Research Paper

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COMPARISON OF DEXMEDETOMIDINE AND FENTANYL AS INTRATHECAL ADJUVANTS TO 0.5% HYPERBARIC BUPIVACAINE FOR TOTAL ABDOMINAL HYSTERECTOMY UNDER SUBARACHNOID BLOCK

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ABSTRACT

To compare the effects of intrathecal dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine regards to time of onset of sensory and motor blockade, Duration of sensory blockade and motor blockade, Two segment sensory regression time, Duration of effective postoperative analgesia and incidence of side effects. A randomized, prospective study, after obtaining ethical committee approval in K.A.P.V Government Medical College Hospital and written informed consent of patients was conducted on 60 Adult Patients of female sex, aged between 40 to 60 years, of physical status ASA Grade I and Grade II undergoing elective Total abdominal hysterectomy surgeries under spinal anaesthesia. Patients were divided into 2 groups of 30 each. Group D received 15mg hyperbaric bupivacaine with 10mcg dexmedetomidine in 0.5ml of normal saline. Group F received 15mg hyperbaric bupivacaine with 25mcg fentanyl. The time of onset of sensory and motor blockade and the duration of two segment sensory regression time, sensory, motor blockade and duration of effective post op analgesia was statistically significant in group D compared to group F. Intrathecal Dexmedetomidine is associated with faster onset of sensory and motor blockade, with significantly prolonged sensory and motor blockade and less requirement of rescue analgesia compared to fentanyl group.

KEYWORD

Hyperbaric Bupivacaine, Intrathecal Adjuvants, Dexmedetomidine, Abdominal Hysterectomy

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INTRODUCTION

Spinal anaesthesia is a simple technique which is easier to perform with rapid onset of anaesthesia, providing adequate analgesia both intra operatively and post operatively[1,2]. Spinal anaesthesia can be provided with a wide range of local anaesthetics and additives that allow control over the level, time of onset and duration of spinal anaesthesia. Postoperative pain control is a major problem, as using only local anaesthetics is associated with relatively short duration of action and thus early analgesic intervention is needed in the postoperative period[3,4]. Opioids produce intense and prolonged analgesic action without gross autonomic changes, loss of motor power or impairment of sensation other than pain when injected into subarachnoid space. Fentanyl a highly lipophilic opioid[5]. Duration of effects of intra thecal fentanyl is dose independent. Recently intra thecal administration of α-2 adreno receptor agonist as adjuvants to local anaesthetics has shown to have sedative[6,7], analgesic, hemodynamic stabilizing effect with prolonged duration of spinal block. It is hypothesized that intrathecal 10 μg dexmedetomidine would produce more postoperative analgesic effect with hyperbaric bupivacaine in spinal anaesthesia with minimal side effects[8,9]. Till date, there are only few studies done that compare the effects of addition of 10 μg dexmedetomidine to hyperbaric bupivacaine and 25 μg fentanyl to hyperbaric bupivacaine with a control group.

MATERIALS AND METHODS

After approval from Institutional Ethical Committee and written informed consent , this study was performed on 60 patients undergoing total abdominal hysterectomy. They were randomly divided into 2 groups of 30 each. Group D received 3 ml of 0.5% Hyperbaric Bupivacaine and 10 μg Dexmedetomidine diluted in 0.5 ml normal saline. Group F received 3 ml of 0.5% Hyperbaric Bupivacaine and 25 μg (0.5 ml) Fentanyl.

Inclusion criteria were age 40 – 60 years, belonging to ASA physical status I or II, Weight 45-70 kg. The exclusion criteria were Patients with any deformity or local sepsis in spinal lumbar region. Bleeding or coagulation abnormalities. History of allergy or hypersensitivity to drugs. History of any comorbid illness, heart rate <60/min.

In the operating room all patients were monitored for ECG, NIBP and SpO2. An intravenous line was established with 16/18G cannula and all patients were preloaded with 500ml of Ringers lactate solution. Baseline heart rate, blood pressure and SPO2 was recorded. Patients were taught how to express degree of pain on visual analogue scale (VAS), 0-10 scale, (0 = pain, 10 = most severe pain). Subarachnoid block was performed in sitting position under strict aseptic technique through midline approach between L2- L3 or L3-L4 intervertebral space using 25G Quincke's spinal needle. After free flow of CSF, 15 mg of 0.5% hyperbaric bupivacaine with 0.5 ml of fentanyl or 15 mg of 0.5% hyperbaric bupivacaine with 10 mcg of dexmedetomidine, diluted in 0.5 ml distilled water, was injected into subarachnoid space. Hemodynamic parameters heart rate, SBP and DBP were comparable between the two groups when observed at base line and was

recorded every 5 minutes for first 15 minutes and then every 10 minutes throughout the intra operative period. Post-operatively monitoring of PR, SPO2, SBP, DBP and MAP was recorded every 30 minutes. The motor block was assessed according to the modified bromage scale.

