Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Comparative Study of Intrathecal Dexmedetomidine vs Fentanyl as an Adjuvant to Hyperbaric Bupivacaine.

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Received: March 2017
Accepted: March 2017

ABSTRACT

Background: Various adjuvants are used to local anaesthetics in neuraxial block to produce prolonged post-operative analgesia. Dexmedetomidine, an α_2 adrenoceptor agonist, has additive action when used in subarachnoid block with local anaesthetics. Fentanyl is also used as an adjuvant to local anaesthetics for prolongation of postoperative analgesia in subarachnoid block. Aim of this study was to compare the onset and duration of sensory & motor block , hemodynamic effects , post-operative analgesia , sedation score and any adverse effects between intrathecal dexmedetomidine and intrathecal fentanyl as adjuvant to hyperbaric bupivacaine. **Methods**: A randomized double blind study was carried out taking 90 patients of ASA grade I & II of age group between 18 -70 years of either sex, randomly allocated into two groups . Group D received dexmedetomidine 5 mcg and Group F received fentanyl 25 mcg with intrathecal hyperbaric bupivacaine 15 mg. **Results:** Patients in Group D had significantly prolonged sensory block , motor block , post-operative analgesia and sedation score in comparison to group F . The hemodynamic parameters were insignificant between the two groups.**Conclusion**: Intrathecal dexmedetomidine is a better alternative to intrathecal fentanyl as it causes prolonged motor and sensory block, minimal hemodynamic variation and less requirements of rescue analgesics in 24 hours when added to hyperbaric bupivacaine

Keywords: Dexmedetomidine, Fentanyl, Spinal anaesthesia , Postoperative analgesia.

INTRODUCTION

Spinal anesthesia is the most common and popular technique for lower limb surgeries. The most common local anesthetic used for this technique is 0.5% hyperbaric bupivacaine: However the anesthesia provided by bupivacaine alone may be short in duration for prolonged surgeries. The current practice in modern anesthesia is to add small doses of adjuvants to local anesthetics to fasten the onset time, improve quality of intra-operative anesthesia, prolong analgesia and decrease the complications associated with intrathecal administrations of high dose of hyperbaric bupivacaine alone.[1,2]

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Fentanyl in various doses when added to hyperbaric bupivacaine for subarachnoid block produce prolonged duration of analgesia .But it is associated with respiratoy dipression, pruritus and retention of urine.[3-5]

Dexmedetomidine a highly slective alfa 2 agonist having numerous benefits when used for nuroaxial block.[6] It acts on both pre and post synaptic sympathetic nerve terminals as well as on central nervous system thereby decreasing the sympathetic outflow and also nonadrenaline release causing sedation, antianxity ,analgesic and sympatholytic effects. However as it lack opoid like properties so opoid related side effects are not found. This has a definite benefit over fentanyl.

So a prospective study was carried out to evaluate and compare perioperative analgesic and other hemodynamic parameters between fentanyl and dexmedetomidine as adjuvant to hyperbaric bupivacaine in subarachnoid block.

MATERIALS AND METHODS

After taking approval from hospital ethical committee, a prospective randomized double blind study was carried out on 90 adult patients of ASA grade I & II of either sex between age group of 18 to 70 years admitted for lower limb orthopaedic surgeries under subarachnoid block between time periods from December 2015 to December 2016. Normal exclusion criteria of spinal anaesthsia were followed. After undergoing pre-anaesthetic checkup & obtaining lab investigation reports , the patients who were fit for surgery were advised to take tab

alprazolam 5 mg & tab ranitidine 150 mg in the night before surgery & also to remain 6 hours of fasting .All the patients were well explained about the procedure of spinal anaesthesia and VAS for expreesing the pain score .

On the day of surgery after taking informed consent, patients were given computer generated random numbers and were allocated into 2 groups of 45 patients in each group.

GROUP – D: (n=45) received 15 mg of 0.5% hyperbaric bupivacaine & 5 mcg of dexmedetomidine in 0.5 ml NS intrathecally.

