ORIGINAL ARTICLE

Comparative Behaviour of two different doses of Dexmedetomidine in Intrathecal Anesthesia as an Adjuvant with Hyperbaric Bupivacaine in Elective Caesarian Section

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ABSTRACT

Background: There is extreme shortage of data regarding effects and safety profile of use of intrathecal dexmedetomidine as an adjunctive agents in Pakistani adult women undergoing caesarian section.
Aims: To observe the outcome of dexmedetomidine utilization in spinal anesthesia as an adjunctive agent, its side effect depiction, and to find the most efficacious and safe dose of intrathecal dexmedetomidine.
Methodology: A total of 135 patients were included in this randomized, prospective study by isolating 45 patients in each of three groups. Each of two study groups were given intrathecal dexmedetomidine 10µg in group D-10 and 15µg in D-15 along 12mg of hyperbaric bupivacaine and bupivacaine only in control group. We recorded onset and regression of sensory and motor blockade, any untoward effect and hemodynamic variability mean arterial BP
Results: Both the study groups [D-10 and D-15] revealed significant results($p<0.05$) in onset and regression of sensory and motor blockade as compared to control group[bupivacaine only]. By addition of adjuncts [dexmedetomidine] in spinal anesthesia, resulted in delayed administration and lower dose of postoperative analgesia and less intraoperative hemodynamic instability and postoperative side effects.
Conclusion: Dexmedetomidine as an adjunctive agent in intrathecal route is a safer and efficacious agent without producing significant side effects. 10 microgram dexmedetomidine is a more appropriate dose than 15 microgram showing comparable efficiency and low untoward effects.
Keywords: Intrathecal anesthesia, dexmedetomidine, bupivacaine.

INTRODUCTION

The advantages and disadvantages, the cost, and the risk benefits ratio between spontaneous vaginal delivery and caesarian section is now so poised that American collage of Obstetrician and gynaecology (ACOG) suggests that probably the patient wish has now become the deciding factor between the two procedures[1]. The trend of CDMR (caesarian delivery on maternal request of primary gravida without any indication) is on the rise with global prevalence of 1-18%[2].

Neuraxial anesthesia has been advocated by anesthesia guidelines as choice of anesthesia technique considering the firm association of general anesthesia with risks of unsuccessful intubation, more chances of aspiration, enhanced intra operative blood loss and overall reduced health related quality of life[3].

Various adjuvants like ketamine, opioids, neostigmine, benzodiazepines, and myriad of other drugs have been employed with local anesthetics in neuraxial blockade to lengthen its effects, to lessen the untoward effects accomplice with larger dose of local anesthetic drugs[4-5], and to boost the postoperative analgesic quality. Many untoward effects associated with these agents have been mentioned such as urinary retention, respiratory depression, pruritus, post-operative gut disturbances which restrict their utilization.

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Dexmedetomidine, a relatively new α-2 adrenergic agonistic agent, is showing very promising results because of its sedative, analgesic sparing, and anesthetic sparing properties. Other important advantages include preserved hemodynamics with minimal side effects like drowsiness and respiratory depression[6].

Dexmedetomidine has got very high affinity for α 2 - adrenoceptor (α2:α1, 1620:1) as compared to clonidine (α2:α1, 220:1). This highly selective α-2 adrenergic agonist manifests all the above mentioned properties without leading to noticeable respiratory depression[7].

Blocking the release of nor-epinephrine at locus coeruleus is its mode of action. Minor doses of dexmedetomidine (3µg) used in conjunction with spinal bupivacaine induces a shorter onset of motor block and an extension in the duration of motor and sensory block with preserved hemodynamics and minimal side effects[8-9]. The complemented antinociceptive effect is attributable to its lipophilicity[10].

Other reason for elongation in the duration of sensory as well as motor blockade alongwith its antinociceptive action is ramification of Dexmedetomidine on local anesthetic from its greater selectivity for α2 receptors[11].

