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INTRATHECAL FENTANYL VERSUS DEXMEDETOMIDINE AS ADJUVANTS TO HYPERBARIC BUPIVACAINE IN INFRAUMBILICAL SURGERIES

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ABSTRACT The study evaluated and compared the efficacy of intrathecal fentanyl 25µg and dexmedetomidine 5µg with 0.5% hyperbaric bupivacaine. Each study group consisted of 25 patients. Patients were randomly divided to receive intrathecally either 0.5% hyperbaric bupivacaine 3ml+0.5 ml of normal saline (control Group B) or (Group F) 0.5% hyperbaric bupivacaine 3ml+25µg fentanyl or (Group D) 0.5% hyperbaric bupivacaine 3ml+5µg dexmedetomidine. Peak sensory level achieved, time to reach Bromage 3, time to two segment regression, regression to Bromage 0, hemodynamic stability, time to rescue analgesia, total analgesic consumption in first 24hrs were recorded.

Results: The peak sensory level reached were T6-T7 (32%) in Group B, whereas T4-T5(44%) in Group F and T4-T5(72%) in Group D. The mean time to regression to Bromage 0 in Group B was 119.60±11.72 min, 159.20±9.09 min in Group F, 402.00±18.71 min in Group D. The mean time to rescue analgesia in Group B was 136.00±5.00 min, 182.40±8.79 min in Group F and 396.40±17.77 min. Total dose of analgesic consumption in Group B was 228±34.10mg, 105±37.50mg in Group F and Group D was 81±20.77mg.

Side effects among the groups were found be not significant statistically (P=0.935)

KEYWORDS : Intrathecal bupivacaine, fentanyl, dexmedetomidine, postoperative analgesia.

INTRODUCTION

Central neuraxial blockade using only local anaesthetics has limited duration of postoperative analgesia. Addition of small doses of opioids with bupivacaine for spinal anesthesia reduces postoperative analgesic requirements. Fentanyl is preferred as an adjuvant in spinal anaesthesia because of its faster onset and short duration of action with lesser incidence of respiratory depression[1,2].

Intrathecal $\alpha_2$agonists are used as adjuvants to local anaesthetics.They potentiate the effect of local anaesthetics[3,4]. They produce analgesia by hyperpolarization of post-synaptic dorsal horn neurons[5]. Dexmedetomidine, a new highly selective α_2-agonist under evaluation as an adjuvant to spinal anaesthesia as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with less side effects[14,17].

PATIENTS AND METHODS

Prospective, randomized, controlled clinical study was conducted following permission from Institutional Ethics Committee. The study participants included 75 patients of ASA grade I and II, aging from 18 to 75 years, weighing 40-70 kgs scheduled for elective infra umbilical surgical procedures under subarachnoid block. Patients with heart block, dysrhythmia, drug therapy with adrenergic receptor antagonists, calcium channel blocker, ACE inhibitors, hypersensitivity to local anaesthetics and adjuvants, uncontrolled / labile hypertension, spine deformities/spinal surgeries, coagulation disorders, H/o of epilepsy/neurological disorders, psychiatric illnesses were all excluded from the study[6,7].

On arrival of the patients to the operating theatre, intravenous access was established with 18 guage venflon cannula on the dorsum of the non-dominant hand after local infiltration. Patients were prehydrated with 15ml/kg of Lactated Ringer's solution, infused over 15 minutes. Standard baseline monitoring included pulse oximetry, 5 lead electrocardiography(ECG), non invasive automated blood pressure (NIBP). Baseline values were noted.

Patients were randomly divided using computer generated list of random numbers to three groups. The sample size required for correctly rejecting the null hypothesis with the power of 80% and 95% confidence interval was calculated and was determined that 25 participants were required in each of the three groups receiving-

Control group (group B) received a premixed solution of 0.5% hyperbaric bupivacaine 3ml (15mg) and 0.5 ml of normal saline

Group fentanyl (group F) received premixed solution of 0.5% hyperbaric bupivacaine 3ml (15mg) and 0.5 ml of fentanyl (25µg)

Group dexmedetomidine (group D) received a premixed solution of 0.5% hyperbaric bupivacaine (15mg) and 0.5ml of dexmedetomidine (5µg).

