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Comparison of Analgesic Effects of Fentanyl, Dexmedetomidine Alone and Combination of Fentanyl and Dexmedetomidine Intrathecally in Active Labor: A Randomized Control Trial

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ABSTRACT

Labor pain is one of the most severe pains the majority of women endure in their lifetime. Effective pain control during childbirth has long been an important health and sociological issue throughout the world and remains so even today. Combined spinal-epidural anaesthesia (CSE) has the advantages of spinal analgesia along with the benefits of epidural analgesia that can be maintained throughout the entire duration of labor. To compare the analgesic effects of administering fentanyl, dexmedetomidine and combination of fentanyl and dexmedetomidine intrathecally in active labor and to evaluate the side effects of fentanyl and dexmedetomidine on mother and new born. A prospective randomized controlled trial was carried out at a tertiary healthcare centre of North India over a period of 7 years. 90 patients participated in this study. These were divided into three groups randomly based on the labor analgesic drugs they recieved and results were analyzed statistically. dxmedetomidine 10 µg aloneand dexmedetomidine 5 µg in combination with 10 µg fentanylused in our study were able to achieve adequate labor analgesia which was comparable to fentanyl alone (group F) as suggested by equivalent minimum VAS (below 2, p = 0.670) among all three groups. Pruritus was the notable side effect with fentanyl (group F, total 6 incidents out of 30 parturients) which was significantly higher than both the groups (group D and Group F+D) (p = 0.021). When dexmedetomidine is combined with fentanyl (group FD) this combination led to longest duration of analgesia among three groups which shows the possibility of synergistic effect of both these drugs without affecting maternal hemodynamics and neonatal outcome.

INTRODUCTION

Labor pain is one of the most severe pains the majority of women endure in their lifetime. Effective pain control during childbirth has long been an important health and sociological issue throughout the world and remains so even today. Painful uterine contractions cause the mother to hyperventilate. The catecholamine levels become high in the mother with the stress of labor pain resulting in maternal and fetal hypoxemia. Pain relief during labor provides the patient with comfort and attenuates the release of stress hormones.

Regional analgesia techniques during labor have been a topic for research recently. These include the epidural alone, combined spinal epidural analgesia, patient-controlled epidural analgesia and continuous spinal analgesia with microcatheters[1,2]. Epidural solutions are administered either by bolus, continuous infusion, or patient-controlled pump. As used in the earlier years, boluses of higher concentrations have been associated with a dense motor block resulting in reduced mobility, decreased pelvic tone and impairment of the bearing down effort in the second stage of labor[3].

Combined spinal-epidural anaesthesia (CSE) has the advantages of spinal analgesia i.e., faster onset of pain relief and more reliable analgesia along with the benefits of epidural analgesia such as continuous infusion for pain relief that can be maintained throughout the entire duration of labor[4,5]. Intrathecal opioids improve the quality and duration of analgesia in these parturients and decrease the risk of hypotension, however, intrathecal opioids have disadvantages of dose-dependent pruritus and respiratory depression[6,7]. A lower concentration of local anaesthetic in combination with a variety of opiates providesan analgesic effect while allowing the woman to maintain some motor function and retain her ability to bear down[2,3].

Dexmedetomidine is a highly selective α2 adrenergic agonist. It has both analgesic and sedative properties. Dexmedetomidine has an analgesic-sparing effect, it significantly reduces opioid requirements. It has a sympatholytic effect that can attenuate the stress response to surgery[8]. Dexmedetomidine shows high placental retention as it does not cross the placenta significantly, so it is safe to use during pregnancy[9]. Also, it had no adverse effects on the mother or fetus in many studies[10].

The study aims to analyze the effect of the combination of intrathecal dexmedetomidine and fentanyl on maternal and neonatal outcomes during labor incomparison with intrathecal dexmedetomidine or intrathecal fentanyl alone.

MATERIALS AND METHODS

The study was planned as a prospective randomized controlled trial. This study was conducted at a tertiary care hospital of North India from November 2015 to December 2022. Approval from the ethical committee of the institute was obtained and a written informed consent was taken from all the patients. Patients posted for delivery meeting the inclusion were enrolled for the study.

