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EFFECT OF INTRATHECAL DEXMEDETOMIDINE AS AN ADJUVANT IN LABOUR ANALGESIA ON OBSTETRICAL AND NEONATAL OUTCOME

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ABSTRACT **Aim and Objectives:**To evaluate the analgesic effect and safety of intrathecal (IT) Dexmedetomidine added as an adjuvant during vaginal delivery. To evaluate the effect of intrathecal (IT) Dexmedetomidine added during Delivery on Neonatal Apgar Score. To evaluate the effect of intrathecal (IT) Dexmedetomidine on progression of labour and its outcome. **Material and Methods:** A Prospective double-blind randomized controlled study in 100 patients in Department of Obstetrics and Gynecology, M.L.B. Medical College & Hospital Jhansi after approval of the Ethical Committee from a period of February 2019 to August 2020. **Result:** Mean age in group A was 26.34±3.26. In group B mean age was 26.64±3.70. p value is 0.6680. In group A 34 (68%) were primigravida and 16 (32%) were multigravida. Out of 50 parturients, in group B 36 (72%) were primigravida and 14 (28%) were multigravida. In group A, the mean gestational age was 37.8±0.90 and group B, the mean gestational age was 38.0±1.03. 16% of the patient in group A and 12% in group B had cervical dilatation of 3cm. 74% of the patient in group A and 78% in group B has cervical dilatation of 4cm. 10% of patients in both groups had cervical dilatation of 5cm. In group A mean VAS score at beginning was 6.68±0.89 and after 30 min it was 1.88±0.80. In group B, mean VAS score at beginning was 6.34±0.94 after 30 min, mean was 3.30±0.74. Mean duration of Ist stage of labor in group A 300 ±22.48. The mean duration of Ist stage of labor in group B 304.88±19. Mean duration of second stage of labor in group A 34.12±1.79. Mean duration of second stage of labor in group B 42.18±1.77. Mean duration of third stage of labor in group A was 4.8±0.4 and group B Was 4.5±0.5. In group A,2(4%) parturients had instrumental vaginal delivery and4(8%) parturients in group B had instrumental delivery. Out of 50 parturients in group A, 82% undergone spontaneous normal vaginal delivery ,18% undergone cesarean section and 76% parturients in group B undergone spontaneous vaginal delivery and 24% undergone caesarean section. Blood loss during delivery in group A 442±117.22 and in group B 445±148.06. In group A, 6 (12%) patients had complain of hypotension and in group B, out of 50 parturients, 5 (10%) patients had developed complain of hypotension. In group A, only 4 (8%) patient developed side effect as compared to group B where 8 (16%) parturients developed side effects. In group A 3 (6%) parturients had meconium stained liquor as compared to group B 4 (8%) parturients had MSL. 2 (4%) babies admitted in NICU in group A and 3 (6%) babies admitted in NICU in group B. mean of umbilical artery blood pH of group A 7.25±0.05 and group B 7.25±0.02. **Conclusion:** Intrathecal dexmedetomidine as an adjuvant prolonged the duration of analgesia and also improve postoperative analgesia without increasing incidence of adverse events with safe outcomes for mother and babies.

KEYWORDS : Bupivacaine, ,dexmedetomidine, Fentanyl, Intrathecal, , Labour Analgesia, Neonatal Outcome.

INTRODUCTION

Pain is a noxious and unpleasant stimulus which produces fear and anxiety. Pathophysiological responses occur in the body during pain. In the respiratory system there is hyperventilation during contraction, increase the work of breathing and oxygen consumption. The pain induced hyperventilation and hypocapnia reduces uteroplacental blood flow by up to 25 %.

The respiratory alkalosis further impair fetomaternal gas exchange by shifting the oxygen –hemoglobin dissociation curve to the left and fetal PaO_2may fall up to 23%.

Epidural analgesia has been extensively used to provide pain relief during labour. Pain relief provide a comfort for the patients and attenuates the release of stress hormone. Epidural Bupivacaine is still the most widely used local anesthetic in the obstretic analgesia. Many drugs are added to bupivacaine to minimize it's total dose and to prolong the analgesic effect.

Dexmedetomidine is a highly selective α_2 adrenergic agonist that has both analgesic and sedative properties when used in combination with regional anesthesia[1-2]. Dexmedetomidine acts by binding to G-protein that coupled a2 adrenergic receptors, which are found in peripheral, central, and autonomic nervous systems, various vital organs, and blood vessels throughout the body[3].

There are three subtypes of these receptors, namely α_2A, α_2B, and a_2C, each having different functions and activities.

Dexmedetomidine is considered to have more affinity for α_2A and α_2C receptors[3].