Total volume of the mixture is 3.5 ml in all groups.

Under aseptic precautions, subarachnoid block was performed with 25g Quinckebach spinal needle at L3 – L4 space through a midline approach in lateral position. After confirming free flow of cerebrospinal fluid (CSF), drug was injected. In case of a discrepancy in the dermatomal level between the right and the left side, the higher level was considered for the statistical analaysis[8]. The following data were measured- peak sensory level, time to two dermatome regression. Surgery was permitted after T8 sensory block was achieved[9].

Motor block was assessed using modified Bromage score[9].
B = 0 No motor loss.
B = 1 Inability to flex the hip
B = 2 Inability to flex the knee
B = 3 Inability to flex the ankle

Motor block data included onset of motor block- time to reach Bromage score 3, time to regression to Bromage score 0.

Hypotension, defined as a decrease in systolic blood pressure by 20% from the baseline was treated with boluses of 6mg mephentermine intravenously and bolus administration of 250ml Lactated Ringer's solution over 10min.

Bradycardia-defined as heart rate < 50 beats per min, treated with boluses of 0.3 – 0.5mg intravenous atropine. Hypoxia was defined as an oxygen saturation value < 90%.

Pruritis[10,11]

Pruritis graded as

0	=	None
1	=	Mild
2	=	Severe

Intravenous ondansetron 4mg was given as for vomiting and severe pruritis.

Pain was assessed using Visual Analogue Scale between 0 and 10. VAS was assessed immediately postoperatively and at 2, 4, 6, 8, 12 and 24 hours. (0 = No pain, 10 = Most severe pain). Injection diclofenac 75mg was given as rescue analgesic when VAS ≥ 4 or if the patient requested additional analgesics. The time for the first request of analgesia and the

total analgesic consumption in the first 24 hours were noted.

OBSERVATIONS AND RESULTS

Statistical analysis was performed using SSPS 17 software. Student's unpaired T-test was used for analysis of mean age, weight distribution,duration of motor blockade, time to two segment regression, time to peak sensory level, rescue analgesic time. Chi square was used for ASA grade, sex, side effects. Fisher's exact test for highest sensory level. Intercomparision between the groups was done by Benferroni test. P value <0.05 was considered highly significant.

Table -1 Demographic data

	Group B(25)	Group F(25)	Group D(25)	P value
Age(yrs)	48.40±13.75	49.36±15.90	41.40±12.21	.223 NS
Weight(kgs)	58.48±5.59	58.84±6.76	58.64±6.89	.896 NS
Gender Male Female	18 7	20 5	19 6	.892 NS
ASA I ASA II	18 7	11 14	12 13	.108 NS

The mean time to two segment dermatomal regression in Group B was 88.60±7.90 min, 111.60±10.28 min in Group F and Group D was 144±8.66min.

The mean time to achieve Bromage 3 in Group B was 12.40±2.00 min , 5.44±2.04 min in Group F and 10.08±1.35 in Group D. The mean time to regression to Bromage 0 in Group B was 119.60±11.72 min, 159.20±9.09 min in Group F, 402.00±18.71 min in Group D.

The mean time to rescue analgesia in Group B was 136.00±5.00 min, 182.40±8.79 min in Group F and 396.40±17.77 min in Group D. Total dose of analgesic consumption in Group B was 228±34.10mg, 105±37.50mg in Group F and Group D was 81±20.77mg.

Side effects among the groups were found be not significant statistically (P=0.935)

Table -2 Sensory and motor block data

	Group B(25)	Group F(25)	Group D(25)	P value
Peak sensory level	T6-T7=8 (32%) T8=17 (56%)	T4-T5=11(44%) T6-T7=10(40%) T8=4 (16%)	T4-T5=18(72%) T6-T7=6 (24%) T8=1 (4%)	P=.000 HS
Time to two segment regression (mins)	89.60±7.90	111.60±10.28	144.00±8.66	P1=.000 HS P2=.000 HS P3=.000 HS
Time to Bromage 3(mins)	12.40±2.00	5.44±2.04	10.08±1.35	P1=.000 HS P2=.000 HS P3=.000 HS
Regression to Bromage 0 (mins)	119.60±11.72	159.20±9.09	402.00±18.71	P1=.000 HS P2=.000 HS P3=.000 HS

