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

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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.

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 α2 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...
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 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 non-parametric. 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            | Test value | P-value | Sig. |
|----------|--------------------|--------------------|------------|---------|------|
| Age (years) | Mean ± SD | 28.28 ± 5.34      | 28.33 ± 5.75 | −0.180  | 0.858 | NS   |
| Range    | 21 – 40           | 21 – 40            |            |         |      |      |
| ASA I    | 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.

| VAS score | Group A            | Group B            | 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 ± 1.12        | 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 – 6              |            |         |      |      |
| 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 – 5              |            |         |      |      |
| 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 – 6              |            |         |      |      |
| 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).

| VAS score | Group A            | Group B            | 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.

| Heart Rate (beats/min) | Group A | Group B | 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.

| Systolic BP (mmHg) | Group A | Group B | 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.

| DBP           | Group A          | Group B          | Test value | P-value | Sig. |
|---------------|------------------|------------------|------------|---------|------|
|               | No. = 32         | No. = 32         |            |         |      |
| **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 – 80          |            |         |      |
| **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     | 68.33 ± 6.17     | 69.07 ± 5.07     | 0.198      | 0.844   | NS   |
| Range         | 60 – 80          | 60 – 75          |            |         |      |
| **At 270 min** |                  |                  |            |         |      |
| Mean ± SD     | 68.00 ± 5.87     | 69.17 ± 4.92     | −0.407     | 0.690   | NS   |
| Range         | 60 – 75          | 60 – 75          |            |         |      |
| **At 300 min** |                  |                  |            |         |      |
| Mean ± SD     | 68.57 ± 4.76     | 70.00 ± 7.07     | −0.405     | 0.695   | NS   |
| Range         | 60 – 75          | 60 – 75          |            |         |      |
| **At 330 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.

| MABP       | Group A          | Group B          | Test value | P-value | Sig. |
|------------|------------------|------------------|------------|---------|------|
|            | No. = 32         | No. = 32         |            |         |      |
| **Before analgesia** |                  |                  |            |         |      |
| Mean ± SD  | 85.22 ± 8.93     | 86.53 ± 6.47     | −0.673     | 0.503   | NS   |
| Range      | 73 – 103         | 78 – 100         |            |         |      |
| **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  | 78.33 ± 6.13     | 80.84 ± 4.02     | −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.

| SpO2       | Group A            | Group B            | 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 99.14 ± 0.73 | 99.17 ± 0.59 | −0.977 | 0.332  | NS   |
| Range      | 98 – 100           | 98 – 100           |            |         |      |
| At 210 min | Mean ± SD 99.13 ± 0.61 | 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 ± 0.66 | −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.

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

Figure 1. CONSORT flowchart demonstrating patient allocation.
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.

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

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 | Test value | P-value | Sig. |
|---------|---------|------------|---------|-----|
| No. = 32 | No. = 32 |            |         |     |
| 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%) | 8 (25.0%) | 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 | Test value | P-value | Sig. |
|---------|---------|------------|---------|-----|
| No. = 32 | No. = 32 |            |         |     |
| 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 SpO2, 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

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