Dexmedetomidine significantly reduces opioid requirements and has sympatholytic effect that can attenuate the stress response to surgery[4]. Dexmedetomidine is used in pregnancy, as it does not significantly cross the placenta because of its high placental retention[5]. In addition, it has no adverse effect on the mother or fetus in many studies.[11] Dexmedetomidine in combination with regional anesthesia provides better intraoperative and postoperative analgesia.

AIMS AND OBJECTIVES

- To evaluate the analgesic effect and safety of intrathecal (IT) Dexmedetomidine added as an adjuvant during vaginal delivery.
- To evaluate the effect of intrathecal (IT) Dexmedetomidine added during Delivery on Neonatal Apgar Score.
- To evaluate the effect of intrathecal (IT) Dexmedetomidine on progression of labour and its outcome.

MATERIAL AND METHODS

Source of data

A Prospective double-blind randomized controlled study will be undertaken in 100 patients in Department of Obstetrics and Gynecology, MLB Medical College & Hospital Jhansi after approval of the Ethical Committee.

Inclusion criteria:

- All patients which are scheduled for normal vaginal delivery with uncomplicated pregnancy, and willing for labor analgesia.
- Patients with cephalic presentation.
- Patients with single fetus.
- Patients is in active labor (had four uterine contractions in 10 min, each contraction lasted for 40-60 s), and cervical dilatation 3 cm or more with head engaged.

Exclusion criteria:

- Patient refusal,

- Patients with cardiac, liver, kidney disease,
- Allergy to local anesthetics or study drugs,
- Patients with fetal distress,
- Contraindications of regional anesthesia,
- Patients intrauterine growth retardation ,fetal distress,
- Past history of sedative drug abuse
- Patients with International normalized ratio (INR) greater than 1.3.
- Patients who have platelet count less than 100,000 were excluded from this study.

Mode of Selection: Random selection

- The analgesic procedure was briefly explained to the patient.
- An informed written consent was obtained from the patient and her relatives then they will be randomly divided into two groups via computer generated random numbers.

Patients were allocated into two groups -
Both groups were receive CSE analgesia:

- **Group A:** 50 patients will receive intrathecal (IT) 2.5 mg hyperbaric levo-bupivacaine+0.05ml of normal saline
- **Group B:** 50 patients will receive IT 2.5 mg hyperbaric levo-bupivacaine+0.05 ml (5 µg) of dexmedetomidine.

Test solution will be diluted with normal saline to a total volume of 2 ml.

In all patients, an intravenous line will secured with an 18-G cannula.

Number of cases belonging to each group – 50
In both the groups epidural catheter was be inserted and levo-bupivacaine will be administered in the concentration of 0.125 % guided by patient's VAS Score & progression of labor.

Standard monitoring devices including-

- Non-invasive blood pressure cuff,
- ECG leads, and
- Pulse-oximetry probe will be attached to the patient and respiratory rate was recorded.

Preloading will be done with Ringer's lactate solution at a dose of 15 ml/kg/body weight over 15 min. Cervical dilatation,stage and progress of labor and fetal heart rate will be monitored.

The onset of administration of IT analgesia will be consider, when the patient will be in active labor. Aseptic precautions will be taken and all instruments of general anesthesia should present during the procedure. Using CSE set at L3—L4 intervertebral space, with the patient in the sitting position, an IT injection of the study drugs will be done and epidural catheter will inserted 5 cm into the epidural space and secured for future administration of 10-12 ml of 0.125% levo-bupivacaine when visual analog scale (VAS) will recorded above 3.

The baseline will be define as time before IT injection of drugs Analgesia onset will be the time of recording VAS less than 3 after IT injection.

Afterward, VAS will recorded every 10 min for 1 h, and then every 1 h until delivery of the baby. The analgesia time will be calculated from IT injection until the time of first rescue of epidural analgesia.

The progress, duration of first and second stage, and modes of delivery (vaginal delivery or CS) will be recorded and maternal side effects will observed, recorded, and treated.

If emergency Cesarean section (CS) will indicated, epidural 10-15 ml of 0.5% levo-bupivacaine will administered and would be mentioned as failure of labor analgesia.

Parameters of comparison:

1) Success rate of labour analgesia and its effect on neonatal outscome.
2) Neonatal Apgar score at 1,3 and 5 minutes.
3) Patient's satisfaction
4) Time between administration of study drug and successful delivery.
5) Any complications

RESULT

TABLE 1: Demographic data

Parameters	Group A [Test Group]	Group B [Control Group]	p value
	Mean±SD	Mean±SD	
Age	26.34±3.26	26.64±3.70	0.6680(NS)
Weight	56.1±5.71	57.78±6.21	0.1622(NS)
BMI	24.20±2.76	25.04±2.86	0.1383(NS)
Height	158.28±5.47	157.5±5.33	0.4719 (NS)
Gestational age	37.88±0.90	38.00±1.03	0.5365 (NS)

