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Effectiveness of Intrathecal Dexmedetomidine and Fentanyl as Adjuvant to Bupivacaine for Labour Analgesia: A Study Protocol

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Study Protocol

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ABSTRACT

Background: The most commonly used labour analgesia is epidural. Another alternative method is intrathecal low dose analgesic, given for providing labour analgesia in the areas where the epidural kit, multiparameter monitors, staff members scarcity is present. Fentanyl has been used widely to decrease motor block effect of local anaesthetics during labour, presence of these opioids along with local anaesthetics can cause pruritus and respiratory depression. Selective α2- agonist Dexmedetomidine (DMT) helps in providing stable haemodynamic parameters, and an effective intraoperative and postoperative analgesia. This study aims to compare the effectiveness of an intrathecal analgesia during labor, using bupivacaine in combination with dexmedetomidine and fentanyl in terms of quality and duration of analgesia.

Materials and Methods: This will be a prospective comparative observational study. Total 80 patients will be included in the study and assigned to two groups by computerized randomization method. GROUP BD (n=40) will receive an intrathecal 0.5% hyperbaric bupivacaine dose 2.5 mg along with dexmedetomidine dose 2.5 µg .GROUP BF (n=40) will receive an intrathecal 0.5% hyperbaric bupivacaine 2.5mg with fentanyl 25mcg. Data will be analysed and Quality and duration of analgesia will be compared for both groups.

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Expected Results: Significant difference is expected in labor analgesia and safety profile with the combination of intrathecal bupivacaine and dexmedetomidine compared to combination of bupivacaine and fentanyl.

Keywords: Labor analgesia; intrathecal; dexmedetomidine; bupivacaine; combination; fentanyl.

1. INTRODUCTION

Normally lack of psychological satisfaction in antenatal patients -fear, anxiety stress highly increases the sensitivity to the pain so relief from pain (analgesic effect) during labour reduces the stress hormones levels in the body and improves the fetal outcome [1].

Although most commonly used in labour analgesia is the utilization of epidural [2] as it has added advantage of providing flexibility according to patients need [3,4]. The another alternative method is intrathecal low dose analgesic, given for providing labour analgesia in the areas where the epidural kit, multiparameter monitors, staff members scarcity is present.

According to several studies the use of bupivacaine Intrathecally for achieving analgesia during labour proved to be effective [5]. Main favourable point of this method is its onset (rapid),with minimal hemodynamic effects. Many adjuvants to intrathecal bupivacaine have been added in various studies for the assessment of sensory block duration.

Example like- fentanyl, sufentanyl, morphine, clonidine, and dexmedetomidine etc. This Fentanyl has been used widely to decrease motor block effect of local anaesthetics during labour, presence of these opioids along with local anaesthetics can cause pruritus and respiratory depression.

Selective α2- agonist Dexmedetomidine (DMT) helps in providing stable haemodynamic parameters, and an effective intraoperative and postoperative analgesia [6].

Research Question: Which combination of study group is more effective for Labour Analgesia and Neonatal outcome.

For labour analgesia, a method to be known as best alternative should provide adequate pain relief, with lesser side-effects on mother and fetus, Like- Intrathecal labour analgesia, it is more economical also as it is proved to be useful method especially in the rural and peripheral areas.

Rationale: Dexmedetomidine and fentanyl like adjuncts when added to bupivacaine reduces the need of additional analgesia, Bupivacaine is being used here for labour because of its property of minimal transfer to placenta. During the second stage of labour pain is of visceral plus somatic origin, it can't be managed alone with neuraxial opioids, thus to assess the effect of these combinations with bupivacaine on labour pain, hemodynamic parameters and Neonatal outcome, the study is evaluated, hence the purpose of the study.

2. AIM AND OBJECTIVES

Aim: Comparing the effectiveness of intrathecal analgesia during labour, using bupivacaine in combination with dexmedetomidine and fentanyl.

2.1 Primary Objective

Comparing the duration and the quality of Analgesia.

