Randomized Comparative Study of Intrathecal Administration of Dexmedetomidine-Fentanyl for Labour Pain

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Abstract: Introduction: Dexmedetomidine used in pregnancy as it does not significantly cross the placenta due to its high placental retention. Also it has no adverse effects on mother or fetus in many studies. Our purpose was to evaluate the effect of combination of IT dexmedetomidine and fentanyl on maternal and neonatal outcomes during labour in comparison to IT dexmedetomidine or IT fentanyl. Methods: Age groups between 20 – 40 years were included in the study. A total of 150 patients were included in the study. All the included patients were scheduled for normal vaginal delivery with uncomplicated delivery. Any patients with liver, kidney disease, cardiac problem, any allergy to local anesthesia, fetal compromise or patient refusal were excluded from the study. The informed consent was taken from all the patient included in the study. Results: Onset of analgesia was faster and duration of analgesia was longer in group C than in the two other groups (p-value <0.001), 18 patients in A group, 19 patients in group B and 15 patients in group C needed top-ups of 10ml of 0.125% bupivacaine till delivery of baby. Discussion & Conclusion: Our study concluded that Addition of 5 µg intrathecal dexmedetomidine to 10 µg fentanyl prolonged the duration of analgesia. The combination decreases the incidence of side effects in comparison to IT 10 µg dexmedetomidine or IT 20 µg fentanyl alone. [V Shah Natl J Integr Res Med, 2018; 9(1):88-91]

Key Words: Combine, Dexmedetomidine, Fentanyl, Labour Pain

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Introduction: The obstetrician-gynecologist is often solely responsible for analgesia/sedation and regional blocks during office-based and outpatient procedures. The American Society of Anesthesiologists guidelines for the provision of analgesia/sedation for nonanesthesiologists provide helpful recommendations to maximize patient safety during office-based and outpatient procedures. Propofol, Midazolam, Fentanyl, Remifentanil, Ketamine can be used as other adjunct to the anesthesia present technique. Pain is a dehumanizing experience that destroys the soul. Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Spinal anesthesia is a commonly used technique for lower abdominal surgeries[1].

Spinal anesthesia is the most commonly used technique for lower abdominal and perineal surgeries. However, local anesthetics-when used alone-is associated with relatively short duration of action, thus early analgesic intervention is needed in the postoperative period[2]. Many adjuncts like fentanyl, ketamine, tramadol, neostigmine, magnesium sulphate, etc. have been used to prolong the analgesic effect of local anaesthetics[3]. Nowadays, apart from lignocaine and bupivacaine, levobupivacaine and ropivacaine are commonly being used for neuraxial anesthesia. Spinal neuraxial blocks result in sympathetic blockade, sensory analgesia, or anesthesia and motor blockade, depending on the dose, concentration or volume of local anesthetic, after insertion of a needle in subarachnoid space[4].

A common problem during lower abdominal surgeries under spinal anesthesia is visceral pain, nausea, and vomiting. The addition of fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block[5].

Spinal anesthesia has some the advantages. These advantages are limited by the short duration of action of local anesthetics when used alone and by side effects as hypotension and bradycardia, many adjutants can been used to prolong the anesthetic and analgesic effect of local anesthetics. The quality of spinal anesthesia can be enhanced by the addition of fentanyl when added to hyperbaric Bupivacaine[6].

Labour pain and painful uterine contractions cause hyperventilation and high catecholamine levels resulting in maternal and fetal hypoxemi. Dexmedetomidine has an analgesic-sparing effect, significantly reducing opioid requirements and has a sympatholytic effect that can attenuate the stress response to surgery. Dexmedetomidine used in pregnancy as it does not significantly cross the

placenta due to its high placental retention. Fentanyl has been used for labor analgesia extensively to decrease motor block of local anaesthetics. Also it has no adverse effects on mother or fetus in many studies. Our purpose was to evaluate the effect of combination of IT dexmedetomidine and fentanyl on maternal and neonatal outcomes during labour in comparison to IT dexmedetomidine or IT fentanyl.

Methods: The present study was done in the department of Anesthesia department in the medical institute for the period of one year from August 2014 to September 2015. The ethical committee of the medical institute was informed before the start of the research and the ethical clearance certificate was obtained from the committee. Official permission was obtained from the institutional review board of the college committee. Age group between 20 – 40 years were included in the study. A total of 150 patients were included in the study. All the included patients were scheduled for normal vaginal delivery with uncomplicated delivery. Any patients with liver, kidney disease, cardiac problem, any allergy to local anesthesia, fetal compromise or patient refusal were excluded from the study. The informed consent was taken from all the patient included in the study.