TABLE 2: PARITY

Parity	Group A [Test Group]		Group B [Control Group]	
	Number of patients	Percentage	Number of patients	Percentage
Primi	34	68.00%	36	72.00%
Multi	16	32.00%	14	28.00%

TABLE 3 : MEAN VAS SCORE

Mean VAS score	Group A [Test Group]	Group B [Control Group]	p value
At beginning	6.68±0.89	6.34±0.94	0.0663 (NS)
At 30 min.after epidural	1.88±0.80	3.30±0.74	0.0001 (S)

TABLE 4: MEAN DURATION OF STAGES OF LABOR(Min) & CERVICAL DILATATION (Cm)

Stages	Mean Duration of Labor (min)	Group A [Test Group]	Group B [Control Group]	p value
First	Mean±SD	300 ± 22.48	304 ± 19	0.57 (NS)
Second	Mean±SD	34.12±1.79	42.18±1.77	0.0001 (S)
Third	Mean±SD	4.8±0.4	4.5±0.5	0.57691(NS)
Cervical Dilataion	Mean±SD	3.94±0.51	3.98±0.47	0.6843 (NS)

TABLE 5: MODE OF DELIVERY

Mode of delivery		Group A [Test Group]		Group B [Control Group]	
		Number of patients	Percentage	Number of patients	Percentage
Vaginal	Spontaneous	41	82.00%	38	76.00%
	Instrumental	2	4.00%	4	8.00%
Caesarean	Dystocia	3	6.00%	2	4.00%
	Fetal distress	4	8.00%	6	12.00%

TABLE 6: MATERNAL HYPOTENSION

Maternal hypotension	Group A [Test Group]		Group B [Control Group]	
	Number of patients	Percentage	Number of patients	Percentage
Yes	6	12.00%	5	10.00%
No	44	88.00%	45	90.00%

TABLE 7: NEONATAL OUTCOME

PARAMETERS	Group A [Test Group]	Group B [Control Group]	p value
1 minute Apgar score	8.2± 0.6	7.8± 0.7	0.02 (S)
3 minute Apgar score	8.22±0.74	8.16±0.89	0.7147 (NS)
5 minute Apgar score	8.38±0.75	8.22±0.82	0.3111 (NS)
Umblical artery blood ph	7.25±0.3	7.28±0.12	0. 6 (NS)
NICU admission	2/50	3/50	NS

DISCUSSION

Our is a clinical prospective observational study conducted at MLB Medical college Jhansi (UP) after approval of the Ethical Committee.A full term parturient women at term pregnancy in latent or active phase of labor who has come for delivery were included in study after obtaining written informed consent.

Age distribution:

Both the group A and group B were similar with respect to the age of parturients. Mean age in group A was 26.34±3.26. In group B mean age

was 26.64±3.70. p value is 0.6680. So result is statistically not significant.

Height:
Height of the parturient studied ranges from 140 cm to 162 cm. shortest height was 140 cm and tallest being 162 cm. The mean height were 158.28±5.47 in group A and 157.5±5.33 in group B respectively. The p value of 0.4719 was statistically not significant.

Weight distribution:
Most of the parturient weight between 50-60kg in both the groups. In group A the mean weight was 56.1±5.71 and in group B the mean weight was 57.78±6.21. The p value is 0.1622. The result is not significant.

BMI distribution:
Mean value of BMI in group A is 24.20 while in group B is 25.4. The result is not significant as p value is 0.1383.

Parity:
Out of 50 parturients, In group A 34 (68%) were primigravida and 16 (32%) were multigravida. Out of 50 parturients, in group B 36 (72%) were primigravida and 14 (28%) were multi gravida.

Gestational age (weeks):
The our study, it was found that in both the groups group A and group B maximum parturients were of 37 weeks (40%).In group A, the mean gestational age was 37.8±0.90.
In group B, the mean gestational age was 38.0±1.03.
The p value is 0.5365, the result is not significant.

Cervical dilatation (cm):
The p value is 0.6843, the result is not significant as p value is not less than 0.05. 16% of the patient in group A and 12% in group B had cervical dilatation of 3cm. 74% of the patient in group A and 78% in group B has cervical dilatation of 4cm. 10% of patients in both groups had cervical dilatation of 5cm.

Mean VAS score:
Out of 50 parturients, In group A mean VAS score at beginning was 6.68±0.89 and after 30 min was 1.88±0.80. In group B, mean VAS score at beginning was 6.34±0.94 after 30 min, mean was 3.30±0.74.The p value is significant ie, 0.0001. VAS score in group B significantly higher than group A.

In our study, dexmedetomidine provided longer duration of spinal analgesia and lower VAS score when added to levo- bupivacaine.