Bromage 0:The patient is able to move the hip, knee and ankle. Bromage 1:The patient is unable to move the hip but is able to move the knee and ankle. Bromage 2:The patient is unable to move hip and the knee but is able to move the ankle. Bromage 3:The patient is unable to move hip, knee and ankle.

Quality of analgesia was assessed by VAS scale.

The incidence of side effects like hypotension, bradycardia, nausea and vomiting was recorded. Hypotension was taken as a decrease in systolic pressure >30% of the baseline value or SBP of <90mmHg, which was treated with crystalloid boluses and intravenous boluses of ephedrine (6mg). Bradycardia was taken as a pulse rate of <50beats/min and was treated with iv atropine (0.6mg).

The data obtained was analyzed statistically using analysis of variance (ANOVA) and student 't' test. A value of <0.05 was considered statistically significant.

RESULTS

The two groups were comparable in demographic parameters like age, weight, ASA status. The two groups were comparable with respect to their age. The mean age was 51.5 years for dexmedetomidine and 52.5 years for fentanyl group. The distribution of the patients according to their age was statistically insignificant(P > 0.05).Two groups which were divided according to the ASA criteria. Dexmedetomidine group had 60% patients in ASA criteria 1 and 40% in ASA criteria 2. Fentanyl group had 53% in ASA criteria 1 and 47% subjects in ASA criterion 2. BMI for dexmedetomidine group was 21.34± 4.7 kg/m2, and that was fentanyl group was 22.34 ± 3.31 kg/m2.

DISCUSSION:

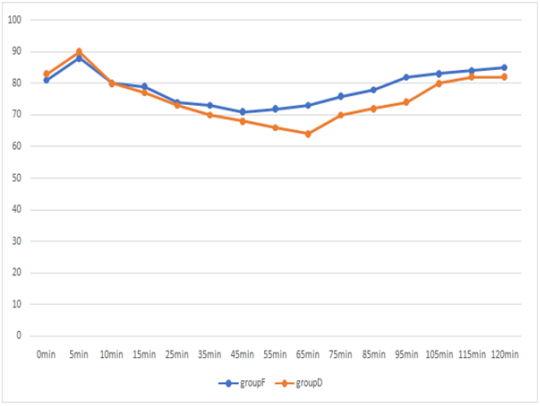
Fentanyl, a highly lipophilic μ-receptor agonist opioid, has rapid onset of action following intra thecal injection. Fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord and may have a supra spinal spread and action. Spinal opiates prolong the duration of analgesia, but they do have drawbacks of late and unpredictable respiratory depression, pruritus, nausea, vomiting and urinary retention[10,11] , which requires constant postoperative monitoring and urinary catheterization. Hence there is a requirement of an adjuvant to be used along with local anaesthetics which can produce prolonged analgesia without the above said side effects of opioids[12,13]. Intra thecal alpha 2 agonists are found to have anti nociceptive action for both somatic and visceral pain. So in this context alpha 2 agonists may be a very useful drug along with the local anaesthetic Bupivacaine 0.5% heavy for spinal anaesthesia[14,18]. The time taken for onset of sensory block was 5.3±0.58minutes in group F while 4.10±.43 minutes in group D The time taken to reach the highest sensory level was 8± 0.42 minutes in group F while 5.95 ± 0.38 minutes in group D. The mean time to reach the bromage 3 was 8.8 ± 1.46 minutes in group F while 7.4 ± 1.72 minutes in group D shown in Table 1. The groups were comparable in terms of hemodynamic parameters, though there had been a statistically significant fall in BP and heart rate when compared to baseline in the dexme detomidine group

TABLE :1

Spinal block characteristic	Group F	Group D	P value
Time taken for onset of sensory blockade (mins)	5.3±0.58	4.10±0.43	0.000(S *)
Time taken to reach highest sensory level (mins)	8±0.42	5.95±0.38	0.000(S *)
Time taken to reach bromage scale 3 (mins)	8.8±1.46	7.4±1.72	0.001(S *)

