].

The analgesic potency of nalbuphine has been found to be equal to morphine, but unlike morphine, it shows a ceiling effect on respiratory depression. It has the potential to provide effective postoperative analgesia with no risk of respiratory depression [7].

This study was planned to compare epidural dexmedetomidine versus nalbuphine added to bupivacaine in labor analgesia and record the advantage of one over the other.

2. Methods

After research Medical Ethical Committee approval (FMASU MS500/2021) and written informed consent, this randomized comparative clinical study was performed in Obstetrics & Gynecology Ain Shams

CONTACT Samar M. Abd El Tawab dr_sm.md@hotmail.com Anesthesia, Faculty of Medicine, Ain Shams University, Cairo, Egypt

University Hospital, Cairo, Egypt, from September 2021 to February 2022. The trial has been registered with a clinical trial registry that allows free online access to the public (NCT05327088).

Inclusion Criteria: This study enrolled 64 parturients between 21 and 40 years old with the American Society of Anesthesiologists (ASA) physical status I–II undergoing labor, requesting analgesia, and having a normal birth canal. The fetus should be a single full-term fetus (37–42 weeks of gestation) with a normal head position and normal development. All parturients should be at the beginning of the active phase of labor, i.e., cervical dilatation of 4 cm with regular uterine contractions.

Exclusion Criteria: Parturients younger than twenty-one and older than 40 years or with contraindication of regional anesthesia, pre-existing neurological disease, history of allergy to the study drugs, cephalopelvic disproportion, fetal distress, amniotic fluid infection, placental insufficiency, or scarred uterus will be excluded from the study.

All the procedures were performed under the supervision of anesthesia senior staff. All parturients were assessed by taking history and physical examination, and routine preoperative investigations were performed to assess the complete blood count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), liver function tests, kidney function tests, fasting blood sugar, and electrocardiogram (ECG).

All parturients completed the recommended fasting hours (6–8 hrs for solid and 2 hrs for clear fluid). Sixty-four patients were randomly allocated by computer-generated randomization and using opaque sealed envelopes to two groups A (the dexmedetomidine group) and B (the nalbuphine group) with 32 parturients in each group. Patients in Group A (dexmedetomidine group) received a bolus of 12 ml volume consisting of 11 ml of 0.25% bupivacaine and 0.5 µg/ml dexmedetomidine (1 ml volume) through the epidural catheter, and then a top-up dose of 6 ml volume consisting of 5 ml of 0.25% bupivacaine and 0.5 µg/ml dexmedetomidine (1 ml volume) was given when the VAS score becomes four or more. Patients in Group B (Nalbuphine group) received a bolus of 12 ml volume consisting of 11 ml of 0.25% bupivacaine and 10 mg nalbuphine (1 ml volume) through the epidural catheter and then a top-up dose of 5 ml of 0.25% bupivacaine and 2 mg nalbuphine (1 ml volume).

All parturients were routinely checked for blood pressure, pulse and respiratory rate, and fetal heart rate during the first stage of labor every 30 mins. When regular uterine contraction appears and the cervix is dilated about 3 cm, the epidural catheter was placed in the operation room. Parturients were asked about the degree of pain experienced before any analgesia was given, by using a visual analog scale (VAS). All parturients were informed about the Visual Analog Scale and how to use it by the investigators.

The visual analog scale (VAS) is a tool widely used to measure pain. A patient is asked to show her perceived pain intensity along with a 100 mm (10 cm) horizontal line, and this rating is then measured from the left edge (=VAS score). The VAS score correlates well with acute pain levels [8]. Using a ruler, the score is decided by measuring the distance (cm) on the 10-cm line between the "no pain" anchor and the patient's mark, providing a range of scores from 0–10. A higher score shows greater pain intensity.

The monitors (electrocardiography, non-invasive blood pressure, and pulse oximetry) were applied to the parturient on arrival at the operation room. Before epidural placement, an intravenous line (18 G cannula) was secured and all the parturients were preloaded with 10 ml/kg of Ringer lactate solution over 15–20 min.

Parturients were in a sitting position. After cleaning and draping with a sterile sheet, L3-L4 intervertebral space was identified, and skin wheal was raised by a 26-gauge needle with xylocaine 2%. Tuohy needle number 18 was introduced, after 2–3 cm insertion, the stylet was withdrawn, and an air-filled syringe was attached to the hub of the needle. The needle was advanced slowly until the epidural space was identified by the loss of the resistance technique. Then, the epidural catheter was inserted. An epidural test dose of 3 ml of xylocaine 2% was injected through the epidural catheter, and the patient was observed for inadvertent subarachnoid injection [9].

Preparation: A 200 µg dexmedetomidine vial (2 ml volume) was withdrawn in a 50 ml syringe, and 31 ml of normal saline was added to get a concentration of 6 µg/ml. One milliliter was withdrawn from this preparation to get the desirable dexmedetomidine dose and volume for the bolus (6 µg in 1 ml volume). For the top-up dexmedetomidine dose, 0.5 ml was withdrawn and 0.5 ml of normal saline was added to get the desired dose and volume (3 µg in 1 ml volume).