Inclusion criteria:

- Booked antenatal cases at term
- American Society of Anesthesiologists (ASA) I and II grade parturient
- Uncomplicated pregnancy scheduled for normal vaginal delivery
- Vertex presentation not in fetal distress
- Singleton fetus and parturients aged between 18-35 years

Exclusion criteria:

- Altered coagulation profile
- Maternal valvular heart disease, kidney disease and liver disease
- Previous caesarean section
- Patient refusal
- Any neuromuscular disorder
- Deformities of spinal column and skin infections at the block area
- Known hypersensitivity to opioids or dexmedetomidine
- Intrauterine growth retardation or fetal compromise

We considered 114 patients for the study; however, 24 patients were excluded from the study as per exclusion criteria. Thus, the study was carried out in 90 patients and participants were randomized in to three groups of 30 each. Randomization was done using computer generated random numbers. Various treatment groups were as follows:

- **Group F:** I/T fentanyl 20 µg in 1 mL normal saline
- **Group D:** I/T dexmedetomidine 10 µg in 1 mL normal saline
- **Group FD:** I/T 5 µg dexmedetomidine plus 10 µg fentanyl in 1 mL normal saline

Detailed pre-anaesthetic check-up was done for all the subjects prior to the study. Basic laboratory data were reviewed.

Patient preparation All patients and labor room staff were familiarized with visual analogue scale (VAS) and its use for measuring the postoperative pain. Patients were not given any premedication or any analgesic agent through any other route other than intrathecal.

CSE tchnique n the labor room, electrocardiogram (ECG), pulse oximetry and noninvasive blood pressure were attached and baseline parameters were recorded and monitoring initiated. A peripheral intravenous access was taken. All the patients eligible for study were preloaded with ringer lactate 10 mL kg^{-1} at the time of performing the combined spinal epidural. The parameters that were observed after the administration of combined spinal epidural were as follows:

- Time to onset of analgesia
- VAS score base line, 5 min after CSE and every 15 min thereafter fot 1st hr then every 30 min till delivery
- Systolic, diastolic blood pressure and heart rate every 15 min for first 1 hr and every 30 min till delivery
- Time to administration of rescue analgesia when VAS is more than 3
- Adverse effects (pruritus, nausea, vomiting) on mother
- Apgar score at 1 min and 5 min after birth

For rescue analgesia, we administered 0.25% bupivacaine 10 mL^{-1} bolus through epidural catheter followed by 0.125% bupivacaine infusion in epidural catheter at the rate of 4-6 mL^{-1} hr targeting VAS below 3 till the time of delivery. All the data are expressed as mean and standard deviation (SD) unless specified.

RESULTS

Demographic variables were comparable among all three groups. Maternal characteristics as age, height, weight and duration of pregnancy were comparable among groups. Mean age was 30.60, 30.10 and 30.57 years in group F, D and group F+D respectively. Mean height was 167.83, 168.73 and 168.03 cms in Group F, D and group F+D respectively. Mean weight was 69.13, 67.87 and 69.03 kgs in group F, D and group F+D, respectively. Mean duration of pregnancy was 38.50 weeks in all three groups. Parity and ASA grade were comparable among groups (Fig. 1 and 2).

Dexmedetomidine 10 µg alone (group D) and dexmedetomidine 5 µg in combination with 10 µg fentanyl (group F+D) used in our study were able to achieve adequate labor analgesia which was comparable to fentanyl alone (group F) as suggested by equivalent minimum VAS (below 2, p = 0.670) among all three groups (Table 1).

The mean duration of analgesia with dexmedetomidine was 184.56±20.23 min (group D) and with combination of fentanyl (group F+D) was 230.17±30.75 min which significantly longer than fentanyl alone (group F) which was 109.61±16.75 min (p<0.001). It shows that intrathecal dexmedetomidine provides significantly longer duration of analgesia than fentanyl (p<0.001).