2.2 Secondary Objective

1. Evaluate haemodynamic effect of Adjuvants when given intrathecally .
2. Neonate Outcome
3. Maternal satisfaction score
4. Side effects

3. MATERIALS

3.1 Study- Design

Study Period: 2 yr. 6 months
Study Area - Department of Anaesthesia & JNMC, AVBRH
Research Design - Prospective observational study
Study Population - Multiparous parturient

3.2 Participants

3.2.1 Inclusion criteria

1. Pts. With Term pregnancy (singleton foetus)

2. Cervical dilatation of atleast 5cm
3. All vertex presentation
4. Uncomplicated pregnancies
5. Multi gravida of physical status ASA grade2

3.2.2 Exclusion criteria

1. Patient refusal.
2. Cephalopelvic disproportion and bad obstetric history.
3. Active maternal haemorrhage
4. Maternal sepsis or infection (needle insertion site)
5. Maternal deranged coagulation profile.
6. Preeclampsia.
7. Preterm labour.
8. Morbid obesity (BMI>35).
9. Twin pregnancy.
10. Scoliosis.
11. Neurologic disorders
12. Previous caesarean section

3.3 Statistical Analysis

Analysis of collected data done by SPSS version 25.0, Continuous co- variables are analysed using ANOVA (Analysis of Variance). Categorical co-variables was studied using chi-squared test or the Fisher's exact test a with the P value at the 95% confidence interval.

3.4 Sample size calculation

In this the level of significance P = 0.05 is used. For calculating the sample size, the power analysis of ([alpha] = 0.05 and [beta] = 0.90), keeping power at 80% shown that 40 patients in each study group needed for observing an increase of 30 min difference in the duration of spinal sensory block between the groups.

We calculate sample size by taking mean and standard deviation of: Time taken for the sensory block to reach T10 dermatome level on a study done A Comparative Study of an Intrathecal 2.5 Mg Dexmedetomidine and the Fentanyl 25 Mg as Adjuvants to Bupivacaine 2.5 Mg for Labour Analgesia value came out to be 38 by using this software, so we have taken sample size as 40 to compensate for possible drop outs.

4. METHODOLOGY

History and clinical examination of each patient was done. All Routine investigations were obtained and noted.

The parturients were attached with the monitor for baseline vitals assessment (pulse rate, blood pressure) the foetal heart rate recorded at different time intervals.

The assessment of uterine contractions and cervical dilatation was done simultaneously. Preloading with fluids- ringer lactate or normal saline was done.

Parturients were positioned in sitting position on attainment of 5 cm cervical dilatation, for the administration of the local anaesthetic.

The skin surface over the L3-L4 intervertebral space was anaesthetized with 2 mL (1% lidocaine). 26 G spinal needle used to inject the drug intrathecally in L3- L4 intervertebral space, at the time of uterine contractions.

The Pelvic examination was done every 2 hours interval for assessing the progress of labour.

The sensory block level assessment:- By absence of sensation on pin prick. The time from giving of intrathecal injection to the time when a sensory level of T10 achieved is define as the onset of sensory blockade.

Sensory regression to S1 dermatome, and the motor block regression to Bromage 0 were recorded. All the durations were calculated in relation to the time of spinal injection. Duration of pain relief is defined as the time from injecting spinal drug to the first demand of patient for analgesics or when the VPS was 4.

Motor block (using Bromage scale): Degree of any motor blockade is assessed in the following manner.

- Grade 0 -No block): complete flexion of knees& feet possible
- Grade1- (Partial block) : pt. is able to flex knees & feet slightly.
- Grade II - (Almost complete): not able to flex knees , but flexion of feet possible
- Grade III – (Complete block): not able to move legs or feet.

Quality of analgesic effect was assessed by using VAS score. VAS was recorded every minute after intrathecal injection for the first 5 min and then at an interval of 15 min. The onset of analgesic effect was defined as the time from giving drug intrathecally to the time of recording a

VAS score came less than 3 during active uterine contraction period.

The Duration of analgesic effect was defined as the time from giving drug intrathecally to the time when VAS value came more than 3.

Using verbal pain score (VPS) ranging from 0 =no pain up to 10 = severe pain, Pain intensity could be assessed. Pain at the peak of a contraction is assessed, immediately before spinal analgesia, every 5 min interval for 30 min and then every 15 min interval until demand for further analgesia by patient.

In cases if labour gets prolonged and the anaesthesia effect reduces before deliver, repeat dose of drug is administered to patient.

Assessment and Monitoring: Following parameters are recorded:

Maternal Heart Rate and Blood Pressure: (manual sphygmomanometer) initially for half an hour every 5min. we will assess, then every 30 min. If decrease in B.P is >20% when compared to initial baseline blood pressure then, considered as maternal hypotension and it is treated with giving more intravenous fluids to patient. and if spo2 <90% (desaturation), it is treated by giving oxygen to patient via facemask

Bradycardia: Defined as heart rate < 50 beats/minute. Bradycardia is treated with atropine given bolus of(0.6mg).

Foetal heart rate: It is monitored continuously by using Doppler(foetal)

Occurrence of any adverse events: Bradycardia, pruritis, nausea, hypotension, respiratory depression are also looked for and appropriately treated.