All the included patients were randomly divided into three groups: Group A: 50 patient were administered with 5ug intrathecal dexemedetomidine in 1 ml of normal saline; Group B: 50 patient were administered with IT 20 ug fentanyl in 1 ml of normal saline and Group C: 50 patient were administered with IT 5 ug dexemedetomidine pluas 10 ug fentanyl in 1 ml of normal saline. All aseptic precautions were taken. All the included patient received 15 ml/kg of Ringer's lactate solution intravenously. The intrathecal injection were administered when the patient were in sitting position. The injection was administered using a combined spinal epidural set (CSE) at L3-L4 intervertebral space. An epidural catheter was inserted 5 cm into the epidural space using the CSE set and secured for future administration of 10-12 ml of 0.125% bupivacaine required when the VAS (Visual analog scale) was recorded above 3 and repeated top-ups of the same dosage were administered as and when the VAS for pain was recorded above 3 till delivery of the baby.[2] 10-15ml of 0.5% bupivacaine was administrated if emergency cesarean section was indicated.

Data Collection: The onset of administration of intrathecal analgesia was considered when the patient was in active labour. The baseline was defined as time before intrathecal injection of drugs. Maternal heart rate and noninvasive blood pressure were recorded every 5 min following the intrathecal injection. Analgesia onset was the time from intrathecal injection to time of recording a VAS less than 3. VAS was recorded thereafter every 1 minute for 10 minutes and then every 10 minutes till VAS reached more than 3. Duration of analgesia was defined as the time from intrathecal injection to the time when VAS reached more than 3 and needed additional analgesia through the epidural catheter. Occurrence of hypotension which was defined as decrease in blood pressure more than 20% from baseline and bradycardia defined as heart rate less than 60 were immediately treated with intravenous fluids, ephedrine or atropine as appropriate. Fetal bradycardia was monitored by cardiotocograph and was initially treated by giving oxygen to mother and ensuring lateral position to avoid aortocaval compression. Other side effects such as pruritus, nausea and vomiting and respiratory depression were recorded pruritus was treated by i.v diphenhydramine 50 mg and 10 mg oral loratidine and nausea and vomiting were treated with ondansetron 4 mg. Modes of delivery were recorded. Neonatal outcome like; neonatal APGAR score and umbilical cord blood pH were recorded.

Statistical analysis: Statistical analysis was performed using the SPSS version 16.0 (IBM, Chicago, IL). A sample size of 50 patients in each group was determined through power analysis (α=0.05; β=0.90) to detect a difference of 30 min in the time analgesia between groups. Data are presented as mean ± SD, or numbers as appropriate. Patient characteristics, onset and duration of analgesia, APGAR score, and pH of 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. The linear mixed model was used for comparison of MAP and HR between the three groups. P values of < 0.05 were considered significant.

Results: A total of 150 women undergoing laboour accepted and participated throughout the study. The three groups, group A (10 µg dexmedetomidine alone), group B (20 µg fentanyl alone), and group C (5 µg Dexmedetomidine and 10 µg fentanyl mixture)

were comparable in terms of demographic variables and labour characteristics (Table 1). Onset of analgesia was faster and duration of analgesia was longer in group C than in the two other groups (p-value <0.001), 18 patients in A group, 19 patients in group B and 15 patients in group C needed top-ups of 10ml of 0.125% bupivacaine till delivery of baby. Regarding to maternal side-effects; hypotension and bradycardia were recorded in group A (patients (30%), patients (16%) respectively) more than the two other groups; the fentanyl group showed significant increase in pruritus patients (43%); lastly nausea and vomiting were detected only in C group 1 patient (7%). The other side effects like shivering, respiratory depression or postdural puncture headache were not noticed in the 3 study groups. APGAR scores (at 1 and 5 minutes) and mean umbilical artery pH in all the groups were within normal values with no significant differences between the groups (P>0.05) (Table 2). There is no statistical difference between the three groups as regard the mode of delivery (Table 3).