Dexmedetomidine has cumulative effects to local response for visceral and somatic analgesia on account of its highly selective α-2 adrenergic agonistic nature. It extends sensory block by obstructing signal transmission through C fibers of spinal cord resulting in hyperpolarization of post synaptic dorsal horn neurons. Enhancement in Motor block duration is by virtue of its α-2 agonistic action

to motor neuron in dorsal horn of spinal cord, besides this direct antinociceptive action for somatic and visceral pain, further results in prolonged pain free duration.

The primary objective of this study is to ascertain the most advantageous intrathecal dose of dexmedetomidine that should result in safe proceeding of a hemodynamically stable caesarian section with least analgesic requirements in comparison to control group in a normal adult Pakistani woman. Secondary objectives were to probe the hemodynamic consequences of two different doses of subarachnoid dexmedetomidine, as adjunct to heavy bupivacaine, alongwith the onset and length of motor and sensory blockade, overall analgesic requirements, as well as other side effects like occurrences of nausea, vomiting, drowsiness and respiratory depression.

MATERIALS AND METHODOLOGY

This is a prospective double-blind randomized observational study was conducted in the Department of Anesthesiology and ICU, Bahawal Victoria Hospital/Quaid-e-Azam Medical College Bahawalpur in patients aged 20 to40 years and undergoing elective lower segment Caesarian section corresponding to American Society of Anesthesiologist I & II[ASA I-II].

Following patients were excluded from the study as per the exclusion criteria:

- Contraindications of subarachnoid blockade, spine deformity, local infection at the site of injection, hypersensitivity to research medicines and local anesthetic, severe hypotension, bleeding diatheses, neuromuscular disorders.
- CNS diseases.
- Gravidity.
- Body Mass Index ≥29
- Patients on treatment with α-adrenergic antagonists.
- Inability to obtain consent.

Sample size was calculated by using calculator of Open Epi based on confidence interval of 85 percent of previous study in this institution which is a total of 135 patients[45 in each of three groups].

The procedure was clearly told to every patient included in the study and informed consent was signed in written from every patients. The patients were urged to remain nil by mouth for 6hours and was premedicated with capsule omeprazole 40mg and tablet domperidone 10mg in the morning with a sip of water. ECG, NIBP and SpO2 were attached to every patient before starting the anesthesia and baseline readings of HR, SBP, DBP, MBP and oxygen saturation in the operation theatre were recorded. Two 18*F cannulas were inserted to preload all the patients with 8ml/kg of Haemaccel 3.5% solution.

A 25G spinal needle (Quincke) was used at a level of space below L3 vertebra by applying pyodine solution, in sitting position by midline approach. Skin was infiltrated with 1% lidocaine solution. Three groups were created by randomized allocation to patients into group-C, group-D10 and group-D15 by using blind technique. Hyperbaric solution of 0.75%bupivacaine (2.0ml) was utilized in a dose of 12mg in controlled group and 10 µg and 15 µg of dexmedetomidine with 0.9% saline to a total volume of 2ml was added in group-D10 and group-D15 alongwith hyperbaric bupivacaine respectively. The intrathecal drug formula was prepared by a separate anesthesiologist under a sterile technique who was blinded to the study. Pulse rate [HR], and blood pressures [SBP, MBP, & DBP] were recorded immediately after subarachnoid anesthesia and every 5 min for the first 30 minutes, then every 15 min for 100minutes and every 30min for the next two hours.

Pinprick sensation using 22G hypodermic needle was used to document level of the sensory dermatome in the center of abdomen above and below the umbilicus. Times for sensory block to compass T10 dermatome and to attain Modified Bromage Scale [MBS] 0 were recorded. The decline of sensory level [T10 and T12] and motor blockade [MBS-0] times were noted. Sedation was determined after end of operation using Ramsay sedation score.