Table -3 Analgesia requirement

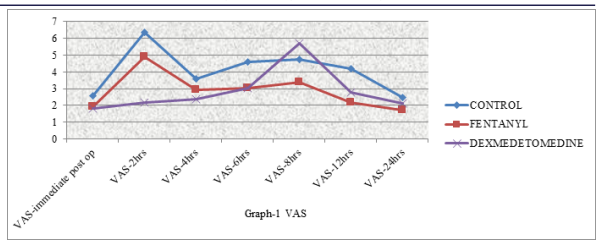
	Group B(25)	Group F(25)	Group D(25)	P value
Rescue time (mins) (VAS >4)	136.00±5.00	182.40±8.79	396.40±17.77	P1=.000 HS P2=.000 HS P3=.000 HS
Total dose (mg)	228.00±34.10	105.00±37.50	81.00±20.77	P1=.000 HS P2=.000 HS P3=.061 Sig

P1=comparision between Group B and F
P2=comparision between Group B and D
P3=comparision between Group F and D

HS-Highly significant
NS-Not significant
Sig-Significant

Table-4 Adverse effects

Adverse effects	Group B(25)	Group F(25)	Group D(25)	P value
Hypotension	3	4	8	.935
Bradycardia	0	0	0	.935
Nausea	4	1	1	.935
Pruritis	0	5	0	.935

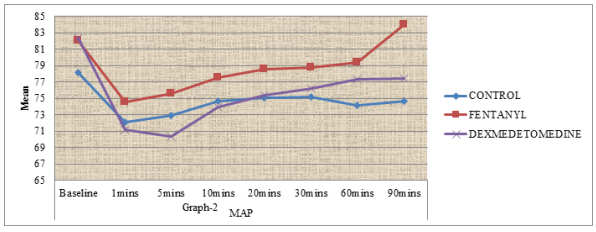


Graph-1 VAS

Visual analogue scores (VAS) were significantly lower (VAS<4) (P<0.001) in Group D - 2hrs,4hrs,6hrs post operatively whereas VAS scores were higher (VAS> 4) in Group B and F 2hrs postoperatively (P<0.001) compared to Group D.

The mean values of MAP in all the three groups were comparable. There was modest fall in MAP in all three groups 1min and 5min after intrathecal drug administration which was higher in Group D compared to other two groups, however all incidence of hypotension was not statistically significant in our study (P=0.935).

The mean values of heart rate were comparable among all four groups, however the incidence of bradycardia was not significant (P=0.916).



Graph-2 MAP

DISCUSSION

Spinal anaesthesia with 0.5% hyperbaric bupivacaine is commonly used in centri-neuraxial blockade performed for lower abdominal and lower limb surgery. In order to maximize post-operative analgesia, a number of adjuvants have been added. Intrathecal comparision of fentanyl and dexmedetomidine was studied based on previous studies comparing either of the drugs. Intrathecal α_2 agonists have been found to have antinociceptive action for somatic and visceral pain[14]. Fentanyl is a lipophilic μ-receptor agonist, acts by combining with opioid receptors in the dorsal horn of spinal cord and also has a supraspinal spread and action[18].

Catherine O Hunt et al.[1], studied the peri-operative analgesia with subarachnoid fentanyl-bupivacaine and concluded that addition of fentanyl greater than 6.25 mcg to hyperbaric bupivacaine was found to reduce the intra-operative opioid requirement in cesarean delivery under spinal anaesthesia. In another study, Harbhej Singh et al.[19], studied the effect of intrathecal fentanyl on onset and duration of hyperbaric bupivacaine induced spinal block for lower extremity surgeries and found that 25μg fentanyl prolonged duration of bupivacaine induced sensory block and reduced analgesic requirements. Yaksh[12], has shown that α_2 agonists when given intrathecally causes dose dependent reduction in motor strength in animals. The newer α_2 agonist dexmedetomidine is highly selective with an affinity of eight times higher than clonidine.