Neonatal Apgar score: HR, RR, skin colour, muscle tone and grimace response to stimulus if these parameters at 1min, 5min. are <7, then it is considered as significant.

Maternal Satisfaction Following Delivery: It is assessed by asking the parturient about pain relief. We also enquired for their willingness to participate in promoting and propagating this technique by sharing their experiences with women residing in remote villages.

Excellent: Patient is comfortable, analgesia effect is adequate, no addition of drugs required during the procedure.

Good: Analgesia effect is adequate, minimum discomfort present to patient during the procedure.

Poor: Patient complaining severe, intolerable pain.

The questions related to maternal satisfaction with delivery and the technique were answered on factors: - Anaesthetic effects, post-op problems, minor side effects.

Other things included in analysis - baseline heart rate of foetus, no. of accelerations/ decelerations(per 20 min), no. of uterine contractions (per 20 min).

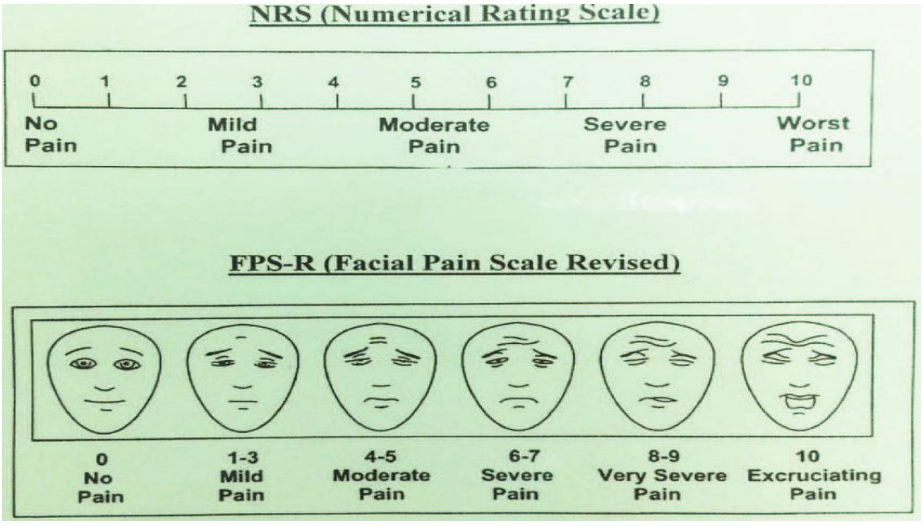

Fig. 1. Numerical rating scale

In postpartum period all the patients were admitted for 48 hrs, for the close observation and they were advised for the bed rest and appropriate intake of fluids and also to inform immediately if headache developed at home upon discharge.

Expected outcome: Duration of labour analgesia and overall effect on labour would be greater in group bupivacaine and dexmedetomidine as compared to other group whereas effect on neonatal outcome would be similar in both the groups.

5. DISCUSSION

In our study use of intrathecal bupivacaine along with dexmedetomidine will prolong the duration of analgesia effect in labouring parturient. These findings result in the addition of intrathecal opioids [7]. Use of local anaesthetics, alpha-2 adrenergic agonist among these patients. The labouring patients group who had received bupivacaine with dexmedetomidine had a (VAS) scores of longer duration as compared to group receiving bupivacaine along with fentanyl. This analgesic effect of dexmedetomidine can be due to the synergistic effect of dexmedetomidine with the local anaesthetics, which can lead to preserving of maternal efforts, as very low dose of intrathecal bupivacaine with dexmedetomidine is used. Few of the related studies were reported [8-11].

S. Fynefac-Ogan and C.E. Enyindah studied intrathecal low dose bupivacaine/ dexmedetomidine in 90 multiparous women in labour, it resulted in prolonged duration of analgesia in significant number. This finding increases the efficacy of intrathecal opioids, local anaesthetics and alpha –2 adrenergic agonist, in laboring women.

The parturient group, received bupivacaine plus dexmedetomidine combination fentanyl combination or only bupivacaine. Mechanism of action of dexmedetomidine is by binding to the presynaptic {C-fibres} and postsynaptic neurons. On the other hand, fentanyl (μ-receptor agonist) creates its effect intrathecally, it combines with opioid receptors in the dorsal horn of the spinal cord and exerts its effect By supraspinal spread and action. This study proves that α2-adrenergic agonist increases analgesia effect from bupivacaine.