GROUP – F: (n=45) received 15 mg of 0.5% hyperbaric bupivacaine & 25 mcg fentanyl intrathecally. Both the groups received 3.5 ml drug solution intrathecally. In the operating room multipara monitor was connected for continuous recording of heart rate (HR), SpO_2, non-invasive blood pressure (NIBP), ECG .The basal parameters were recorded. IV line secured with 18G cannula & preloaded with crystalloid 10 ml/kg body weight. Under all aseptic precautions, spinal anaesthesia was given with either of the study drug in sitting position at L_3-L_4 intervertebral space by a 25G quincke's spinal needle and the patint made to supine immediately . Here both the patient and treating anaesthesist were blind about the study drug injected.

The following parameters were studied

1. Sensory block - tested by pin prick method every 2 minutes & following observations were noted
   a) Time to reach sensory block at T10 dermatome
   b) Maximum level of upward spread
   c) Time to reach peak block hight
   d) Time for two segment regression
   e) Time for requirement for rescue analgesia (VAS pain score >3)
2. Motor block level was assessed by modified Bromage scale.[7]
3. Quantification of pain score was assessed by VAS pain score 0 – 10, where 0 being no pain & 10 being worst possible pain.
4. Haemodynamic variables were studied at 5 minutes interval during intra-operative period & 30 minute interval in post-operative period for 8 hours in ward. HR, SpO_2, NIBP & ECG were recorded. Hypotension (ie. SBP < 90 mm of Hg or MAP < 20 % from baseline) was treated with i.v. injection mephenteramine 5 mg incremental doses as needed. Bradycardia (HR <60 beats/min) was treated with inj. Atropin 0.6 mg i.v. O_2 supplementation was given through face mask @ 5 l/min if SpO_2 falls <90 %.
5. Perioperative side effects like nausea, vomiting, tremor, headache or any transient neurological symptoms were noted.
6. Level of sedation was assessed by Modified Ramsay Sedation Score.[8]

Statistical analysis

Collected data were analyased with the help of SPSS software version 16. Neumerical parametric data were compared by unpaired t-test. Nominal & ordinal data were compared by Fisher's exact test .P < 0.05 was considered statistically significant. Frequencies expressed as number and percentage.

RESULTS

Table 1: Demographic profile

	GROUP D (Mean ± SD)	GROUP F (Mean ± SD)	P value
Age (years)	57.95 ± 8.91	58.32 ± 8.79	> 0.05
Sex (M:F)	33:12	38 :07	
Height (cm)	162.35 ±1.96	162.35 ± 1.55	>0.05
Weight (kg)	73.55 ±10.1	72.53 ±10.2	>0.05
Duration of surgey (min)	98.86 ±8.56	98.36 ± 8.69	>0.05

This table shows there is no significant difference in demographic characteristics between the two groups.

Table 2 Comparison of subarachnoid block characteristics

	GROUP D (Mean ± SD)	GROUP F(Mean ± SD)	P value
Time to reach T10segment (min)	5.36 ±0.61	4.6 ±0.49	0.00
Highest level of sensory block	T4 / T5 / T6	T4 / T5 / T6	
Number of patients	4 / 26 / 15	3 / 25 / 17	
Time to reach highest level of sensory block (min)	10.90 ±0.61	10.16 ±0.83	0.004
Time to reach Bromage 3 motor block (min)	8.73 ±0.69	8.73±0.64	1.00
Time for two segment regression (min)	153.17 ±12.22	98.5 ±9.48	0.00
Duration of analgesia (min)	291.33 ±13.55	180.33 ±10.08	<0.05

It is found that, to achieve T_{10} level of sensory block was significantly prolonged in group D in comparison to group F. The highest level of sensory block reached is comparable in both the groups. But the time to reach highest level was significantly prolonged in group D in comparison to group F. The onset of motor block (Bromage 3) is comparable between two groups. Two segment sensory regression time was significantly prolonged in group D. Duration of analgesia is prolonged significantly in group D in comparison to group F. Rescue analgesia is given when VAS > 3 by inj.Diclofenac 75 mg i.m.