Maternal vitals were recorded at baseline and at regular intervals after CSE. Heart rate, systolic blood pressure and diastolic blood pressure were comparable among groups at base line and after CSE till the time of delivery (Fig. 3-5).

Pruritus was the notable side effect with fentanyl (group F, total 6 incidents out of 30 parturients) which was significantly higher than both the groups (group D and Group F+D) (p = 0.021) (Table 2).

There was no significant difference in the rates of emergency LSCS between the three groups in our study (6.7% in group D, 6.7% in Group F and 3.3% in group F+D). About 90 % parturients delivered vaginally in all three groups which were comparable among groups (p = 0.840) (Table 3).

APGAR scores were also comparable in all groups at 1 min (group F 7.53±0.51, group D 7.60±0.50 and group F+D 7.50±0.51) and at 5 min (group F 9.53±0.51, group D 9.43±0.57 and group F+D 9.47±0.51). There was no significant difference in all three groups (p = 0.738 and 0.758) (Table 4).

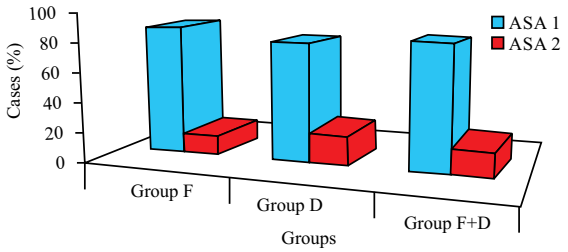

Fig. 1: ASA grades of parturients

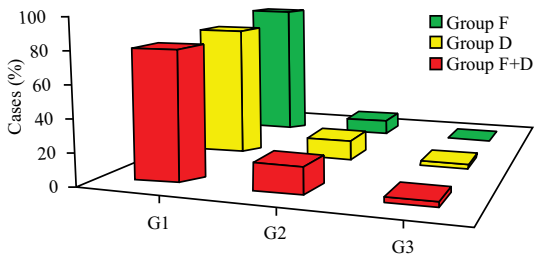

Fig. 2: Distribution of primigravida and multigravida among groups

Table 1: Depth of analgesia

	Group F	Group D	Group F+D				
	----------Mean±SD ----------			p-value	Group F V/S group D	Group F V/S group F+D	Group D V/S group F+D
VAS (baseline)	7.77±0.73	7.90±0.66	7.83±0.70	0.760	0.74	0.927	0.927
VAS (minimum	1.60±0.89	1.67±0.66	1.70±0.65	0.670	0.72	0.680	0.983