Duration of analgesia measured from the time of intrathecal injection to the first request of analgesia [VAS > 4] was monitored. Incidence of side effects like nausea, vomiting, hypotension, bradycardia and shivering were noted. Patients were taught how to express degree of pain on Visual analogue scale (VAS), 0-10 scale, (0 = pain, 10) was used to assess the intensity of pain and requirements of analgesia telling the patient how to express the pain and were advised to label the severity according to VAS from 'No pain' at 0 to 'Maximum pain' at 10 point. At VAS > 5, inj. ketorolac 30mg IM was given as rescue analgesic and study terminated.

Hypotension was defined in our study by systolic pressure if recorded below 60mmHg and bradycardia as HR less than 50beats/min.

Statistical analysis: Analysis of variance (ANOVA) and students 't' test was used to compare and calculate the variables values to reach a statistical significance of <0.05. A Statistical Package of Social Sciences [SPSS] version 20 was used for statistical analysis.

RESULTS

Any obvious statistical disparity was not observed in the demographic characteristics of the patients in all the groups (p>0.05) (Table 1). Duration of surgery was approximately the same and oxygen saturations was shown similar trends [p>0.05](Table:1). The mean time for first analgesic was statistically noticeable between controlled and study groups [G-C; 201.67 ± 20.05, G-D10; 338.46 ± 38.66, G-D15; 361.46 ± 41.72 min] and the p-value was equal to 0.011.

Onset of sensory blockade was statistically discernible (<.005) between groups (Table 2). Minimum onset time for sensory blockade was contemplated in group-D15 where it was 2.7289±1.264 minutes as compared to group-C and group-D10 [4.45±1.058 & 3.3789±.457 minutes] respectively. Whereas time taken to attain Bromage zero score was the least in group-D15 [4.44±1.166 minutes] as confronted in group-C and group-D10 [5.66±1.663 & 5.95±2.204minutes] respectively, the difference was statistically significant in term of p-value (.001).

Regression of sensory block from T6 to T12 was taken the mean time of 175.42±13.971 minutes in group-D15 which was comparable with group-D10 [170.93±13.342min] whereas regression of sensory level in group-C was 109.24±37.482 minutes, leading to the statistical significance of .000p with control but study group showed a p-value of 0.094[table;4]. The same results have been found when we observed this regression of sensory level of T10 (Table 4). Mean time to wear off the motor

blockade was delayed in both of research groups [G-D10 (143.62±14.64) & G-D15 (211.73±9.240)minutes] in comparison of control group[132.20±8.267mins] leading to statistical significance[p-value=.001].

When we stared hemodynamic characteristics [Table;3] where we have been found statistical difference [p<0.05] in mean heart rates between each of three groups immediately after one and five minutes of spinal blockade but later on, no obvious difference was seen. Mixed trends were perceptible in systolic and mean arterial pressures during the early readings recorded after execution of subarachnoid block with study medicines where some statistical differences have been revealed (Table 4).

Sedation was seen in 2 of patients(6.66%) in study groups[D-10 & D-15] as no patient seen in controlled, while total dose of analgesia [Ketorolac] administered was lessened in study groups as compared to control. Lastly we have seen untoward effects (Table 5) where incidence of nausea and vomiting showed indistinguishable frequencies and shivering was only seen in two patients of controlled groups only. Bradycardia was seen in equal number in all 3 groups but hypotension was noted in only one patient in group-c and group D-15. Drowsiness was also seen in one patient of group D-15(2.2%).

Table 1: (n=45)

Variables	Group-C	Group-D10	Group-D15	P value
Age(years)	25.51±28.50084	21.48±21.17956	23.53±26.11652	0.284
Weight (kgs)	59.47±733	58.57±7.09	59.99±7.06	0.443
Height (cms)	156.67±8.01	155.55±8.89	158.69±7.99	0.224
Time for first analgesics(min)	201.67 ± 20.05	338.46 ± 38.66	361.46 ± 41.72	0.011
Mean o2 saturation (%)	98.87±0.32	99.01±0.02	98.95±0345	0.245
Duration of surgery[min]	50.72±8.01	48.40±7.88	49.45±8.10	0.443