A 10 mg nalbuphine ampule (1 ml volume) was used without dilution for the bolus dose. For the top-up dose, a 10 mg nalbuphine ampule was withdrawn in a 5 ml syringe and 4 ml of normal saline was added to get a concentration of 2 mg/ml. One milliliter was

withdrawn from this preparation to get the desirable top-up nalbuphine dose and volume for the study (2 mg in 1 ml volume).

Eleven milliliters of 0.25% bupivacaine was prepared by adding 5.5 ml of normal saline to 5.5 ml of 0.5% bupivacaine.

Five milliliters of 0.25% bupivacaine was prepared by adding 2.5 ml of normal saline to 2.5 ml of 0.5% bupivacaine.

2.1. Measurements

The patient's demographic and clinical characteristics, including age, ASA classification, and parity, were noted.

Primary outcome: Assessment of pain using the VAS score: visual analog scale "from 0–10, 0 = no pain and 10 = worst pain" was adopted: before analgesia (T0), 30 min after the onset of analgesia (T30), every 30 mins until delivery (T60-Td) and during delivery (Td). The scores of 1–3, 4–7, and 8–10 are mild, moderate, and severe pain, respectively.

Secondary outcomes: (1) The vital signs of the parturient: the heart rate, blood pressure, and oxygen saturation at 30 min before analgesia and 30 min after analgesia and then every 30 min as long as the epidural catheter is inserted. (2) Duration of labor: the active phase of labor at the first stage, second stage, and third stage. (3) Neonatal condition: APGAR scores at 1 and 5 min after the birth. (4) The adverse reactions: itching, nausea, vomiting, bradycardia, hypotension, etc.

All these data were recorded by an assistant who was blinded to the drugs given. Data were collected using a case report form.

2.1.1. Management of possible adverse reactions

Nausea and vomiting were managed by antiemetics (Metoclopramide 10 mg IV over 1–2 mins) [10]. Bradycardia is defined as a drop of heart rate more than 20% of the baseline and was managed by Atropine (0.5–1 mg IV and can be repeated if needed, not to exceed 3 mg) [11]. Hypotension is defined as a drop of blood pressure more than 20% of the baseline and was managed by IV fluids and Ephedrine (5–10 mg IV bolus and, administer additional doses as needed, not to exceed a total cumulative dosage of 50 mg) [12].

2.2. Statistical analysis

Data were collected, revised, coded, and entered into the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations, and ranges when data were parametric, and median and interquartile range (IQR) when data were found nonparametric. Also, qualitative variables were presented as numbers and percentages. The comparison between groups regarding qualitative data was done by using the ***Chi-square test*** and/or ***Fisher exact test*** when the expected count in any cell was found to be less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using an **independent t-test**, while non-parametric distribution was done by using the ***Mann-Whitney test.*** The confidence interval was set to 95%, and the margin of error accepted was set to 5%. So, the p-value was considered significant as follows: P-value > 0.05: nonsignificant (NS); P-value < 0.05: significant (S); and P-value < 0.01: highly significant (HS).

Sample Size: By using the G power program for sample size calculation, setting power at 80% and alpha error at 5%, and after reviewing previous study results [13] assuming a medium effect size difference (0.3) in VAS score for pain between the two groups (epidural dexmedetomidine versus nalbuphine either added to bupivacaine for labor analgesia), a sample size of at least 64 patients undergoing labor (32 patients in each group) was sufficient to achieve the study objective.

3. Results

The analgesic effects of bupivacaine 0.25% in combination with dexmedetomidine (Group A) in comparison to nalbuphine (Group B) in women in labor were studied. After analyzing the data, there were no significant differences in the demographic data between both groups. The demographic data were controlled to avoid any bias or confounding factor in the study. We found out that both groups were satisfied with epidural analgesia, but the parturient in group A (the dexmedetomidine group) had a lower VAS score all over the study than group B (the nalbuphine group) with a significant difference at 30 mins and 60 mins after analgesia. There was no statistically significant difference between the two groups as regard age, ASA classification, and parity as shown in Table 1. There was a significant decrease in VAS score after 30 mins and 60 mins in group A than in group B, denoting delayed onset of nalbuphine more than dexmedetomidine. However, there was no statistically significant difference between the two groups in VAS scores as shown in Tables 2 and 3. There was a significant decrease in heart rate after 30 mins and 60 mins in group A than in group B. However, there was no statistically significant difference between the two groups in heart rate after that as shown in Table 4. There was a significant

Table 1. Comparison between group A and group B of demographic data.