There was no significant difference in systolic blood pressure (SBP) among two groups.

It shows no significant change in HR among two groups.

Group D patients are more sedated in comparison to Group F.

Among other side effects, only two cases in Group F developed vomiting & three cases pruritis. No cases in Group D developed pruritus or vomiting.

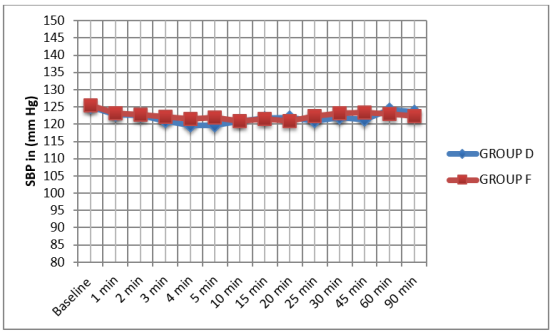

Figure 1: Comparison of mean systolic blood pressures.

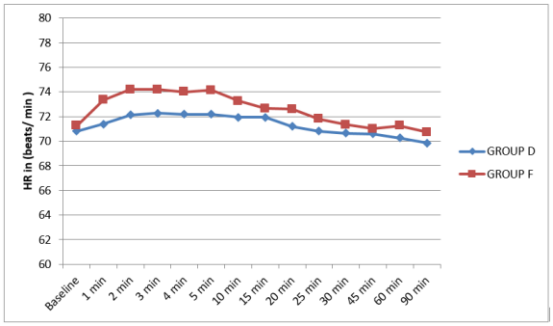

Figure 2: Comparison of HR (beats / min).

Table 3: Comparison of intraoperative sedation [Ramsay sedation score (RSS)]

	GROUP D	GROUP F
RSS	1/2/3	1/2/3
No. of patients	3 / 12 / 30	4 / 30 / 11
% of patients	6.6 % / 26 % / 66.6 %	8.8% / 66.6 % / 24.4 %

DISCUSSION

The use of conventional local anaesthetics like bupivacaine has been unable to provide analgesia for an extended duration.[11] Most patients require further analgesics during the postoperative period. Various adjuvants are added to local anesthetics for this purpose. Among the myriad list of LA adjuncts, magnesium seems to have several advantages.[1]

Safety of intrathecal magnesium sulphate has been studied in animal models. Though earlier studies encouraged the use of intrathecal magnesium concurrent animal research published recently has raised questions regarding safety of intrathecal magnesium.[12-15] However, IT magnesium has been used in significant number of humans and there were no documented neurological complications.[16] Histopathological and ultra-structural human spinal cord studies may sound interesting but are practically next to impossible. In such circumstances off label use of magnesium intrathecally is supposed to thrive because of its advantages.

Optimum dose and concentration of IT magnesium for antinociceptive action is an untrodden area in research. In the first human study on IT magnesium the dose was fluked out from within the safety range extrapolated from animal studies Recently,[9] few studies have used higher doses and shown antinociceptive action but regression analysis of dose response relationship has not been performed and there is still scope for further higher doses. [10]