Table 2: Sensory and motor block characteristics [Mean±SD]

Variables(min)	Group-c(n=45)	Group D-10(n=45)	Group D-15 (n=45)	GC & GD10	GC & GD 15	GD10 & GD15
Onset of Sensory blockade(T6)	4.45±1.058	3.3789±.457	2.7289±1.264	.000	.000	.005
Onset of Motor blockade(Bromage 0)	5.66±1.663	5.95±2.204	4.44±1.166	.434	.001	.000
Regression of Sensory Blockade to T10	89.24±37.482	150.87±15.215	155.42±23.875	.001	.001	.061
Regression of Sensory blockade(T12)	109.24±37.482	170.93±13.342	175.42±13.971	.000	.000	.094
Regression of Motor blockade (Bromage3)	132.20±8.267	143.62±14.64	211.73±9.240	.000	.000	.000

Fig.1: Comparison of onset and regression of sensory and motor blockade

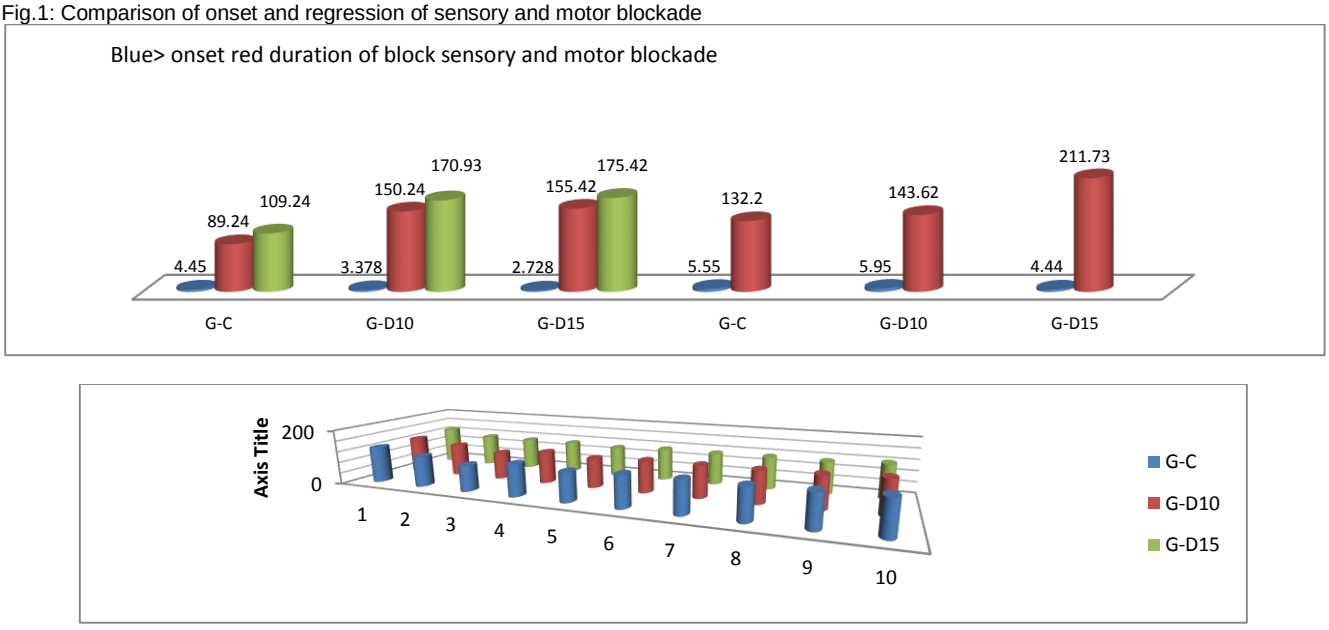

Table 3: Changes in mean pulse rate[mean±sd]