Chauhan et al. Ain-Shams conducted a prospective study, among 100 labouring parturients. GROUP S (n= 50) have received intrathecal dose 0.5 ml of heavy bupivacaine (2.5 mg) & 0.5 ml of fentanyl (25 μg), and also 1 ml of preservative free morphine (250 μg/ml) was given (total volume of 2 ml) using 26 G Quincke needle. GROUP C n= 50) patients were managed for normal vaginal delivery. They concluded that intrathecal low dose analgesia with heavy Bupivacaine + fentanyl + morphine can be used effectively in both primi & multi parturients with no increase in risk of C-section among patients. Few more studies on similar aspects were reviewed [12-15].

In a study by O. Adeyemi, R. Vernon, and O. Medge, Intrathecal dexmedetomidine-fentanyl combination was used for labour analgesia. This randomized comparative study was done in 90 patients aged (19-39 yr.). Patients randomly divided into 3 groups: GROUP D: 30 patients received 10 μg dexmedetomidine intrathecally in 1 ml of NS(normal saline), GROUP F: 30 patients received 20 μg fentanyl intrathecally in 1 ml of NS and GROUP DF: 30 patients received 5 μg dexmedetomidine plus 10 μg fentanyl intrathecally in 1 ml of NS. Side effects, neonatal outcome, neonatal Apgar score and other parameters recorded. They concluded that the dexmedetomidine group & dexmedetomidine-fentanyl combination group have prolonged duration of analgesia. Pulse rate and MAP was lowest in the group receiving dexmedetomedine as compared to other 2 groups, whereas increase in the adverse effect incidence (pruritus) was seen in fentanyl group [16-17].

Murphy J.D et al in 1991**,** compared a combination of the Bupivacaine with fentanyl and the Bupivacaine alone for spinal analgesia effect in labouring patients and evaluated for the parameters that can influence the maternal satisfaction. This study was prospective randomised study. GROUP 1 mothers were given Bupivacaine (0.25%) 5mL top up doses when requested for, GROUP 2 mothers given Bupivacaine (0.25%) 4mL if pain was restricted to the abdomen whereas(0.1%) Bupivacaine with Fentanyl (50micgm), concentration given if pain appeared in perineum also. Main outcome measures-Overall maternal satisfaction. Result of study showed that maternal satisfaction was higher in group 2, and was associated with more no. of normal deliveries, Group 1 patients have restricted movements. When Fentanyl was added to Bupivacaine, it reduced the need for local anaesthetic use without affecting analgesia. They concluded - Fentanyl can be effectively

combined with Bupivacaine as it provides beneficial effect on maternal satisfaction score.

Mohamed Fouad Selim et al studied doppler velocimetry of uterine & umbilical arteries during epidural and spinal labour analgesia with bupivacaine-fentanyl combination / bupivacaine-dexmedetomidine in 130 labour patients. Control group consists of 30 women who did not receive epidural analgesia and remaining hundred divided into study group, 50 each. Study group showed side-effects like- hypotension, incidence of nausea & vomiting as compared to the control group . Pulsatile indices of uterine & umbilical arteries at various time intervals at the baseline, 30min., 60 & 120 min. recorded. Group BD and BF (epidural analgesia groups) showed marked increase in UtA-PI (pulsatility indices) when compared with the control group during uterine contractions & relaxations [18-19].

6. CONCLUSION

Rapid action of onset of analgesia with minimal haemodynamic changes and minimal side-effects when given intrathecally provides the flexibility to meet the needs of patients widely and provides maternal satisfaction. Thus increases the effectiveness and safety of intrathecal analgesia for labour.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent will be collected and preserved by the author(s).

ETHICAL APPROVAL

The study will be conducted after approval of the Ethics committee of Datta Meghe Institute of Medical Sciences, (JNMC), (AVBRH), Sawangi, Wardha, during the period of September 2020 to September 2022.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Onah HE, Obi SN, Oguanuo TC, Ezike HA, Ogbuokiri CM, Ezugworie JO. Pain perception among parturients in Enugu, South-Eastern Nigeria. Journal of Obstetrics and Gynaecology. 2007;27(6): 585–588.
2. Fyneface-Ogan S, Mato CN, Anya SE. Epidural anesthesia: Views and outcomes of women in labor in a Nigerian hospital. Annals of African Medicine. 2009;8(4): 250–256.
3. Reynolds F, Crowhurst JA. Opioids in labour—no analgesic effect. The Lancet. 1997;349:4–5.
4. Lebovits AH, Zenetos P, O'Neill DK, et al, Satisfaction with epidural and intravenous patient-controlled analgesia," Pain Medicine. 2001;2(4):280–286.
5. Adeyemi O, Vernon R, Medge O. A spinal labour analgesia protocol for Ghana. In Proceedings of the 4th All Africa Anaesthesia Congress. 2009;67–68.
6. Martin E, Ramsay G, Mantz J, Sum-Ping STJ. The role of the α2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. Journal of Intensive Care Medicine. 2003;18(1): 29–41.
7. Wong CA, Scavone BM, Slavenas JP, et al. Efficacy and side effect profile of varying doses of intrathecal fentanyl added to bupivacaine for labor analgesia. International Journal of Obstetric Anesthesia. 2004;13(1):19–24.
8. Singh S, Sen J. The Effect of Intrathecal Magnesium Sulfate to Bupivacaine-Fentanyl Subarchanoid Block for Infraumblical Surgeries. Journal of Datta Meghe Institute of Medical Sciences University. 2019;14(3):196–201. Available:https://doi.org/10.4103/jdmimsu.jdmimsu_83_19.
9. Bhuyan D, Chandak AV, Singam A, Chaudhari SS. A Study on Analgesic Efficacy of Intrathecal Bupivacaine and Fentanyl with Intrathecal Midazolam for Lower Limb Surgeries. International

