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Original Research Article

A Comparative Prospective Study of Intrathecal Dexmedetomidine-Fentanyl for Labor Analgesia

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Abstract

Background: Particularly in developing countries, women have described the intense and frequent pain they endure during childbirth as well as the lack of options for pain management. Sedatives and parenteral opioids are the most regularly prescribed drugs for women in labor in many low-resource settings. It has been shown that his method of treating pain has very little to no effect on the discomfort experienced during birth. Relieving pain during childbirth is one of the primary goals of maternity care. It is generally established that combining spinal and epidural analgesics can reduce labor pain without endangering the mother or fetus. For extended postoperative analgesia, intrathecally administered dexmedetomidine and bupivacaine have been employed. It is an analgesic alpha 2 adrenoreceptor agonist that is very selective.

Material and Method: The department of Anesthesia conducted this comparative prospective observational study. All participants gave their informed written agreement regarding their participation in the study and the use of their data for the current research project. One hundred full-term pregnant women who were admitted to the obstetric department for safe confinement were the participants. A tertiary care teaching hospital's obstetrics department's dedicated labor room served as the study's location. A multipara monitor, an ultrasound machine, an anesthetic workstation, and resuscitation supplies are all included in the labor room's setup. The benefits of labor analgesia have been discussed by the pregnant moms. The consent of an obstetrician was sought before any patient could be included in the study.

Results: Out of the 120 parturients that met the inclusion criteria, 110 patients gave their assent and were added to the study when the inclusion criteria were applied. According to the exclusion criteria, ten patients were not accepted. once the 100 patients in the predetermined sample size have been reached. The quality of the block analysis showed that Group A experienced analgesia earlier than Group B. There was statistical significance in the discrepancies. Group A also had analgesia for a longer period of time. Group A exhibits a greater degree of motor block than Group B, according to the examination of motor block. The most frequent adverse effect, according to the analysis of side effects, was pruritus, which was followed by bradycardia, hypotension, shivering, and nausea.

Conclusion: Intrathecal dexmedetomidine decreases the frequency of side effects and extends the duration of analgesia, in contrast to dexmedetomidine or fentanyl used alone. Intracerecal adjuvant walking epidural is a safe and effective method for labor analgesia. The duration and severity of the block are higher with intrathecal dexmedetomidine. Fentanyl increases the chance of a vaginal birth going well. Fentanyl, not dexmedetomidine, should be utilized as an intrathecal adjuvant for labor analgesia. It provides a longer duration of analgesia with an appropriate level of labor analgesia when compared to fentanyl.

Keywords: Analgesia, Dexmedetomidine, Fentanyl, Labor, Neonatal, labor analgesia.

Introduction

Labor is one of the most physically taxing experiences that women have in their lifetimes. Labor pain usually scores a minimum of 7, ranking it second or third among all painful conditions on a scale of 1 to 10. [1,2] Since the Middle Ages, physicians have been employing methods to decrease the intensity of labor pain. The modern period of labor analgesia began with the

"etherization of labor" by James Young Simpson, who effectively administered the medication to a woman whose pelvis was deformed. [3] The excruciating labor pain has a number of detrimental physical and psychological impacts on the mother and fetus. Torture-induced hyperventilation and elevated catecholamine levels in the mother and fetus are the main causes of hypoxemia. With minimal risk to the mother or fetus, the commonly used technique of combined spinal epidural (CSE) analgesia lessens labor discomfort. [4] The agonizing pain of labor causes the mother and fetus to experience a variety of negative physical and psychological stresses.

Hyperventilation and high catecholamine levels resulting from labor pain and unpleasant uterine contractions cause hypoxemia in both the mother and the fetus. [5,6] Pain relief has two advantages: it soothes the patient and lowers the release of stress chemicals. [7] Painkillers not only make the patient feel better, but they also stop stress hormones from being released, which can exhaust the parturient's reserves and starve the fetus of oxygen and nutrients. [8]

Combined spinal epidural (CSE) analgesia is a widely accepted technique to alleviate labor pain with minimal side effects to the mother and fetus. [9] Although the use of intrathecal opioids for labor analgesia is becoming more common, there is not much data to back this up. Phenyl piperidine is the source of fentanyl, a potent and fast-acting synthetic drug. Because of its short half-life, fentanyl is thought to be a great substitute for managing labor pain. During childbirth, fentanyl and bupivacaine have been used extensively to lessen motor block. Nevertheless, itching and respiratory depression are side effects of combining opioids with local anesthetics.