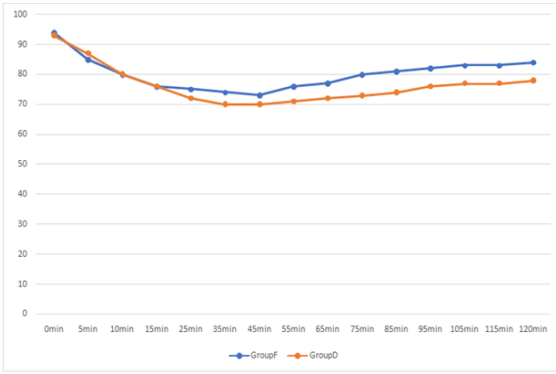
One of the main disadvantages of spinal anesthesia is adverse changes in hemodynamic parameters. In our study, Two patients in the dexmedetomidine group had episodes of bradycardia, whereas nine patients in fentanyl group had the same. This was treated with injection Atropine 0.6 mg IV single dose. On intragroup analysis, there was a significant Drop in heart rate in the dexmedetomidine group continued to be stable throughout the intraoperative and into the postoperative period (figure 1). There has been statistically significant fall in systolic and DBP from baseline in each group of patients (intragroup analysis). In our study, we found that there was decrease in BP starting from 6 to 8 min after administration of subarachnoid block up to 75 min in group dexmedetomidine and 105 min in group fentanyl in postoperative period in a dose dependent manner. However, on the intergroup comparison, results have been statistically insignificant both intra operatively and postoperatively (P > 0.05) (figure 2).

Figure 1: Mean HEART RATE at various interval



Dexmedetomidine evokes a biphasic BP response: a short hypertensive phase and subsequent hypotension. The two phases are considered to be mediated by two different α2-AR subtype; the α2B receptor is responsible for initial hypertensive phase whereas hypotension is mediated by α2A receptor. α2 receptors are located in blood vessels where they mediate vasoconstriction and on sympathetic terminals, they inhibit norepinephrine release. The responses of activation of α2 receptors cause contraction of vascular smooth muscles leading to hypertension. The initial response lasts for 4–5 min and is followed by decrease in BP of 10%–20% below baseline and also stabilization of the heart rate below the baseline values. Both these effects are caused by the inhibition of central sympathetic outflow overriding the direct stimulating effect. Hence, this could be the plausible cause in our case. The postoperative pain relief and hemodynamics were better with the addition of fentanyl. Bradycardia was found in 10%–15% of the cases which was not statistically significant. In our study, the baseline (preoperative) SBP in dexmedetomidine group was 129.97 ± 11.81 mmHg and DBP was 81.10 ± 7.84 mmHg. During the surgery, highest SBP was seen at 4th min (143.53 ± 14.83 mmHg) immediately after giving subarachnoid block, and a minimum of at 20th min (104.93 ± 11.12 mmHg) and the lowest diastole recorded was at 25th min at (59.10 ± 5.29 mmHg). During the postoperative period, these patients had a stable hemodynamic state, owing to probably to good analgesia period. The baseline (preoperative) SBP in fentanyl group was 120.33 ± 11.95 mmHg which was incidentally also the highest noted. During the surgery, lowest recorded at 6th min (99.40 ± 7.17 mmhg). In our study, the dose of bupivacaine used was 15 mg in all groups which is likely to produce dense axonal blockade as discussed above and hence could mask the hypotensive effect of dexmedetomidine even in higher doses. Around ten patients in the dexmedetomidine group experienced hypotension, whereas 13 patients in the fentanyl group.

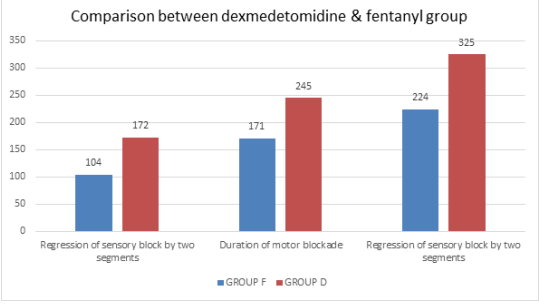
Figure 2: Mean MAP at various interval



In dexmedetomidine group, the mean time was 172 ± 22.27 min, while in fentanyl group, the mean time was 104 ± 19.11 min. The difference in the mean times was highly significant across groups as indicated by P 0.0002 using one-way ANOVA. Tukey's post hoc analysis revealed significant difference of mean time between all the three groups. These observations have been consistent with Al-Mustafa et al.,[10] Eid et al.,[15] who found statistically significant difference in two-segment regression time. They also found the time to two-segment sensory regression to be 172 ± 22.27 min with 10 µg dexmedetomidine while it was 104 ± 19.11 min in group of patients receiving 25 µg fentanyl (TABLE 2). It has been postulated that dexmedetomidine stimulate α2 receptors directly in the spinal cord, thus inhibiting the firing of nociceptive neurons. The local anesthetics act by blocking sodium channels whereas the α2 adrenoceptor agonist acts by binding to presynaptic C-fibres and postsynaptic dorsal horn neurons. The effect of dexmedetomidine is additive or synergistic effect secondary to the action of local anaesthetics. Hence, the prolonged action of dexmedetomidine was noted. The dexmedetomidine group took maximum time for regression of sensory block by two segments. This clearly states that both fentanyl and dexmedetomidine is far superior to plain bupivacaine. While comparing between the studies groups, dexmedetomidine is appreciably remarkable, with extended time for the same effect.