Our study with addition of 25μg fentanyl or 5μg dexmedetomidine with hyperbaric bupivacaine showed significant prolongation of both sensory and motor block. Both drugs provided good quality intraoperative and post operative analgesia and hemodynamic stability. The analgesia was clinically better in group D than group F but it was not highly significant.

Al Mustafa etal.[17], studied the effect of dexmedetomidine 5 and 10μg in bupivacaine in urological procedures and found onset of sensory blockade was 6.3±2.7 min and 4.7±2.0 min, blockade to Bromage 3 was 13.0±3.4 min and 10.4±3.4 min in 5μg and 10μg groups and found that dexmedetomidine acted in a dose dependant manner. In this study the mean time of onset of sensory blockade was 6.48±8.7min and motor blockade to Bromage 3 was 10.08±1.35 in Group D which was comparable with study done by Al Mustafa et al. The peak sensory level reached was T6-T7(32%) in Group B, whereas T4-T5(44%) in Group F, T4-T5(72%) in Group D in our study. Al Ghanem et al.[14], compared the effect of dexmedetomidine 5μg(D) and fentanyl 25μg(F) intrathecally with 0.5% bupivacaine for spinal anaesthesia and noted

that the peak level reached was T6(T4-T9) in gr F.

Rajani et al.[6],Compared the effect of 5µg dexmedetomidine and 25µg fentanyl with 2.5ml of hyperbaric bupivacaine. Time to regress to Bromage 0 was 421±21 min in dexmedetomidine group, 149±18 min the fentanyl group (P value <0001). They concluded dexmedetomidine as an alternative to fentanyl to produce an excellent quality of introperative analgesia, stable hemodynamic conditions, minimal side effects and good post operative analgesia. The intrathecal 5µg dexmedetomidine used in our study had shown significantly prolonged duration of motor blockade, which is in consonance with the results observed by investigators in comparision with various adjuvants (clonidine, fentanyl and sufentanil) used in their studies[13,14,15].,The duration of motor blockade observed in present study was markedly prolonged (402.00±18.71 min) when compared to duration of motor blockade250±76 min in kanazi et al.,'s study(P>0.001) and 240±64 min in Al Ghanem et al.,'s study (P>0.001), which could be attributed to higher intrathecal volume of drug(3.5 ml) used in our study as compared to 1.9 and 2.5ml drug used in the respective studies.We noted significantly delayed requirement of rescue analgesic (P=.000) and significantly reduced 24 hr rescue analgesic requirement (P=.621) with Group D when compared to Group F which supports the analgesic efficacy of dexmedetomidine as an intrathecal adjunct. Similarly, significantly improved analgesia was seen by Gupta et al.[15], on comparision of dexmedetomidine and fentanyl as intrathecal adjuvant (P>0.001).The most significant side effects reported with the use of intrathecal α_2 agonists are bradycardia and hypotension. G.E Kanazi et al.[13], noted that addition of dexmedetomidine to bupivacaine caused no significant decrease in the BP either intra operatively or post operatively. Bradycardia and Hypotension were seen in both fentanyl and dexmedetomidine groups but was not significant (P=0.935) probably due to small doses of intrathecal fentanyl, dexmedetomidine with high dose local anaesthetics used.

CONCLUSION

We evaluated the effect of addition of intrathecal fentanyl and dexmedetomidine to hyperbaric bupivacaine on sensory, motor block characteristics, postoperative analgesia and requirement of rescue analgesics in first 24 hours following surgical procedures. Both drugs are comparable and provided stable hemodynamic conditions, good quality of prolonged intra and postoperative analgesia with minimal side effects and are attractive alternatives as adjuvants to spinal bupivacaine for long duration surgical procedures. Addition of fentanyl is useful for short surgical procedures or for ambulatory surgeries as it has shorter duration of action.