		Group A	Group B			
		No. = 32	No. = 32	Test value	P-value	Sig.
Age (years)	Mean ± SD	28.28 ± 5.34	28.53 ± 5.75	−0.180	0.858	NS
	Range	21 – 40	21 – 40			
ASA	II	32 (100.0%)	32 (100.0%)	–	–	–
Parity	P1	16 (50.0%)	17 (53.1%)	0.063	0.802	NS
	P2	16 (50.0%)	15 (46.9%)			

P-value > 0.05: Nonsignificant

Table 2. Comparison between group A and group B of VAS scores before and after epidural analgesia.

		Group A	Group B			
VAS score		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia (T0)	Median (IQR)	7 (7 – 8)	7 (7 – 8)	−0.962	0.336	NS
	Mean ± SD	7.47 ± 1.16	7.19 ± 0.78			
	Range	5 – 10	6 – 9			
30 min	Median (IQR)	3 (2 – 3)	4 (2 – 6)	−2.431	0.015*	S
	Mean ± SD	2.78 ± 0.91	4.06 ± 2.03			
	Range	1 – 5	1 – 8			
60 min	Median (IQR)	3 (2 – 4)	4 (3 – 5)	−2.284	0.022*	S
	Mean ± SD	3.03 ± 0.97	3.75 ± 1.27			
	Range	1 – 5	1 – 6			
90 min	Median (IQR)	1.5 (1,2)	2 (1 – 2.5)	−1.480	0.139	NS
	Mean ± SD	1.69 ± 0.93	2.25 ± 1.44			
	Range	1 – 5	1 – 5			
120 min	Median (IQR)	3 (2 – 4.5)	4 (3 – 5)	−1.128	0.259	NS
	Mean ± SD	3.25 ± 1.46	3.66 ± 1.15			
	Range	1 – 6	2 – 6			
150 min	Median (IQR)	2 (2,3)	3 (2 – 4)	−1.598	0.110	NS
	Mean ± SD	2.31 ± 1.2	2.84 ± 1.42			
	Range	1 – 6	1 – 6			
180 min	Median (IQR)	2 (2 – 4)	3 (2 – 4)	−1.669	0.095	NS
	Mean ± SD	2.71 ± 1.22	3.3 ± 1.42			
	Range	1 – 5	1 – 6			
210 min	Median (IQR)	3 (2 – 4)	3.5 (3,4)	−1.896	0.058	NS
	Mean ± SD	2.76 ± 1.35	3.46 ± 1.17			
	Range	1 – 5	1 – 5			
240 min	Median (IQR)	2 (1 – 3.5)	3 (1 – 4)	−1.102	0.271	NS
	Mean ± SD	2.33 ± 1.43	2.93 ± 1.67			
	Range	1 – 5	1 – 6			
270 min	Median (IQR)	2 (1 – 4)	3 (2 – 4)	−0.558	0.577	NS
	Mean ± SD	2.67 ± 1.59	2.91 ± 1.22			
	Range	1 – 5	1 – 5			
300 min	Median (IQR)	2 (1 – 4)	3.5 (3,4)	−0.723	0.470	NS
	Mean ± SD	2.7 ± 1.89	3.33 ± 1.37			
	Range	1 – 6	1 – 5			
330 min	Median (IQR)	3 (2 – 4)	3 (1.5 – 4.5)	−0.096	0.923	NS
	Mean ± SD	2.86 ± 1.35	3 ± 1.83			
	Range	1 – 5	1 – 5			
360 min	Median (IQR)	2 (1 – 3)	2 (1 – 4)	−0.289	0.772	NS
	Mean ± SD	2 ± 1.29	2.5 ± 1.91			
	Range	0 – 4	1 – 5			

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; *: Significant

Table 3. Comparison between group A and group B of VAS scores before analgesia, at 30 mins after analgesia and at the time of delivery (Td).

		Group A	Group B			
VAS score		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia (T0)	Median (IQR)	7 (7 – 8)	7 (7 – 8)	−0.962	0.336	NS
	Mean ± SD	7.47 ± 1.16	7.19 ± 0.78			
	Range	5 – 10	6 – 9			
30 min (T30)	Median (IQR)	3 (2 – 3)	4 (2 – 6)	−2.431	0.015*	S
	Mean ± SD	2.78 ± 0.91	4.06 ± 2.03			
	Range	1 – 5	1 – 8			
Time of delivery (Td)	Median (IQR)	2 (1 – 2)	2.5 (1 – 4)	−1.946	0.052	NS
	Mean ± SD	1.94 ± 0.95	2.59 ± 1.34			
	Range	1 – 4	1 – 5			

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; *: Significant

Table 4. Comparison between group A and group B of heart rates before and after epidural analgesia.