Seyhan et al.[17] studied the effect of three different doses of Mg on postoperative consumption of morphine, and a single dose of 40 mg/kg was found to decrease postoperative morphine consumption, when this dose was followed by a continuous infusion of 10 mg/kg/hr, the effect was enhanced. However, increasing the infusion dose to 20 mg/kg/hr led to hemodynamic instability without additional analgesic effect. Perioperative administration of Mg sulphate (50 mg/kg) and continuous infusion of (15 mg/kg/hr) in gynecology patients receiving total i.v. anesthesia decreased rocuronium requirements and improved postoperative analgesia without significant side effects.[18] Several studies have investigated the effect of intrathecal and i.v. Mg as adjuvant to bupivacaine and fentanyl spinal anesthesia on postoperative pain and analgesic consumption and have shown that both intrathecal and i.v. Mg are safe and prolong the time to first analgesic requirement. Based on the previous studies, a bolus dose of magnesium sulfate (50mg/kg) and continuous infusion of (15mg/kg/hr) in group B and a dose of 75 mg magnesium sulphate as intrathecal adjuvant to bupivacaine in group A was used. In the present study, the incidence of complications was very minimal. Others studies conducted using 50mg of intrathecal magnesium did not show any increased incidence of complications.[7,19] However Jabalameli et al showed that 100mg of intrathecal magnesium is associated with increased incidence of intraoperative and postoperative complications like hypotension, [20] nausea, vomiting compared with lower doses and with placebo. However, he did not find any difference in the requirements of ephedrine or atropine. Nevertheless, IT magnesium has been used in significant number of humans and there have been no documented neurological complications.[16]

Onset of analgesia at T6 was delayed with intrathecal magnesium sulphate compared to intravenous magnesium and placebo. Time to 2 segment regression of sensory block, duration of spinal anaesthesia as well as duration of effective analgesia were significantly prolonged in intrathecal as well as intravenous magnesium as compared to placebo. Duration and onset of motor block was similar across all three groups. Intrathecal or intravenous magnesium were not associated with significant side effects. In the present study, serum Mg concentrations in group B were significantly higher than the other 2 groups, at 6 h postoperative.

These high levels, however, were safely less than the toxic levels (Mg toxicity begins at serum concentration of 2.5–5mmol/L, cardiac arrest occurs at 12.5mmol/L). An inverse relationship has been found between the severity of postoperative pain and serum magnesium level. Accordingly, prevention of perioperative hypomagnesaemia is an important factor for antinociceptive mechanism.[18]

Co-administration of intravenous Mg sulfate or intrathecal Mg given to patients undergoing spinal anesthesia for elective infraumbilical surgeries could improve pain control for the first 24 h after surgery. While there was no significant difference between the two modalities as regard pain scores, however, i.v. Magnesium led to relative hypotension and decreased blood loss. Intrathecal as well as intravenous magnesium sulphate significantly prolonged the time for the first analgesic request, thus substantiating their use in postoperative analgesia.

The present study has the following limitations:

1. In the inclusion criteria, patients undergoing infraumbilical surgeries including lower limb surgeries were selected. This was done to have a larger sample size. This could have been narrowed down to specific surgeries like hip replacement surgery, arthroscopy, etc.
2. Postoperative opioid consumption was not compared between the groups due to technical problems.
3. Prolonged follow up of patients for neurological deficits was not done.

Comparison of magnesium with other agents was not studied.