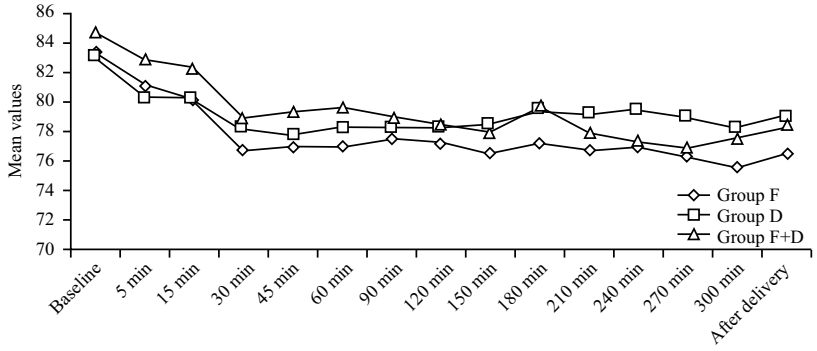

Fig. 3: Mean heart rate variation with time among three groups

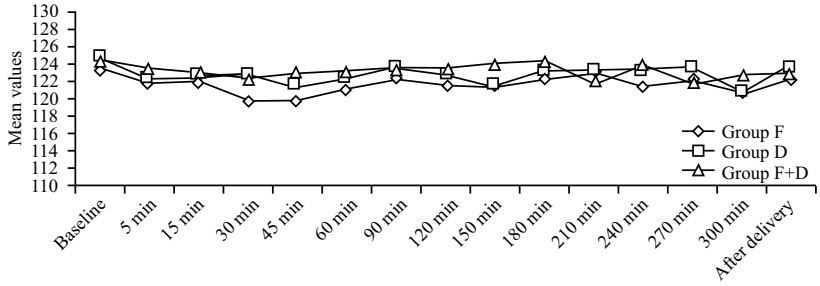

Fig. 4: Comparison of Mean SBP changes with time among groups

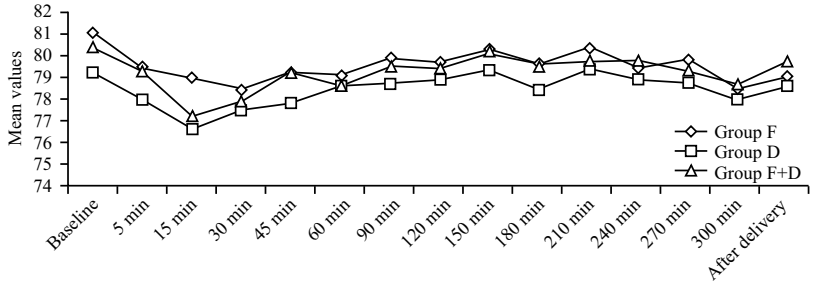

Fig. 5: Comparison of Mean DBP changes with time among groups

Table 2: Comparison of Maternal side effects among groups

	Group						
Maternal Adverse effects	Group F Frequency (%)	Group D Frequency (%)	Group F+D Frequency (%)	p-value	Group F V/S group D	Group F V/S group F+D	Group D V/S croup F+D
Hypotension	1 (3.3)	1 (3.3)	1 (3.3)	1.000	1.000	1.000	1.000
Nausea	1 (3.3)	1 (3.3)	1 (3.3)	1.000	1.000	1.000	1.000
Pruritus	6 (20.0)	0 (0.0)	2 (6.7)	0.021	0.024	0.254	0.492
Vomiting	0 (0.0)	0 (0.0)	1 (3.3)	1.000	1.000	1.000	1.000

Table 3: Mode of Delivery

	Groups			
Mode of delivery	Group F Frequency (%)	Group D Frequency (%)	Group F+D Frequency (%)	p-value
Forceps	1 (3.3)	0 (0.0)	1 (3.3)	0.840
LSCS	2 (6.7)	2 (6.7)	1 (3.3)	
Vaginal	27 (90.0)	28 (93.3)	28 (93.3)	
Total	30 (100)	30 (100)	30 (100)	

Table 4: Comparison of APGAR score at 1 min and 5 min among groups

Fetal outcome apgar score	Group F	Group D	Group F+D		Group F V/S group D	Group F V/S group F+D	Group D V/S group F+D
	----------Mean±SD----------			p-value			
At 1 min	7.53±0.51	7.60±0.50	7.50±0.51	0.738	0.866	0.965	0.724
At 5 min	9.53±0.51	9.43±0.57	9.47±0.51	0.758	0.745	0.877	0.968

DISCUSSIONS

Over the years labor analgesia has progressed towards minimizing or eliminating motor blockade and avoid any adverse effects on progress of labor and maternal or fetal outcome. Opioids are commonly used in to intrathecal space and via epidural route for labor analgesia with or without local anesthetics. Many previous studies have shown that intrathecal opioids

provide more satisfactory analgesia during labor in comparison to epidural or intravenous opioids[11,12]. As a sole agent, doses of intrathecal fentanyl reportedly used for labor analgesia range from 10-50 µg. In previous studies the ED^{50} ofintrathecal fentanyl for labor analgesia was found 14 +/- 1 micro gram. When fentanyl is used as the sole intrathecal agent mean duration of labor analgesia does not increase as the dose is increased beyond 25 micro gram of fentanyl[13].