		Group A	Group B			
Heart Rate (beats/min)		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia	Mean ± SD	103.28 ± 11.82	99.53 ± 13.58	1.178	0.243	NS
	Range	80 – 130	70 – 130			
30 min	Mean ± SD	70.00 ± 16.21	79.69 ± 12.18	−2.702	0.009**	HS
	Range	40 – 90	50 – 95			
60 min	Mean ± SD	72.66 ± 7.40	78.28 ± 10.37	−2.498	0.015*	S
	Range	60 – 85	65 – 95			
90 min	Mean ± SD	73.75 ± 8.98	71.41 ± 9.61	1.008	0.317	NS
	Range	60 – 90	60 – 90			
120 min	Mean ± SD	75.47 ± 6.76	78.13 ± 10.38	−1.213	0.230	NS
	Range	65 – 85	65 – 100			
150 min	Mean ± SD	75.00 ± 9.07	76.41 ± 7.75	−0.667	0.507	NS
	Range	60 – 95	65 – 90			
180 min	Mean ± SD	79.03 ± 11.43	75.67 ± 11.80	1.132	0.262	NS
	Range	60 – 95	60 – 105			
210 min	Mean ± SD	74.14 ± 8.56	77.50 ± 7.52	−1.539	0.130	NS
	Range	60 – 90	65 – 90			
240 min	Mean ± SD	75.63 ± 10.03	77.00 ± 8.19	−0.445	0.659	NS
	Range	60 – 95	65 – 90			
270 min	Mean ± SD	72.00 ± 9.02	75.50 ± 4.97	−1.114	0.277	NS
	Range	60 – 85	70 – 85			
300 min	Mean ± SD	73.50 ± 6.69	76.67 ± 6.06	−0.948	0.359	NS
	Range	65 – 85	70 – 85			
330 min	Mean ± SD	67.86 ± 9.51	77.50 ± 6.45	−1.786	0.108	NS
	Range	60 – 85	70 – 85			
360 min	Mean ± SD	74.29 ± 6.73	76.25 ± 6.29	−0.476	0.645	NS
	Range	65 – 85	70 – 85			

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; P-value < 0.01: Highly significant; **: Highly significant; *: Significant

Table 5. Comparison between group A and group B of systolic BP before and after epidural analgesia.

		Group A	Group B			
Systolic BP (mmHg)		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia	Mean ± SD	114.38 ± 8.68	112.34 ± 9.16	0.911	0.366	NS
	Range	100 – 130	95 – 130			
30 min after	Mean ± SD	90.38 ± 16.18	98.44 ± 12.21	−2.250	0.028*	S
	Range	70 – 118	80 – 120			
At 60 min	Mean ± SD	92.59 ± 13.53	99.06 ± 9.79	−2.191	0.032*	S
	Range	70 – 113	85 – 120			
At 90 min	Mean ± SD	98.13 ± 14.07	102.63 ± 10.46	−1.537	0.129	NS
	Range	78 – 119	87 – 124			
At 120 min	Mean ± SD	105.00 ± 11.64	105.94 ± 9.28	−0.356	0.723	NS
	Range	90 – 120	90 – 120			
At 150 min	Mean ± SD	107.97 ± 8.12	106.88 ± 9.90	0.483	0.631	NS
	Range	95 – 120	90 – 120			
At 180 min	Mean ± SD	106.45 ± 6.85	103.83 ± 7.62	1.412	0.163	NS
	Range	95 – 120	90 – 120			
At 210 min	Mean ± SD	107.24 ± 9.50	103.85 ± 5.88	1.571	0.122	NS
	Range	90 – 120	95 – 115			
At 240 min	Mean ± SD	111.46 ± 10.68	112.00 ± 7.27	−0.173	0.864	NS
	Range	90 – 130	100 – 120			
At 270 min	Mean ± SD	115.33 ± 7.67	109.00 ± 8.43	1.945	0.064	NS
	Range	100 – 130	100 – 120			
At 300 min	Mean ± SD	116.50 ± 6.26	110.00 ± 5.48	2.101	0.054	NS
	Range	110 – 125	100 – 115			
At 330 min	Mean ± SD	112.14 ± 6.36	112.50 ± 6.45	−0.089	0.931	NS
	Range	100 – 120	105 – 120			
At 360 min	Mean ± SD	113.57 ± 6.90	111.25 ± 6.29	0.552	0.594	NS
	Range	100 – 120	105 – 120			

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; *: Significant

decrease in arterial blood pressure (systolic, diastolic, and mean blood pressure) after 30 mins and 60 mins in group A than in group B. However, there was no statistically significant difference between the two groups in blood pressure after that as shown in Tables 5, 6, and 7. There was no statistically significant difference between group A and group B as regards the duration of the active phase of the first stage and third stage of labor as shown in Table 8 and Figure 1. The duration of the second stage of labor was highly significantly longer in group A than in group B as shown in Table 9. Group B had a significantly higher incidence of developing itching than group A. However, group

Table 6. Comparison between group A and group B of diastolic BP before and after epidural analgesia at separate times.