During childbirth, fentanyl and bupivacaine have been used extensively to lessen motor block. Nevertheless, itching and respiratory depression are side effects of combining opioids with local anesthetics. [10] Because of its inherent analgesic properties, dexmedetomidine—a highly powerful and selective alpha 2 adrenergic agonist—has been used in conjunction with spinal bupivacaine to prolong postoperative analgesia. Recent studies on the usage of dexmedetomidine during pregnancy have shown that it does not pass the placenta very much because of its high placental retention. [11] Several studies have used dexmedetomidine intravenously and epidurally in labor without any adverse effects on the mother or fetus. [12,13] Dexmedetomidine is a highly selective alpha-2 adrenergic agonist that has intrinsic analgesic properties and has been used intrathecally to prolong postoperative analgesia. [14,15] Since there is little placental transfer, the fetus should experience little to no change. Dexmedetomidine offers the benefit of lowering blood pressure because it controls catecholamine release. Dexmedetomidine occasionally causes bradycardia and hypotension in the mother, which could be harmful. [16] Intrathecally or intravenously administering dexmedetomidine during pregnancy is still considered off-label. Dexmedetomidine has a sympatholytic action that can lessen the stress response to surgery and an analgesic-sparing effect that considerably reduces the need for opioids. [17, 18]

Material and Methods

The department of Anesthesia conducted this comparative prospective observational study. All participants gave their informed written agreement regarding their participation in the study and the use of their data for the current research project. One hundred full-term pregnant women who were admitted to the obstetric department for safe confinement were the participants. A tertiary care teaching hospital's obstetrics department's dedicated labor room served as the study's location. A multipara monitor, an ultrasound machine, an anesthetic workstation, and resuscitation supplies are all included in the labor room's setup. The benefits of labor analgesia have been discussed by the pregnant moms. Obstetrician concurrence was obtained for the inclusion of any patient in the study. Written and informed consent after explaining the effects of drugs being used for labor analgesia was obtained from the patient for their participation in the observational study.

All participants who met the inclusion criteria were randomized into two groups (A and B) using computer-generated randomization. Under aseptic precautions, labor analgesia was administered through a combined spinal–epidural technique using an 18G Tuohy needle and a 27G spinal needle in the left lateral position. The drugs and volumes administered were as follows:

- Group A: Bupivacaine 2.5 mg (0.5 mL diluted to 2 mL) + 20 µg dexmedetomidine in 1 mL saline intrathecally (total volume: 3 mL)
- Group B: Bupivacaine 2.5 mg (0.5 mL diluted to 2 mL) + fentanyl (15 µg) in 1 mL saline intrathecally (total volume: 3 mL).

The syringes were masked, and the drug administration and subsequent patient monitoring were performed by the medical team who does not know about the composition. In both groups, epidural top-up was administered through the catheter upon the patient's request. The drug used was 0.125% bupivacaine.

Hepatic data Non-invasive methods were used to measure the following: respiration rate, blood pressure, pulse rate, and oxygen saturation. The fetal heart rate, cervical dilation, and labor stage

and progress were all exhibited by the physician. Intracerecal analgesia should have been administered as soon as the patient entered active labor. The baseline was the amount of time before the intrathecal medicine injection. Analgesia started when an intrathecal injection resulted in a VAS score of less than 3. Subsequently, the VAS was recorded once every minute for ten minutes, and subsequently once every ten minutes until a value of three was reached. The period from the intrathecal injection until the VAS reached more than 3 and required further analgesia through the epidural catheter was used to define the duration of analgesia.

Every five minutes after the intrathecal injection, the mother's non-invasive blood pressure and heart rate were recorded. Intravenous fluids, ephedrine, or atropine, if needed, were administered promptly to treat bradycardia (defined as a heart rate ≤ 60 beats per minute) and hypotension (defined as a 20% or higher reduction in blood pressure from baseline). Fetal bradycardia was diagnosed and treated with a cardiotocograph; initially, the mother was given oxygen while being positioned on her side to avoid aortic compression. Other side effects that have been observed include nausea, respiratory depression, and itching. In order to reduce pruritus, IV diphenhydramine 50 mg and oral loratadine 10 mg were administered, while ondansetron 4 mg was used to manage nausea and vomiting. The delivery methods were noted. Neonatal outcomes such as pH of the umbilical cord blood and neonatal Apgar score were noted.