Time	Group-c(n=45)	Group d-10(n=45)	Group d-15(n=45)	Gc & gd10	Gc & gd15	Gd10 & gd15
BASELINE	95.6667±17.23	96.13±12.5	94.48±17.29	.872	.781	.673
AT Imin	94.48±21.079	94.88±11.658	91.44±12.205	.001	.000	.006
AT 5min	92.97±16.840	89.75±9.7261	83.80±13.081	.036	.007	.018
At 10min	94.84±18.359	90.28±12.844	88.42±17.363	.175	.068	.601
At 15min	89.91±17.889	90.00±11.453	81.31±11.606	.978	.010	.001
At 20min	91.00±18.596	86.71±11.203	81.44±12.119	.160	.003	.027
At 30min	91.71±17.517	88.60±10.344	84.95±12.356	.282	.009	.173
At 45 min	71.13±6.838	71.91±8.585	77.60±9.252	.203	.183	.112
At 60 min	71.84±14.904	65.15±16.810	64.77±16.630	.241	.315	.082
At100min	84.71±14.221	78.84±14.409	77.77±38.413	.067	.202	.338

Table 4: Changes in SBP and MBP

Time	Group-C	Group-D10	Group-D15	GC & GD-10	GC & GD-15	GC & GD -15
Baseline	131.15±15.060	128.93±12.02	133.82±13.586	.147	.429	.063
AT Imin	111.15±3.717	114.26±4.783	114.24±4.046	.001	.001	.982
AT 5min	94.71±14.221	98.84±14.494	112.77±38.331	.109	.002	.024
At 10min	115.53±4.251	115.86±4.159	113.82±4.672	.685	.039	.008
At 15min	104.71±2.616	106.57±2.230	107.33±2.868	.001	.000	.127
At 20min	113.48±4.590	114.42±4.234	115.51±3.108	.299	.007	.131
At 30min	115.13±4.224	114.46±5.132	113.37±4.427	.435	.033	.272
At 45min	113.48±4.59061	114.42±4.234	115.51±3.108	.299	.007	.131
At 60min	116.44±4.545	116.44±4.545	114.42±3.683	.405	.032	.135
100min	122.26±21.64	124.44±18.401	123.88±20.280	.470	.652	.837
Changes In MBP						
Baseline	80.40±14.17	80.77±17.965	82.17±19.278	.883	.065	.076
AT Imin	71.13±6.838	71.91±8.585	77.60±9.252	.339	.000	.004
AT 5min	71.84±14.904	65.15±16.810	64.77±16.630	.046	.051	.881
At 10min	64.44±15.324	67.35±18.095	67.24±17.612	.405	.247	.970
At 15min	65.82±16.677	67.60±17.547	67.64±16.833	.536	.501	.986
At 20min	68.57±25.729	71.22±18.447	76.08±27.476	.318	.067	.115
At 30min	68.46±16.520	65.88±17.216	70.06±17.052	.448	.657	.236
At 45min	63.95±13.090	67.17±14.343	68.06±15.235	.221	.154	.775
At 60min	68.37±16.680	67.77±17.413	68.11±16.918	.758	.943	.928
At 100min	67.82±13.873	66.86±14.741	69.4±15.709	.689	.609	.438

Table:5 Untoward consequences [%]

Side effects	Group-C	Group –d10	Group –d15	P-value
Nausea & Vomiting	1(2.22%)	2(4.44%)	2(4.44%)	0.445
Bradycardia	2(4.44%)	2(4.44%)	3(6.66%)	0.210
Hypotention	1[2.2%]	0	1[2,2%]	0.541
Drowsiness	0	0	1[2.2%]	0.894
Shivering	2[4.4%]	0	0	0.972