		Group A	Group B			
DBP		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia	Mean ± SD	70.94 ± 9.71	73.91 ± 7.27	−1.385	0.171	NS
	Range	60 – 90	60 – 85			
30 min after	Mean ± SD	60.00 ± 12.70	67.03 ± 11.35	−2.335	0.023*	S
	Range	40 – 80	40 – 80			
At 60 min	Mean ± SD	65.78 ± 7.63	70.00 ± 6.35	−2.404	0.019*	S
	Range	50 – 80	60 – 80			
At 90 min	Mean ± SD	68.16 ± 8.08	70.00 ± 6.35	−1.015	0.314	NS
	Range	57 – 82	60 – 80			
At 120 min	Mean ± SD	66.72 ± 6.79	66.41 ± 5.85	0.197	0.844	NS
	Range	60 – 80	60 – 80			
At 150 min	Mean ± SD	67.50 ± 4.92	65.16 ± 4.83	1.923	0.059	NS
	Range	60 – 75	60 – 75			
At 180 min	Mean ± SD	67.58 ± 6.31	66.33 ± 7.18	0.721	0.474	NS
	Range	60 – 75	60 – 95			
At 210 min	Mean ± SD	68.28 ± 5.05	66.73 ± 3.14	1.344	0.185	NS
	Range	60 – 75	60 – 70			
At 240 min	Mean ± SD	69.38 ± 6.13	69 ± 5.07	0.198	0.844	NS
	Range	60 – 80	60 – 75			
At 270 min	Mean ± SD	68.33 ± 6.17	70 ± 3.33	−0.778	0.445	NS
	Range	60 – 80	65 – 75			
At 300 min	Mean ± SD	68.00 ± 5.87	69.17 ± 4.92	−0.407	0.690	NS
	Range	60 – 75	60 – 75			
At 330 min	Mean ± SD	68.57 ± 4.76	70.00 ± 7.07	−0.405	0.695	NS
	Range	60 – 75	60 – 75			
At 360 min	Mean ± SD	70.00 ± 5.77	68.75 ± 2.50	0.405	0.695	NS
	Range	60 – 80	65 – 70			

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; *: Significant

Table 7. Comparison between group A and group B of MABP before and after epidural analgesia at separate times.

		Group A	Group B			
MABP		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia	Mean ± SD	85.22 ± 8.93	86.53 ± 6.47	−0.673	0.503	NS
	Range	73 – 103	78 – 100			
At 30 min	Mean ± SD	70.22 ± 12.37	77.53 ± 10.43	−2.557	0.013*	S
	Range	50 – 93	53 – 90			
At 60 min	Mean ± SD	74.69 ± 8.74	79.56 ± 6.75	−2.497	0.015*	S
	Range	57 – 88	68 – 90			
At 90 min	Mean ± SD	78.13 ± 8.97	80.84 ± 6.92	−1.357	0.180	NS
	Range	65 – 92	69 – 91			
At 120 min	Mean ± SD	79.47 ± 7.60	80.44 ± 6.04	−0.564	0.574	NS
	Range	70 – 93	70 – 93			
At 150 min	Mean ± SD	79.00 ± 5.23	81.25 ± 5.37	−1.698	0.095	NS
	Range	70 – 90	73 – 90			
At 180 min	Mean ± SD	78.87 ± 5.29	80.77 ± 4.79	−1.477	0.145	NS
	Range	70 – 93	73 – 88			
At 210 min	Mean ± SD	79.12 ± 3.04	81.66 ± 5.91	−1.970	0.054	NS
	Range	72 – 85	70 – 90			
At 240 min	Mean ± SD	83.27 ± 4.28	83.46 ± 7.11	−0.094	0.926	NS
	Range	73 – 90	70 – 97			
At 270 min	Mean ± SD	83.10 ± 4.68	84.25 ± 6.07	−0.510	0.614	NS
	Range	77 – 90	78 – 97			
At 300 min	Mean ± SD	82.50 ± 5.05	84.45 ± 4.93	−0.775	0.450	NS
	Range	73 – 88	77 – 92			
At 330 min	Mean ± SD	84.50 ± 7.14	86.25 ± 4.50	−0.527	0.610	NS
	Range	75 – 90	77 – 93			
At 360 min	Mean ± SD	83.00 ± 2.94	87.38 ± 4.47	−1.754	0.110	NS
	Range	80 – 87	83 – 95			

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; *: Significant

A had a significantly higher incidence of bradycardia than group B as shown in Table 10. There was no statistically significant difference between the two groups regarding the APGAR score at 1 min and 5 min as shown in Table 11.

4. Discussion

Epidural analgesia has been the most convenient way of labor analgesia. However, the selection of more effective and safer additive drugs remains under discussion [14].

Table 8. Comparison between group A and group B among SO2 before and after epidural analgesia at separate times.