Dexmedetomidine has been used in spinal and epidural anesthesia as an adjuvant and has shown several advantages of increased duration of analgesia in comparison to local anesthetics or fentanyl alone with no adverse neurological effects[14]. Intrathecal dexmedetomidine increases the duration of spinal anesthesia and provides improved postoperative analgesia and does not increase the incidence of hypotension and adverse events[15]. Being highly lipophilic like fentanyl it is retained in placental tissue[9]. Studies that described the use of dexmedetomidine in parturients have mentioned that babies delivered were with normal APGAR scores which indicates that it doesn't affect the fetal well-being[9,10,14].

In a comparison of intrathecal fentanyl and intrathecal dexmedetomidine Dilesh *et al*.[16] found that VAS recorded in both groups were below 3 and quality of analgesia was satisfactory in both groups. He also observed that VAS at maximal analgesia was significantly lesser in the fentanyl group compared to dexmedetomidine group, denoting a significantly deeper level of analgesia with fentanyl compared to dexmedetomidine. Mahendru *et al*.[14] compared intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery and he found that minimum VAS scores were recorded in Group bupivacaine with dexmedetomidine in comparison to Group bupivacaine with fentanyl.

Both these studies show that satisfactory VAS score is achieved with intrathecal dexmedetomidine though Dilesh *et al*.[16] shows maximum analgesia is achieved with fentanyl while Mahendru *et al*.[14] shows maximum analgesia is achieved with dexmedetomidine. In our study we were able to achieve VAS less than 3 in all three groups which shows that intrathecal dexmedetomidine and fentanyl provides adequate labor analgesia. Minimum VAS achieved was comparable among all three groups.

Fyneface-Ogan conducted a study to determine the effect of adding dexmedetomidine to hyperbaric bupivacaine for neuraxial analgesia for labor. Ninety laboring multiparous women were allocated in to three groups of 30 each to have single shot intrathecal bupivacaine alone (B), bupivacaine with fentanyl (BF), or bupivacaine with dexmedetomidine (BD). Sensory and motor block characteristics, time from injection to two dermatome sensory regression, sensory regression to S1 dermatome, and motor block regression to Bromage 1 were recorded. The time for sensory regression to S1 was significantly prolonged in the group BD (268.9±15.58 min) ($p = 0.0001$) in comparison to group B (107.9±22.11 min) and group BF (122.9±10.42 min). Authors concluded that shot intrathecal bupivacaine/dexmedetomidine significantly prolonged sensory block in laboring women[15]. Though they have used intrathecal bupivacaine which resulted in motor block that is not the case in our study as bupivacaine was not used into intrathecal space. They demonstrated that intrathecal dexmedetomidine prolongs duration of analgesia in comparison to adding fentanyl to bupivacaine. In our study also dexmedetomidine has shown prolongation of duration of labor analgesia in comparison to fentanyl.

Dilesh *et al*.[16] concluded that 10 µg dexmedetomidine intrathecally provides a longer duration of analgesia with lesser incidence of pruritus compared to 20 µg fentanyl intrathecally for CSE labor analgesia. In our study combination of fentanyl and dexmedetomidine (Group F+D) showed duration of analgesia 230.17 min which was significantly prolonged than Group F (109.61 min) and Group D (184.56 min) ($p<0.001$) (Table 11 and Fig. 11). This shows the possibility of synergistic effect of fentanyl and dexmedetomidine though further studies with larger study groups would be required to establish this fact. Our results are comparable to study done by Dilesh et al as they compared labor analgesia with intrathecal dexmedetomidine and intrathecal fentanyl through CSE followed by epidural bupivacaine. In our study one patient in each group complained of nausea and only one patient had vomiting in Group F+D. These findings were not significant and comparable among groups. Studies done by Fyneface-Ogan *et al*.[15] and Dilesh *et al*.[16] also shows that intrathecal fentanyl and dexmedetomidine in above mentioned doses does not cause significant nausea and vomiting in laboring women.