Journal of Pharmaceutical Research. 2019;11(4): 2054–59.
Available:https://doi.org/10.31838/ijpr/2019.11.04.511.

10. Singh S, Sen J. The Effect of Intrathecal Magnesium Sulfate to Bupivacaine-Fentanyl Subarchanoid Block for Infraumblical Surgeries. Journal of Datta Meghe Institute of Medical Sciences University. 2019;14(3):196–201.
Available:https://doi.org/10.4103/jdmimsu.jdmimsu_83_19.
11. Dongre P, Chandak AV, Singam A, Bapat AV. Evaluation of Low Dose Dexmedetomidine and Neostigmine with Bupivacaine for Post-Operative Epidural Analgesia in Lower Limb Orthopedic Surgeries. International Journal of Pharmaceutical Research. 2019;11(2): 1874–77.
Available:https://doi.org/10.31838/ijpr/2019.11.02.216.
12. Jejani AS, Chaudhari A, Singam A. Study of Intrathecal Buprenorphine for Postoperative Analgesia after Cesarean Section. Research Journal of Pharmacy and Technology. 2019;12(12):6062–66.
Available: https://doi.org/10.5958/0974-360X.2019.01052.7.
13. Rajan R, Gosavi SN, Dhakate V, Ninave S. A Comparative Study of Equipotent Doses of Intrathecal Clonidine and Dexmedetomidine on Characteristics of Bupivacaine Spinal Anesthesia. Journal of Datta Meghe Institute of Medical Sciences University. 2018;13(1): 4–8.
Available:https://doi.org/10.4103/jdmimsu.jdmimsu.
14. Varghese LA, Taksande K. A Comparison between Intrathecal Dexmedetomidine with Hyperbaric Bupivacaine and Intrathecal Fentanyl with Hyperbaric Bupivacaine in Lower Abdominal Surgeries: A Prospective Double-Blinded Study. Journal of Datta Meghe Institute of Medical Sciences University. 2017;12(2):99–109.
Available:https://doi.org/10.4103/jdmimsu.jdmimsu_55_17.
15. Deshmukh P, Sangawar M, Dhumne N, Chakole V. The Spinal Adjuvent-Intrathecal Nalbuphine as Effective as Intrathecal Fentanyl. International Journal of Research in Pharmaceutical Sciences. 2020;11(3): 4492–98.
Available:https://doi.org/10.26452/ijrps.v11i3.2676.
16. Rai A, Datarkar A, Borle RM. Are maxillomandibular fixation screws a better option than Erich arch bars in achieving maxillomandibular fixation? A randomized clinical study. Journal of oral and maxillofacial surgery. 2011;69(12):3015-8.
17. Bourne R, Steinmetz JD, Flaxman S, Briant PS, Taylor HR, Resnikoff S, Casson RJ, Abdoli A, Abu-Gharbieh E, Afshin A, Ahmadieh H. Trends in prevalence of blindness and distance and near vision impairment over 30 years: an analysis for the Global Burden of Disease Study. The Lancet Global Health. 2021;9(2):e130-43.
18. Borle RM, Nimonkar PV, Rajan R. Extended nasolabial flaps in the management of oral submucous fibrosis. British Journal of Oral and Maxillofacial Surgery. 2009;47(5):382-5.
19. Franklin RC, Peden AE, Hamilton EB, Bisignano C, Castle CD, Dingels ZV, Hay SI, Liu Z, Mokdad AH, Roberts NL, Sylte DO. The burden of unintentional drowning: global, regional and national estimates of mortality from the Global Burden of Disease 2017 Study. Injury prevention. 2020;26(Supp 1):i83-95.

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