TABLE:2

	GROUP F	GROUP D	P VALUE
Regression of sensory block by two segments (mins)	104±19.11	172±22.27	0.00002
Duration of motor blockade (mins)	171.42±20.30	245±25.65	0.000251
Duration of analgesia (mins)	224±16.24	325±17.46	0.000(s*)



VAS SCORE:

	Group F	Group D	P value
1hour	0.0±0.0(0,0)	0.0±0.0(0,0)	-
2hours	1.8±1.6(1,3)	0.0±0.0(0,0)	0.025 (S*)
4hours	4.9±0.94(1,6)	2.8±0.97(1,4)	0.00020(S*)
6hours	4.6±1.42(1,7)	3.2±0.97(,4)	0.0260 (S*)

SIDE EFFECT:

Respiratory depression is defined as a respiratory rate of <10 breaths/min, and this was not observed in any patient in dexmedetomidine group. Two patients in the fentanyl group was noted to have mild respiratory depression, which did not require to be managed. In dexmedetomidine group, 10 (33.3%) patients had hypotension for with injection Ephedrine IV 6 mg was given, around two patients had bradycardia which was treated with injection Atropine IV 0.6 mg. Incidence of hypotension more in dexmedetomidine compare to fentanyl group. (TABLE.3)

TABLE 3:

SIDE EFFECT	D group		F group		P value
	n	%	n	%	
Nausea &vomiting	3	10	4	13.3	0.690
shivering	2	6.7	1	3.3	0.557
Respiratory depression	3	10	2	6.7	0.643
Hypotension	10	33.3	3	10	0.452

CONCLUSION

To conclude, 10 mcg dexmedetomidine as an adjuvant to intrathecal bupivacaine provides good quality of anaesthesia, prolonged analgesia and minimal hemo dynamic changes responding to vasopressors.

REFERENCES

1. Adams BW. Lignocaine spinal analgesia. Anaesthesia. 1956;11:297-307.
2. Mackenzie AR. Influence of anaesthesia on blood loss in transurethral prostectomy. Scott Med J. 1990;35:14-16.
3. Bubanendran A, Kroin JS. Useful adjuvants for postoperative management. Best Pract Res Clin Anaesthesiol. 2007;21:31-49.
4. Grewal A. Dexmedetomidine: new avenues. Journal of Anaesthesiology clinical pharmacology. 2011;27:297-302.
5. Chaiari A, Lorber C, Eisenach JC. Analgesic and hemodynamic effects of intrathecal clonidine as a soul analgesic agent during first stage of labour, a dose response study. Anaesthesiology. 1999;91:338-96.
6. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small dose intrathecal clonidine and isobaric bupivacaine for orthopaedic surgery: a dose response study. Anesth Analg. 2004;99:1231-8.
7. Juliao MC, Lauretti GR. Low dose intrathecal clonidine combined with sufentanil as analgesic drugs in abdominal gynecological surgery. J Clin Anesth. 2000;12:357-62.
8. Asano T, Dohi S, Ohta S, Shimonaka H, Lida H. Antinociception by epidural and systemic α2 adrenoreceptor agonists and their binding affinity in rat spinal cord and brain. Anesth Analg. 2000;90:400-7.
9. Klaso EA, Poyhia R, Rosenberg PH. Spinal antinociception by dexmedetomidine, a highly selective alpha-2 adrenergic agonist. Pharmacol Toxicol. 1991;68:140-43.
10. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben RK, Qudaisat IY et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedure. Am JA Appl Sci. 2009;6:882-7.
11. Mantz J, Josserand J, Hamada S. Dexmedetomidine: New insights. Eur J Anaesthesiol. 2011;8:3-6.
12. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965;16:55-69.
13. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J. 1974;2:656-9.
14. Salgado PF, Sabbag AT, Silva PC, Brienze SL, Dalto HP, et al. Synergistic effect between dexmedetomidine and .75% ropivacaine in epidural anesthesia. Rev Assoc Med Bras. 2008;54:110-5.
15. Eisanach JC, De Kock M, Klimscha W. α2 aderenergic agonists for regional anesthesia. Anesthesiology. 1996;85:655-74.
16. Harada Y, Nishioka K, Kitahata LM, Kishkawa K, Collins JG. Viseral antinocepetive effects of spinal clonidine combine with morphine, ankephalin or U50,488H. Anaesthesiology. 1995;83:344-52.
17. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. Saudi Med J. 2009;30:365-70.
18. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM et al. Effect of low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand. 2006;50:222-7.
19. Mohammad AA, Fares KM, Mohammad SA. Efficacy of intrathecally administered dexmedetomidine versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. Pain physican. 2012;15;