		Group A	Group B			
SpO2		No. = 32	No. = 32	Test value	P-value	Sig.
Before analgesia	Mean ± SD	97.84 ± 1.53	98.38 ± 1.26	−1.517	0.134	NS
	Range	95 – 100	96 – 100			
30 mins after	Mean ± SD	97.47 ± 3.09	98.25 ± 2.41	−1.128	0.264	NS
	Range	90 – 100	92 – 100			
At 60 min	Mean ± SD	98.91 ± 1.73	99.00 ± 0.98	−0.267	0.791	NS
	Range	94 – 100	97 – 100			
At 90 min	Mean ± SD	99.00 ± 0.76	98.94 ± 0.67	0.349	0.729	NS
	Range	98 – 100	98 – 100			
At 120 min	Mean ± SD	99.00 ± 0.98	99.34 ± 0.75	−1.576	0.120	NS
	Range	97 – 100	98 – 100			
At 150 min	Mean ± SD	98.91 ± 0.93	99.22 ± 0.55	−1.636	0.107	NS
	Range	97 – 100	98 – 100			
At 180 min	Mean ± SD	99.00 ± 0.73	99.17 ± 0.59	−0.977	0.332	NS
	Range	98 – 100	98 – 100			
At 210 min	Mean ± SD	99.14 ± 0.83	99.19 ± 0.63	−0.270	0.788	NS
	Range	98 – 100	98 – 100			
At 240 min	Mean ± SD	99.13 ± 0.61	99.13 ± 0.52	−0.044	0.965	NS
	Range	98 – 100	98 – 100			
At 270 min	Mean ± SD	99.00 ± 0.65	99.40 ± 0.70	−1.457	0.159	NS
	Range	98 – 100	98 – 100			
At 300 min	Mean ± SD	99.00 ± 0.47	99.33 ± 0.82	−1.046	0.313	NS
	Range	98 – 100	98 – 100			
At 330 min	Mean ± SD	99.00 ± 0.58	99.25 ± 0.96	−0.549	0.596	NS
	Range	98 – 100	98 – 100			
At 360 min	Mean ± SD	98.86 ± 0.69	99.50 ± 0.58	−1.567	0.152	NS
	Range	98 – 100	99 – 100			

P-value > 0.05: Nonsignificant
There was no statistically significant difference between the two groups in SO2 as shown in Table 8.

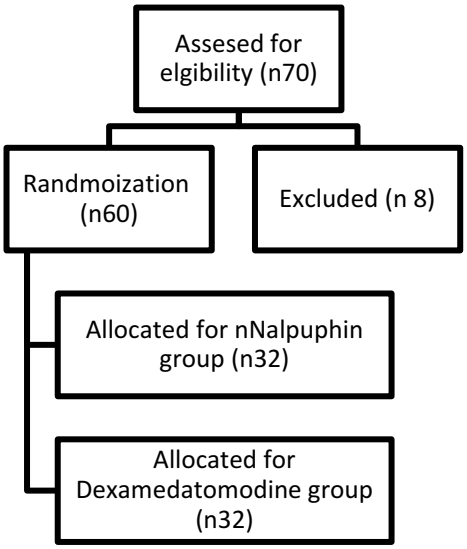

Figure 1. CONSORT flowchart demonstrating patient allocation.

In this study, the analgesic effects of bupivacaine 0.25% in combination with dexmedetomidine (Group A) in comparison to nalbuphine (Group B) in women in labor were recorded. We used a starting dose of 12 ml volume. This volume shows a satisfactory analgesic effect in general practice as it covers up to the level of T10, which is the desirable level in our study. Also, the results of many studies using the epidural volume between 10 and 15 ml showed satisfactory labor analgesia such as the study conducted by Gupta et al. [15].

There were no significant differences in the demographic data between both groups. The demographic data were controlled to avoid any bias or confounding factor in the study. We found out that both groups were satisfied with epidural analgesia, but the parturient in group A (the dexmedetomidine group) had a lower VAS score all over the study than group B (the nalbuphine group) with a significant difference at 30 mins and 60 mins after analgesia. This is like what was recorded when comparing epidural

Table 9. Comparison between group A and group B among the duration of the active phase of the first stage, second stage, and third stage of labor of the studied cases.

		Group A	Group B			
		No. = 32	No. = 32	Test value	P-value	Sig.
Duration of the active phase of the first stage in mins	Mean ± SD	174.38 ± 35.01	172.97 ± 29.78	0.173	0.863	NS
	Range	100 – 250	110 – 230			
Duration of the second stage in mins	Mean ± SD	90.78 ± 44.99	61.25 ± 42.08	2.712	0.009**	HS
	Range	30 – 180	30 – 180			
Duration of the third stage in mins	Mean ± SD	7.66 ± 1.84	6.94 ± 1.85	1.558	0.124	NS
	Range	5 – 10	5 – 10			

P-value > 0.05: Nonsignificant; P-value < 0.01: Highly significant; **: Highly significant

Table 10. Comparison between group A and group B among side effects.