REFERENCES

1. Morrison AP, Hunter JM, Halpern SH, Banerjee A. Effect of intrathecal magnesium in the presence or absence of local anaesthetic with and without lipophilic opoids: a systematic review and meta – analysis. British Journal of Anaesthesia. 2013; 110(5):702-12.
2. Khangure N. Adjuvant agents in neuraxial blockade. Anaesthesia tutorial of the week. 230 (2011). Available from http://totw.anaesthesiologists.org/category/atotw/
3. Christiansson L. Update on adjuvants in regional anaesthesia. Periodicum Biologorum. 2009;111(2):161–170
4. Hodgson PS, Neal JM, Pollock JE, and Liu SS. The Neurotoxicity of Drugs Given Intrathecally (Spinal). Anesth Analg. 1999;88:797–809.
5. Woolf CJ, Thompson SW. The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation: implications for the treatment of post injury pain and hypersensitivity states. Pain. 1991; 44:293-9.
6. Thurnau GR, Kemp DB, Jarvis A. Cerebrospinal fluid levels of magnesium in patients with preeclampsia after treatment with intravenous magnesium sulphate: a preliminary report. Am J Obstet Gynaecol. 1987; 157:1435-8.
7. Paul S, Bhattactarjee DP, Ghosh S, Chatterjee N. Efficacy and safety of intrathecal magesium sulphate as a adjuct to bupivacaine for lower limb orthopaeadic surgery. Pharmacology online. 2009; 2:570-574.
8. Malleeswaran S, Panda N, Mathew P, Bagga R. A randomized study of magnesium sulphate as an adjuvant to intrathecal bupivacaine in patients with mild preeclampsia undergoing caesarean section. International Journal of Obstetric Anesthesia. 2010; 19:161-6.
9. Buvanendran A, McCarthy RJ, Kroin JS, Leong W, Perry P, Tuman KJ. Intrathecal magnesium prolongs fentanyl analgesia: A prospective, randomised, controlled trial. Anesth Analg. 2002; 95:661-6.
10. Lee JW, Kim MK, Shin Y, Koo B. The analgesic effect of single dose of intrathecal magnesium sulphate. Korean J Anesthesiol. 2007; 52:72-6.
11. Safiya I Shaikh, M Kiran. Intrathecal buprenorphine for postoperative analgesia: A prospective randomised double blind study. J Anaesth Clin Pharmacol. 2010; 26(1):35-8.
12. Chanimov M, Cohen ML, Grinspun Y, Herbert M, Reif R, Kafman I and Bahar M. Neurotoxicity after spinal anaesthesia induced by serial intrathecal injections of magnesium sulphate. Anaesthesia. 1997; 52: 223-228.
13. Hiroshi Saeki, Mishiya Matsumoto, Shuichi Kaneko, Shunsuke Tsuruta, Ying Jun Cui, Kazunobu Ohtake, et al Is Intrathecal Magnesium Sulfate Safe and Protective Against Ischemic Spinal Cord Injury in Rabbits? Anesth Analg. 2004; 99:1805–12.
14. Simpson JI, Eide TR, Schiff GA, et al. Intrathecal magnesium sulfate protects the spinal cord from ischemic injury during thoracic aortic cross clamping. Anesthesiology. 1994; 81: 1493–9.
15. Levent Ozdogan , Handan Sastim , Dilsen Ornek, Aysun Postaci , Taner Ayerden , Bayazit Dikmen Neurotoxic Effects of Intrathecal Magnesium Sulphate.Rev Bras Anestesiol. 2013; 63(1):139-148
16. Albrecht E, Kirkham KR, Liu SS and Brull R. The analgesic efficacy and safety of neuraxial magnesium sulphate: a quantitative review. Anaesthesia. 2013; 68: 190–202
17. Seyhan TO, Tugrul M, Sungur MO, Kayacan S, Telci L, Pembeci K, Akpir K. Effects of three different dose regimens of magnesium on propofol requirements, haemodynamic variables and postoperative pain relief in gynaecological surgery. Br J Anaesth. 2006;96(2):247–52.
18. Ryu JH, Kang MH, Park KS, Do SH. Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth. 2008;100:397–403.
19. Khezri MB, Yaghobi S, Hajikhani M, Asefzadeh S. Comparison of postoperative analgesic effect of intrathecal magnesium and fentanyl added to bupivacaine in patients undergoing lower limb orthopedic surgery. Acta Anaesthesiologica Taiwanica. 2012; 50:19-24.
20. Mitra Jabalameli, Seyed Hamid Pakzadmoghadam. Adding different doses of intrathecal magnesium sulfate for spinal anesthesia in the cesarean section: A prospective double blind randomized trial. Adv Biomed Res. 2012; 1: 7.

How to cite this article: Mishra PR, Mishra SK, Sarkar K, Satapathy R, Pavan HR. Comparative study of intrathecal Dexmedetomidine vs Fentanyl as an adjuvant to hyperbaric Bupivacaine. Ann. Int. Med. Den. Res. 2017; 3(3):AN28-AN31.

Source of Support: Nil, **Conflict of Interest:** None declared