DISCUSSION

We found that both, the fastest inception of sensory block and shortest time to reach Bromage score 3 (initiation of motor block) , was , associated with group of patients with heaviest dose of dexmedetomidine (Group D-15 as compared to D-10 and Group D-C).Various researches have proved different results in this regard. A large meta-analysis comprising more than one thousand patients from sixteen randomized control trails assessed various effects of different doses of DEX in neuraxial anaesthesia[12].The analysis concluded that time for initiation of sensory block was shorter as dose of dexmedetomidine increases but increasing the dose of dexmedetomidine did not affect the onset of motor block. Quite the reverse, Al-Mustafa et al, proved that 10 microgram dexmedetomidine took least time in initiating the sensory and motor block in comparison to 5 microgram dexmedetomidine and the control group, proving same results as that of our study[13]. Analogously, Hala et al[14] did a study to see the effects of two different intrathecal doses of 10 and 15 micrograms of dexmedetomidine alongwith hyperbaric bupivacaine, the showed the same results as ours that increasing the dose of dexmedetomidine shortens the initiation time of sensory and motor block.

Although the duration of sensory block and time to regression of sensory level to T10 and T12 was significantly prolonged between control group and the groups with DEX (p-value<.05 between GC and D-10 and D-15), the difference was insignificant between groups with two doses (p-value> .05). While the duration of motor block was significantly prolonged between not only control group and groups with dexmedetomidine (p-value <.05), but also it was prolonged significantly with increasing dose of dexmedetomidine (p-value <.05 between D-10 and D-15). Various researchers have proved that adding dexmedetomidine intrathecally increases the duration of sensory and motor block, while, contrary to our results, GUPTA[15] and Yektas et al [16] further showed increasing duration of sensory and motor block with increasing dose. Corresponding to our results, Sudheesh et al[17], proved that though sensory block increases with adding dexmedetomidine intrathecally but with increasing dose the difference was insignificant(p value>.05).

It is admitted on all hands that adding dexmedetomidine intrathecally not only prolonged the analgesic effects but also results in decreased requirements of analgesics for the next 24 hours[14-16]. Evenly, our patients followed the same above mentioned rule and showed significantly reduced requirement of analgesic drugs.

Considering the hemodynamic changes, the mean heart rate between all three groups was comparable (although heart rate was dropped in D-15 group at 1minute and 5minutes but it was within normal range). Gupta et al[15], Sudheesh et al[17] and Esmaoğlu et al[18] also showed even values of mean heart rates between dexmedetomidine groups and control. Halder et al, however showed that bradycardia is a statistically significant occurrence in dexmedetomidine group[19]. Similarly, the mean B.P had comparable values between three groups. This results goes with results of various other studies as well[17, 18, 20], while yektas et al[16] showed statistically significant occurrence of hypotension in dexmedetomidine group.

There is 55% incidence of shivering in c-section[21]. It increases O_2 consumption, increase in CO_2 synthesis ultimately producing maternal metabolic derangements. Intrathecal dexmedetomidine suppresses the central thermoregulatory mechanism by blocking the transference of body temperature details thus inhibiting shivering[22]. None of our patients in dexmedetomidine group showed shivering while single patient in control group had the event. A meta-analysis by Wang et al[23] also showed that intrathecal dexmedetomidine effectively reduces the incidence of shivering.

Comparing the two groups of intrathecal dexmedetomidine (D-10 & D-15), we found that they were statistically non-significant in duration of sensory block (p-value >.05). Recovery of motor function is more rapid in D-10 group which is rather a sigh of relief for patient. Hemodynamic profile is comparable, while, incidences of nausea, vomiting and prevention of shivering are also equivalent in both groups. Side effects like bradycardia, hypotension and drowsiness, though, not statistically significant, but, nevertheless, are more in D-15 group.

Our study is not short of limitations .we did not take into account the no of caesarian sections each woman had before being enrolled in this study as the adaptability to pain and maternal receptiveness of primary gravida is different than multi gravida[24]. The comprehension and education level of all participants were also not similar. The affirmation of our results is also required from other centers with bigger cohorts considering a shorter sample and single center focused study.

CONCLUSION

Adjuvant Intrathecal dexmedetomidine with hyperbaric bupivacaine is a safer, hemodynamically favorable and analgesic sparing technique. 10microgram dexmedetomidine is an optimal dose for intrathecal administration.

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