	Group A	Group B			
	No. = 32	No. = 32	Test value	P-value	Sig.
Itching	0 (0.0%)	4 (12.5%)	4.267	0.039*	S
Nausea	6 (18.8%)	5 (15.6%)	0.110	0.740	NS
Vomiting	1 (3.1%)	0 (0.0%)	1.016	0.313	NS
Bradycardia	6 (18.8%)	1 (3.1%)	4.010	0.045*	S
Hypotension	8 (25.0%)	6 (18.8%)	0.366	0.545	NS

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; *: Significant

Table 11. Comparison between group A and group B among APGAR scores of the studied cases.

		Group A	Group B			
		No. = 32	No. = 32	Test value	P-value	Sig.
APGAR SCORE at 1 min	Median (IQR)	7 (6.5 – 8)	7 (7,8)	−1.584	0.113	NS
	Range	4 – 8	5 – 10			
APGAR SCORE at 5 mins	Median (IQR)	9 (9,10)	9 (8–10)	−0.043	0.966	NS
	Range	6 – 10	8 – 10			

P-value > 0.05: Nonsignificant

dexmedetomidine and fentanyl for lower limb vascular surgeries. This can be explained by the more rapid onset of dexmedetomidine than nalbuphine due to the high lipid solubility and rapid tissue uptake of dexmedetomidine more than nalbuphine [16]. Some of the epidural dexmedetomidine is absorbed back into the bloodstream and produces analgesia by stimulating the receptors at the brain level. The degree of this absorption is determined by the lipophilicity of the drug. Highly lipid-soluble drugs like dexmedetomidine diffuse into the bloodstream quickly, therefore, producing rapid onset of analgesia.

Similarly, the results were consistent with the results found by Jun et al [14] when using epidural dexmedetomidine for labor analgesia. The VAS score significantly decreased in *Jun's* study at 30 mins after analgesia as in our study.

The results in our study also agreed with the results reported by Baxter et al. [17] when comparing different concentrations of epidural nalbuphine (0.5 mg/ml, 1 mg/ml, 1.5 mg/ml, and 2 mg/ml) and epidural morphine for post-thoracotomy analgesia. The VAS score was found to be least in the 2 mg/ml nalbuphine group, which is like the top-up dose of nalbuphine in our study. As regards the hemodynamics, there was a statistically significant decrease in heart rate and arterial blood pressure (systolic, diastolic, and mean blood pressure) at 30 mins and 60 mins after analgesia in group A (the dexmedetomidine group) than in group B (the nalbuphine group) with no significant difference after that.

The study conducted by Jun et al. [14] using epidural dexmedetomidine for labor analgesia agreed with our study in the decrease of heart rate and blood pressure at 30 min. Another study conducted to assess the effect of epidural dexmedetomidine in lower limb vascular surgeries showed a significant decrease in heart rate at 25 mins in the dexmedetomidine group and a significant decrease in blood pressure 15 mins after analgesia [17]. Dexmedetomidine can reduce the blood pressure and HR due to its binding to α2 receptors in the locus coeruleus, decreasing the release of norepinephrine, and inhibiting the sympathetic activity.

Also, the rapid onset of dexmedetomidine can explain the significant decrease in heart rate and blood pressure at 30 min and 60 min in comparison to nalbuphine. As regards SpO_2, there was no significant difference between the two groups all over the study. When recording the duration of distinct stages of labor in our study parturient, we noticed that there was no significant difference between the 2 groups in the active phase of first stage and the

third stage durations. However, the second stage of labor was prolonged in group A (the dexmedetomidine group) than in group B (the nalbuphine group) with a statistically significant difference.

Jun et al. (2018) who used epidural dexmedetomidine in labor analgesia disagreed with our study on this point. In his study, the first stage and the second stage of labor were shorter in duration in the dexmedetomidine group than in the other group with no difference in the duration of the third stage. The prolongation of the second stage of labor in our study was still within the normal range, and no parturient experienced arrest of labor. This may be due to the absence of pain, therefore the decreased urge of the parturient to push the fetus through the birth canal.

As regards the adverse effects, there was a statistically significant difference between the two groups regarding itching and bradycardia. Group B (the nalbuphine group) showed a significantly higher incidence of itching (4 cases) than group A (the dexmedetomidine group) (no cases). On the other hand, group A showed a significantly higher incidence of bradycardia (6 cases) than group B (1 case).

There was no significant difference between the two groups as regards nausea, vomiting, or hypotension. In the study conducted comparing the nalbuphine and morphine regarding the incidence of itching and nausea, they found no difference between both groups [17].

Although *Pongraweewan et al*. were studying the effect of epidural nalbuphine in reducing itching induced by epidural morphine, he found that the incidence of itching did not decrease by using epidural nalbuphine and only the severity of itching decreased. This agrees with our study that epidural nalbuphine induces itching [18].