Statistical Analysis: Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM, Chicago, IL). Data are presented as mean ±SD or numbers as appropriate. Patient characteristics (age, weight, height, parity, and gestational age), onset and duration of analgesia, and pH of the umbilical artery were analyzed using the independent two-sample t-test. Other parameters were studied using the Chi-square test or Fisher's exact test as appropriate.

Result

A total of 120 parturient fulfilled the inclusion criteria, of whom 110 patients provided consent and were subsequently enrolled in the study after applying the inclusion criteria. Ten patients were excluded based on the exclusion criteria. After reaching the preselected sample size of 100 patients. The demographic and baseline variables are shown in Table 1 and were statistically similar

Table 1: Demographic and baseline parameters among participants

Parameters	Mean±SD	
	Group A (n=50)	Group B (n=50)
Age (years)	23.80±2.76	24.66±1.86
Weight (kg)	61.27±5.52	55.05±6.86
Height (cm)	152.85±3.18	153.50±3.93
Heart rate (bpm)	106.12±5.12	102.80±6.51
SBP (mmHg)	113.38±3.33	112.29±6.32
DBP (mmHg)	70.18±5.81	71.12±6.73
MAP (mmHg)	81.22±3.52	83.10±6.42
SpO_2 (%)	94.31±0.64	92.33±0.69
VAS score	7.87±0.86	6.72±1.02

Table 2: Mode of delivery among participants

Mode of delivery	Group A (N=50)	Group B (N=50)
Normal (n=65)	30	35
Instrumental vaginal delivery (n=8)	5	3
Cesarean delivery (n=27)	15	12

A total of 100 patients reported sufficient analgesia (Group A: 50; Group B: 50), and 65 patients delivered vaginally (Group A: 30; Group B: 35), indicating an overall success rate of 61.66%; however, the success rate was significantly higher in Group B. The rates of forceps-assisted vaginal delivery and cesarean delivery were higher in Group A.

Table 3: Quality of block among the participants

Parameter	Mean±SD	
	Group A (N=50)	Group B (N=50)
Onset time (s)	57.22±15.20	85.50±23.30
Duration of analgesia (min)(VAS score <3)	117.11±21.17	102.21±15.81
Degree of the motor block ason the Bromage Scale	3.10±0.88	3.77±0.83
Top-up required in first 6 h	6.20±1.33	10.32±3.34

The analysis of the quality of the block revealed an earlier onset of analgesia in Group A than in Group B. The differences were statistically significant. The duration of analgesia was also higher in Group A. The analysis of motor block reveals a higher degree of motor block in Group A than that in Group B.

Table 4: Incidence of maternal and fetal side effects in both the groups

Parameter	Mean±SD	
	Group A (N=50)	Group B (N=50)
Pruritus	0	21
Hypotension	5	3
Bradycardia	4	2
Nausea	1	3
Vomiting	0	1

Pruritus was shown to be the most frequent side effect (although it was only noticed in Group B), followed by hypotension, bradycardia, shivering, and nausea, according to the analysis of negative effects. There were no abnormalities in the umbilical artery and uterine blood flow, according to fetal ultrasonography and Doppler study. With a lower pulsatility index, Group A saw less variation in heart rate. Both procedures were safe, as shown by the study of fetal data, and all neonates in both groups were confirmed to be safe and healthy after 6 weeks of birth.

Discussion

There have long been controversies and myths around labor pain treatment. As such, the challenge of delivering safe and effective analgesia during labor has persisted. Labor analgesia has evolved over time to minimize motor obstruction, permit walking epidurals, and stop labor from going into overdrive. Lipophilic opioids, such as fentanyl, have been routinely used intrathecally and epidurally for labor analgesia in addition to local anesthetics. A selective alpha 2 adrenoreceptor agonist, dexmedetomidine has been applied as an adjuvant in spinal and epidural anesthetic procedures. Compared to local anesthetics alone, it has several advantages, such as a longer duration of analgesia and no adverse neurological consequences. [19,20] However, the degree of the block must be balanced during labor analgesia to avoid any motor block, which is necessary for a good vaginal delivery. Adjuvants are increasingly being used in labor spinal analgesia, as they have long been used in clinical practice for spinal anesthesia. [21]