Mean duration of first stage of labor (min):
The mean duration of first stage of labor in group A 300 ±22.48. The mean duration of firststage of labor in group B 304.88±19. The p value is 0.57, which is not significant. There is no effect on the duration of first stage of labor in our study.

Systematic review done by *Halpern*[6] *and Leighton* demonstrated no difference in the duration of first stage of labor among women who received epidural analgesia.

Cochrane 2005[7] review supported that duration of first stage of labor not affected by increasing epidural demand.

Duration of second stage of labor:
The mean duration of second stage of labor in group A 34.12±1.79. The mean duration of second stage of labor in group 42.18±1.77.The p value is 0.0001 which is significant.

There is significant reduction in duration of second stage of labor.

Previous studied demonstrated that high concentration of neuraxial local anesthetic might relax pelvic floor musculature, interfere with fetal rotation during descent and prolong the second stage of labor. Our study, comparable with study done by Grace Lim et al[8].

Duration of third stage of labor:
The mean duration and of third stage of labor in group A was 4.8±0.4
The mean duration and of third stage of labor in group B was 4.5±0.5
The p value is 0.57691, which was not significant.

Mode of delivery:
Our of 50 parturients,In group A, 2% parturients had instrumental vaginal delivery and 4% parturients in group B had instrumental delivery. Out of 50 parturients in group A, 82% undergone spontaneous normal vaginal delivery ,18% undergone CS and 76% parturients in group B undergone spontaneous vaginal delivery and 24% undergone caesarean section.

Dipti et al[9], found no relation between epidural analgesia and cesarean section this was also supported by Segal et al in their meta analysis that included nine studies, showing no association between epidural analgesia and cesarean section

Mean amount of blood loss during delivery:
The mean amount of blood loss during delivery in group A 442±117.22 and in group B 445±148.06. The p value is not significant. The amount of blood was comparable in both the groups.

Maternal hypotension:
Among 50 parturients in group A, 6 (12%) patients had complain of hypotension and in group B, out of 50 parturients, 5 (10%) patients had developed complain of hypotension. Intrathecal dexmedetomidine does not increase the risk of hypotension. There goes along the results of meta analysis conducted by Neetu et al[10].

Side effect (Headache, Nausea, Vomiting, Pruritus and shivering):
Out of 50 parturients in group A, only 4 (8%) patient developed side effect as compared to group B where 8 (16%) parturients developed side effects. Comparable to the study conducted by Hine et al showing that intrathecal dexmedetomidine prolonged the duration of spinal anesthesia and improved post operative analgesia without increasing the side effects.

Meconium stained liquor:
Out of 50 parturients, in group A 3 (6%) parturients had meconium stained liquor as compared to group B 4 (8%) parturients has MSL. Comparable to the study done by Fyneface ogan et al[11].

Mean APGAR score at 1,3 and 5 minute of delivery:
With regard to neonatal outcomes APGAR score at 3rd and 5th minute showed normal values with no significant difference between two groups.

Except 1st minute APGAR score, which was significantly higher in group A. Comparable with the study done by Fyneface organ et al[11].

NICU admission:
Out of 50 parturients, 2 (4%) babies admitted in NICU in group A.
Group B, out of 50 parturients 3 (6%) babies admitted in NICU.
The result are comparable in the groups. NICU admission was of infant with meconium stained liquor.

Mean umbilical artery blood PH:
The mean of umbilical artery blood pH of group A 7.25±0.05.
The mean of umbilical artery blood pH of group B 7.25±0.02.
In our study, it was found that no significant difference in the mean umbilical artery blood Ph.

Comparable with the study done by Fyne face ogan et al[11].

Abu- Halaweh et al[12] used intravenous dexmedetomidine as an adjunct to opioid based PCA and general anesthesia for labor analgesia and cesarean section in a parturients with favorable maternal and neonatal outcome.

There was no significant difference between the two groups with respect to maternal patient characteristics such as age, weight, parity. Baseline VAS for pain and cervical dilatation at initiation of labor analgesia.

CONCLUSION

- Epidural analgesia during labor using levo-bupivacaine with dexmedetomidine is associated with significant reduction in duration of second stage of labor.
- The onset of analgesia was faster and longer in group A.
- The baseline VAS was comparable in the two groups,but the subsequent records higher VAS in group B.
- Dexmedetomidine provided longer duration of spinal analgesia and lower VAS when added to levo-bupovacaine.
- 1st minute APGAR score, which was significantly higher in group

A.

- No association between epidural analgesia and cesarean section in our study.
- Maternal hypotension and other side effects were comparable in both groups and were controllable
- Our study showed that intrathecal dexmedetomidine as an adjuvant prolonged the duration of analgesia and also improve postoperative analgesia without increasing incidence of adverse events with safe outcomes for mother and babies.

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