Table 1: Demographic data of the patients

Characteristic	Group A	Group B	Group C	P value
Age	27 years	32 years	28 years	>0.05
Weight	80 kg	75 kg	73 kg	>0.05
Height	160 cm	170 cm	165 cm	>0.05
Gestational Age	39 weeks	40 weeks	38 weeks	>0.05

Table 2: Fetal Outcome

		Group A	Group B	Group C	P value
APGAR score	1 min	7.73 ± 0.9	8.0 ± 0.5	7.73 ± 0.7	> 0.05
	5 min	9.3 ± 0.5	9.0 ± 0.3	9.5 ± 0.2	> 0.05
Umbilical artery pH		6.73 ± 0.5	7.17 ± 0.04	7.05 ± 0.02	> 0.05

Table 3: Mode of delivery in the three groups

	Group A N = 50	Group B N = 50	Group C N = 50	P value
Vaccum Vaginal delivery	10	8	6	>0.05
Vaginal Delivery	30	28	32	>0.05
Fetal distress	4	7	6	>0.05
Failure of progress	6	7	6	>0.05

All patients in the three groups had baseline VAS ranged from 6-10, at 5 minutes reading VAS became less than 3 in the three groups and reached the lowest level (0-1) at 30 minutes reading and started to increase in the next readings. VAS became more than 3 earlier in the group B than group A and group C.

Discussion: It is well recognized that postoperative pain is most often being undertreated. The routine use of regional anesthesia for lower abdominal surgeries is associated with a short duration of analgesia postoperatively[7]. The current study attempted to compare dexmedetomidine (DEX) and fentanyl as the appropriate adjunct drugs for spinal block in addicted patients. Addicted patients may need higher doses of bupivacaine in combination with an adjunct drug[8].

Labour analgesia has been evolved over the last years to minimize labour pain. Fentanyl have been used extensively intrathecally and epidurally for labour analgesia along with local anesthetics[8]. Dexmedetomidine, is a highly selective α2 adrenoreceptor agonist has been used in spinal and epidural anesthesia as an adjuvant to local anesthetics and has several advantages of increased duration of analgesia compared to local anesthetics alone with no adverse neurological effects[9].

Local anesthetics are commonly used for intrathecal anesthesia, but the major problem is the relatively short duration of action, thus early analgesic intervention is needed in the postoperative period. A number of adjutants, such as clonidine and midazolam, and others have been studied to prolong the effect of spinal anesthesia[10].

Dexmedetomidine, an imidazole compound, is the pharmacologically active dextroisomer of medetomidine that displays specific and selective α2-adrenoceptor agonism. Activation of the receptors in the brain and spinal cord inhibits neuronal firing and results in symoathlytic effect, causing hypotension, bradycardia, sedation, and analgesia[11]

Our study used 5 µg dexmedetomidine plus 10 µg fentanyl intrathecally in labour with minimal adverse effects on the mother or newborn were noted. In agree with our results, a recent study done by Niu et al., has shown that intrathecal dexmedetomidine prolonged the duration of spinal anesthesia and

improved postoperative analgesia and did not increase the incidence of hypotension and adverse events[12]. The onset of analgesia with dexmedetomidine+fentanyl was faster than dexmedetomidine or fentanyl only. Duration of analgesia was better in group C compared to groups A and B. All patients achieved a VAS <3 after 5 minutes. The present study showed that addition of spinal 5 µg dexmedetomidine to fentanyl significantly prolonged duration of analgesia compared with either use of intrathecal 20 µg fentanyl or 10 µg dexmedetomidine. Similar study, showed significantly improved analgesic efficacy was seen by Gupta et al., on comparison of dexmedetomidine and fentanyl as intrathecal adjuvant (P<0.001). As regard to neonatal outcomes: APGAR scores (at 1 and 5 minutes) and mean umbilical artery pH in all the groups were within normal values with the differences between the groups were not statistically significant (P>0.05). Mahdy et al., found that after intrathecal dexmedetomidine and fentanyl injection there were no adverse effects on mothers or babies in any group. Adverse effects in the form of hypotension and bradycardia were markedly observed in A group than in the 2 other groups. Fyneface-Ogan et al., agreed with our results by observing minimal change of maternal blood pressure after intrathecal administration of dexmedetomidine. Clinical studies have demonstrated the safety of intrathecal dexmedetomidine in humans. However it has been shown that dexmedetomidine in relatively high doses can lead to hypotension when administered either neuraxially or intravenously[12].

Conclusion: Our study concluded that Addition of 5 µg intrathecal dexmedetomidine to 10 µg fentanyl prolonged the duration of analgesia. The combination decreases the incidence of side effects in comparison to IT 10 µg dexmedetomidine or IT 20 µg fentanyl alone.

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