Niu et al 2013 [14] in their meta-analysis showed that intrathecal dexmedetomidine prolonged the duration of spinal anesthesia and improved postoperative analgesia and did not increase the incidence of hypotension and adverse events. Wong et al.2004 [22] investigated the efficacy of various doses of fentanyl as an adjuvant for labor spinal analgesia; they concluded that 15 μg was a safe and effective dose of fentanyl. This forms the basis of using a 15 μg dose of fentanyl in the current study. Ezz Gehan et al.2017 [23] used 20 μg dexmedetomidine intrathecally, which formed the basis of the dexmedetomidine dose in this study. Dexmedetomidine has high placental retention (0.77 maternal/fetal index) and does not cross the placenta significantly. Being highly lipophilic like fentanyl it is retained in placental tissue. Studies show that dexmedetomidine has high placental retention and increases the frequency and amplitude of uterine contractions directly and in a dose-dependent fashion suggesting advantages for use as an analgesic adjunct during labor. [24] Fyneface-Ogan et al.2012 [25] compared 2.5 μg dexmedetomidine intrathecally along with 2.5 mg hyperbaric bupivacaine versus bupivacaine and fentanyl intrathecally in labor and has shown that dexmedetomidine along with bupivacaine intrathecally significantly prolonged sensory block in laboring women.

Research findings indicate that dexmedetomidine has a high degree of placental retention and directly and dose-dependently increases the frequency and amplitude of uterine contractions, indicating potential benefits for usage as an adjuvant analgesic during labor. [11] Therefore, excellent analgesia and the absence of motor block were anticipated upon intrathecal dexmedetomidine injection, indicating that this medication is appropriate for labor analgesia. Its intrathecal usage in labor, however, is still not approved for use. This study's 10 μg dose was lower than intravenous doses utilized in the past during pregnancy, and no negative effects on the unborn child were predicted. Dexmedetomidine acts on the receptors of the substantia gelatinosa of the dorsal horn of the spinal cord which inhibit the firing of nociceptive neurons stimulated by peripheral Aδ and C fibers. It also inhibits the release of the nociceptive neurotransmitter substance P. [26]

Al-Mustafa et al 2009 [27] and Hala et al 2011 [28] observed dose-dependent prolongation of the duration of action of analgesia with reduced analgesic requirement when intrathecal dexmedetomidine dosages increased (5, 10, and 15

μg). Similar to our findings Mahdy et al 2011 [29] found that after intrathecal dexmedetomidine and fentanyl injection, there were no adverse effects on mothers or babies in any group. Palanisamy et al 2009 [30] used i.v. dexmedetomidine successfully as an adjunct to opioid-based PCA and general anesthesia for the respective provider of labor analgesia and cesarean delivery anesthesia in a parturient with a tethered spinal cord, with favorable maternal and neonatal outcomes.

Consequently, it is proposed that intrathecal dexmedetomidine and fentanyl, with their longer duration of analgesia and lack of adverse effects (like sedation, respiratory depression, mother hypotension, and neonatal depression), could be a desirable substitute for labor analgesia. The results of this study will be crucial in low-resource nations where the tools, supplies, and expertise required to provide an epidural analgesic service are lacking. [31] Given the lengthy duration of analgesia it demonstrated in our trial, intrathecal bupivacaine/dexmedetomidine may be the only medicine administered as a single shot to multiparous women in labor. Because dexmedetomidine has no adverse effects, such as drowsiness, respiratory depression, maternal hypotension, or newborn depression, it may offer extra advantages to women undergoing labor and delivery. Even though this study adds to our knowledge of dexmedetomidine, further investigation might be necessary to completely comprehend how this medication relieves labor pain. Nonetheless, this experiment showed that a single intrathecal injection of low-dose dexmedetomidine had a substantial potential to lessen labor and delivery discomfort. To obtain a more effective and prolonged block during labor and delivery in primiparous women, a higher intrathecal DMT dose would be necessary.

Conclusion:

Intrathecal dexmedetomidine decreases the frequency of side effects and extends the duration of analgesia, in contrast to dexmedetomidine or fentanyl used alone. Intracerecal adjuvant walking epidural is a safe and effective method for labor analgesia. The duration and severity of the block are higher with intrathecal dexmedetomidine. Fentanyl increases the chance of a vaginal birth going well. Fentanyl, not dexmedetomidine, should be utilized as an intrathecal adjuvant for labor analgesia. It provides a longer duration of analgesia with an appropriate level of labor analgesia when compared to fentanyl. It does not harm the mother or the baby while maintaining hemodynamic stability.

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