CONCLUSION

Intrathecal dexmedetomidine (Group D) provided longer duration of analgesia in comparison to intrathecal fentanyl (Group F) as part of labor analgesia. When dexmedetomidine is combined with fentanyl (Group FD) this combination led to longest duration of analgesia among three groups which shows the possibility of synergistic effect of both these drugs without affecting maternal hemodynamics and neonatal outcome.

REFERENCES

1. Howell, C.J., T. Dean, L. Lucking, K. Dziedzic, P.W. Jones and R.B. Johanson, 2002. Randomised study of long term outcome after epidural versus non-epidural analgesia during labour. BMJ, 325: 357-357.

2. Howell, C.J., C. Kidd, W. Roberts, P. Upton, L. Lucking, P.W. Jones and R.B. Johanson, 2001. A randomised controlled trial of epidural compared with non-epidural analgesia in labour. BJOG: An Int. J. Obstet. Gynaecol., 108: 27-33
3. Thornton, J. and G. Capogna, 2001. Reducing likelihood of instrumental delivery with epidural anaesthesia. Lancet, Vol. 358. 10.1016/s0140-6736(00)05295-8
4. Scavone, B.M., J.T. Sullivan, A.M. Peaceman, T.P. Strauss Hoder and C.A. Wong, 2002. Fetal heart rate and uterine contraction pattern abnormalities after combined spinal/epidural vs systemic labor analgesia. Anesthesiol., Vol. 96.
5. Anim-Somuah, M., R.M. Smyth and L. Jones, 2011. Epidural versus non-epidural or no analgesia in labour. Cochrane. Database. Syst. Rev., Vol. 12. 10.1002/14651858.cd000331.pub3
6. Harsten, A., L. Gillberg, L. Hakansson and M. Olsson, 1997. Intrathecal sufentanil compared with epidural bupivacaine analgesia in labour. Eur. J. Anaesthesiol., 14: 642-645.
7. Cascio, M., B. Pygon, C. Bernett and S. Ramanathan, 1997. Labour analgesia with intrathecal fentanyl decreases maternal stress. Can. J. Anaesth., 44: 605-609.
8. Verma, R., R. Gupta, J. Bogra, M. Kohli, R. Raman and J. Kushwaha, 2011. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. J. Anaesthesiol. Clin. Pharmacol., 27: 339-343.
9. Nair, A. and K. Sriprakash, 2013. Dexmedetomidine in pregnancy: Review of literature and possible use. J. Obstetric. Anaesth. Crit. Care., 3: 3-6.
10. Hanoura, S., R. Hassanin and R. Singh, 2013. Intraoperative conditions and quality of postoperative analgesia after adding dexmedetomidine to epidural bupivacaine and fentanyl in elective cesarean section using combined spinal-epidural anesthesia. Anesth. Essays Res.es, 7: 168-172.
11. Herpolsheimer, A., and J. Schretenthaler, 1994. The use of intrapartum intrathecal narcotic analgesia in a community-based hospital. Obstet. Gynecol., 84: 931-936.
12. Zapp, J. and T. Thorne, 1995. Comfortable labor with intrathecal narcotics. Mil. Med., 160: 217-219.
13. Palmer, C.M., R.C. Cork, R. Hays, G.V. Maren and D. Alves, 1998. The dose-response relation of intrathecal fentanyl for labor analgesia. Anesthesiology, 88: 355-361.
14. Mahendru, V., A. Tewari, S. Katyal, A. Grewal, M. Singh and R. Katyal, 2013. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. J. Anaesthesiol. Clin. Pharmacol., 29: 496-502.
15. Fyneface-Ogan, S., O.G. Job and C.E. Enyindah, 2012. Comparative effects of single shot intrathecal bupivacaine with dexmedetomidine and bupivacaine with fentanyl on labor outcome. ISRN Anesthesiol., 2012: 1-6.
16. Kiran, S., P. Dilesh, S. Eapen and V. Chopra, 2014. A comparison of intrathecal dexmedetomidine verses intrathecal fentanyl with epidural bupivacaine for combined spinal epidural labor analgesia. J. Obstetric. Anaesth. Crit. Care., 4: 69-74.