References

1. Hunt CO, Naulty JS, Bader AM, Hauch MA, Vartikar JV, Datta S, Hertwig LM, Ostheimer GW: Perioperative analgesia with subarachnoid fentanyl -bupivacaine for cesarean delivery. Anaesthesiology, 1989; 71(4):274-278.
2. Choi DW, Ahn HJ, Kim MH. Bupivacaine-sparing effect of fentanyl in spinal anaesthesia for cesarean delivery. RegAnesth Pain Med 2000;25:240-5.
3. Dobrydnjov I, Axelsson K, Thorn S E et al. Clonidine combined with small dose bupivacaine during spinal anaesthesia for inguinal herniorraphy:A randomised double blind study. Anaesth Analg 2003;96:1496-503.
4. De Kock M, Gautier P, Fanard L, Hody J, Lavand'homme P.Intrathecal ropivacaine and clonidine for ambulatory knee arthroscopy. Anaesthesiology 2001;94:574-578.
5. Eisanach JC, De Kock M, Klimscha W. α2 adrenergic agonists for regional anaesthesia. Anesthesiology1996;85:655-674.
6. Rajani Gupta, Reethu Verma, Jaishri Bogra, Monica Kohli, Rajesh Raman, Jitendra Kumar Kushwaha: A comparative study of intrathecal Dexmedetomidine and fentanyl as adjutants to Bupivacaine.Journal of Anaesthesiology Clinical Pharmacology. July – September 2011; Vo.27 issue 3 : 339-343.
7. Ashraf Amin Mohamed, Khaled Mohamed Fares, Sahar Abd-Elbaky Mohamed. Efficacy of intrathecally administered dexmedetomidine Versus dexmedetomidine with fentanyl in patients undergoing major abdominal cancer surgery. Pain Physician 2012; 15 : 339 – 348. ISSN 1533– 3159. www.painphysicianjournal.com
8. D.Marhofer, S.C.Kettner, P. Marhofer, S.Pils, M.weber and M. Zeitlinger. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block : a volunteer study. Br J. Anaesthesia 110 (3) : 438 – 42 (2013)
9. Bromage PR . A Comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anesthesiologica scandavica1965;16:55–69. http: www.ncbi.nim.nih.gov/pubmed/532204
10. Huban dayioglu, Zehra N. Baykara, Asena Salbes, Mine Solak, Karnil Toker. Effect of adding Magnesium to bupivacaine and fentanyl for spinal anaesthesia in knee arthroscopy .Journal of Anaesthesia February 2009, Vol 23, issue1, pp19-25.
11. Chia YY, Liu K, Liu YC, chang HC, wong CS. Adding Ketamine in multimodal patient controlled epidural regimen reduces post-operativepain and analgesic consumption. Anesthesia Analgesia 1998;86: 1245-9.
12. Yaksh T L, Pharmacology of spinal adrenergic systems which modulate spinal nociceptive processing. Pharmacol Biochem Behav 1985;22:845-858.
13. Kanazi GE, Aonad T, Jabbour J, Al-Jazzar M,Al-Yaman,Bulbul M. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiologica Scandinavica 2006; 50:222-227.
14. Subhi M, Mahmoud M,Khaled R,Ibrahim Y,Ayman M,Hamdi M. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynaecological procedures. American Journal of Applied Sciences 2009; 6(5):882-887.
15. Gupta R, Verma R, Bogra J, Kohli M, Raman R. Kushwaha JK. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. Journal of Anaesthesiology Clinical Pharmacology.2011;27(3):339-43.
16. Hala EA, Mohammed A.Abdelkarms. Mojalli M. Bassam A, Ziad M. Dose-related prolongation of hyperbaric bupivacaine spinal anaesthesia by dexmedetomidine . A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. Journal of Anaesthesiology Clinical Pharmacology.2011;27(3):339-43.
17. Al Mustafa M M, Abu-Halaweh SA, Alowedi A S, Murshidi M M,Ammari B A, awwad Z M:Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. Saudi Med J.2009; Vol.30(3): 365-370.
18. Kalso E, Poyhia R, Rosenberg P. Spinal antinociception by dexmedetomidine, a highly selective α2-adrenergic agonist. Pharmacol Toxicol 1991;68:140-3.
19. Singh H, Yang J, Thornton K, Giesecke AH, Intrathecal fentanyl prolongs sesory bupivacaine spinal block. Canadian Journal of Anesthesia 1995; 42:987-91.