Jun et al. (2018) used ropivacaine and 0.5 μg/ml dexmedetomidine for labor analgesia, and the results came out as no bradycardia in any case and two cases of itching out of seventy-five in the dexmedetomidine group. This does not agree with our study. As for the neonatal outcome of the studied groups, the APGAR score was recorded at 1 min and 5 min and there was no significant difference between the two groups. The APGAR score at 5 mins was around nine in most of the cases in both groups. This result agrees with the results recorded by *Jun et al. (2018)* using epidural dexmedetomidine in labor analgesia who recorded the APGAR score at 5 mins and showed no significant difference between the two groups. Also, *Wangping and Ming* recorded an APGAR score at 1 min and 5 min when studying the optimal epidural dexmedetomidine dose used in labor. Their results agree with our study [13].

5. Conclusion

Both epidural dexmedetomidine and nalbuphine added to 0.25% bupivacaine achieved satisfactory labor analgesia, and both promoted the progress of labor without severe side effects. Taking into consideration that, dexmedetomidine has a faster onset than nalbuphine.

Disclosure statement

The authors declare no conflict of interest

References

[1] Paramasivan A, Lopez-Olivo MA, Foong TW, et al. Intrathecal dexmedetomidine and postoperative pain: a systematic review and meta-analysis of randomized controlled trials. Eur J Pain. 2020;24(7):1215–1227.
[2] Verghese T, Dixit N, John L, et al. Effect of intravenous dexmedetomidine on duration of spinal anaesthesia with hyperbaric bupivacaine - A comparative study. Indian J Clin Anaesth. 2019;6(1):97–101.
[3] Senapati LK, Samanta P. Effect of intravenous versus intrathecal dexmedetomidine on characteristics of hyperbaric bupivacaine spinal anesthesia in lower limb surgery. Asian J Pharm Clin Res. 2018;11:427–430.
[4] Santpur MU, Kahalekar GM, Saraf N, et al. Effect of intravenous dexmedetomidine on spinal anesthesia with 0.5% hyperbaric bupivacaine in lower abdominal surgeries: a prospective randomized control study. Anesth Essays Res. 2016;10(3):497–501.
[5] Niu XY, Ding XB, Guo T, et al. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: a meta-analysis. CNS Neurosci Ther. 2013;19(11):897–904.
[6] Camann WR, Hurley RH, Gilbertson LI, et al. Epidural nalbuphine for analgesia following caesarean delivery: dose-response and effect of local anaesthetic choice. Can J Anaesth. 1991;38(6):728–732.
[7] Chatrath V, Attri JP, Bala A, et al. Epidural nalbuphine for postoperative analgesia in orthopedic surgery. Anesth Essays Res. 2015;9(3):326.
[8] Myles PS, Troedel S, Boquest M, et al. The pain visual analog scale: is it linear or nonlinear? Anesth Analg. 1999;87(6):1517.
[9] Abdalla W, Ammar MA, Tharwat A, et al. Combination of dexmedetomidine and remifentanil for labor analgesia: a double blinded, randomized, controlled study. Saudi J Anaesth. 2015;9(4):433–438.
[10] Ayele T, Aregawi A, Negash T, et al. Anti-emetic effect of low dose metoclopramide with dexamethasone and metoclopramide alone for post-operative nausea and vomiting after thyroidectomy. A prospective cohort studies. 2021.
[11] McLendon K, Preuss C. Atropine [Internet]. 2021 [cited 2021 Sep 2]. Available from 2021 Sep 2: https://www.ncbi.nlm.nih.gov/books/NBK470551/
[12] Vercauteren MP, Coppejans HC, Hoffmann VH, et al. Prevention of hypotension by a single 5-mg dose of ephedrine during small-dose spinal anesthesia in prehydrated cesarean delivery patients. Anesth Analg. 2000;90(2):324–327.

[13] Wangping Z, Ming R. Optimal dose of epidural dexmedetomidine added to ropivacaine for epidural labor analgesia: a pilot study. Evid Based Complement Alternat Med. 2017;2017:7924148.

[14] Jun W, Zhengzhuang A, Li O. Analgesic efficacy of dexmedetomidine used for epidural anesthesia on labor analgesia. Biomed Res. 2018;29(3).

[15] Gupta S, Partani S. Neuraxial techniques of labour analgesia. Indian J Anaesth. 2018;62(9):658–666.

[16] Soliman AA, Melika AS. Epidural bupivacaine and dexmedetomidine versus bupivacaine and opioids for lower vascular surgery. J Med Sci Res. 2021;1(3):158.

[17] Baxter AD, Laganiere S, Samson B, et al. A dose-response study of nalbuphine for post-thoracotomy epidural analgesia. Can J Anaesthesia. 1991;38(2):175–182.

[18] Pongraweewan O, Santawata U, Weerasarn L, et al. Epidural nalbuphine for post cesarean epidural morphine induced pruritus. Med J Med Assoc Thailand. 2009;92(6):782.