Original Research Article

Comparison of intrathecal clonidine and dexmedetomidine as adjuvant to bupivacaine for hemodynamic response and postoperative analgesia in infraumbilical surgeries

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Abstract

Background: Clonidine and Dexmedetomidine is commonly used adjuncts with hyperbaric Bupivacaine in spinal anaesthesia. Both are α2 adrenergic agoinsts. Dexmedetomidine is comparatively newer drug with lesser side effects. Though both drugs were used commonly their effectiveness in subarachnoid block remains a debate. Aim of the study is to compare the Postoperative Analgesia and Heamodynamic response to intrathecal Clonidine and Dexmedetomidine as adjuvant to Bupivacaine in infraumbilical surgeries. **Method:** 60 patients of ASA 1 and 2 between age groups undergoing infraumbilical surgeries under spinal anaesthesia were selected and randomly allocated into 2 groups. Group D received 3 ml Bupivacaine heavy and 3 µg Dexmedetomidine. Group C received 3 ml Bupivacaine heavy and 30 µg Clonidine. Constant drug solution volume of 3.3ml was injected at L3-L4 space intrathecally. Onset and duration of sensory and motor block, duration of effective analgesia, heamodynamic changes and side effects were recorded. **Result:** Onset of sensory block was 3.34min in Group D and 4.032min in Group C. Onset of motor block was 3.2min in Group C and 3.8 min in Group D. Duration of sensory block was 337.98 min in group D and 265.46 min in group C. Duration of motor block measured was 262.42 min in group D and 205.8 min in group C. Rapid onset and prolonged duration of sensory and motor block was seen in group D compared to group C. Two segmental regression was 99.54 min in Group C and 136.54 min in Group C. Duration of analgesia was 305.7min in Group C and Group D was 366.4min.Two segmental regression and Duration of analgesia was prolonged in Group D. Both Dexmedetomidine and Clonidine decreased vitals, PR, SBP, DBP but were comparable. Clonidine produced more sustained and prolonged hypotension with lesser plane of sedation when compared to Dexmedetomidine. **Conclusion:** Intrathecal Dexmedetomidine 3 µg added as additive with intrathecal Bupivacaine proved to be better than 30 µg Clonidine.

Key Word: Spinal Anaesthesia, Clonidine, Dexmedetomidine, α2 adrenergic agonist.

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INTRODUCTION

Spinal anesthesia provides good quality of anesthesia and very less side effects than general anesthesia[1]. It is used for perineal, abdominal, lower limb and gynecological operations. Spinal anesthesia provides immediate onset and prolonged duration of motor blockade. It is also easy to perform. Usually Bupivacaine is the most commonly used local anesthetic interathecally, which produce long lasting sensory and motor blockade. In order to decrease dose of local anaesthetic and to provide good quality and prolonged duration of anesthesia, additives are added

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intrathecally along with local anesthetics[2]. Commonly added adjuvants are Opioids ie, Fentanyl, Morphine, etc, Midazolam, α 2 adrenergic agonists ie, Clonidine and Dexmedetomidine. In this study we had added Clonidine and Dexmedetomidine as adjuvant to intrathecal Bupivacaine. Clonidine is an α 2 adrenergic agonist. It's commonly used intrathecally as adjuvant with Bupivacaine[3]. Dexmedetomidine is also an α2 adrenergic agonist. Use of Dexmedetomidine intrathecally proved its potent antinociceptive[4] character and also drug has been used safely in epidural space and intrathecally, without any evidence of neurological deficits. Dexmedetomidine is ten times more potent than Clonidine[5].Hence in this study equipotent dose of Dexmedetomidine 3µg and clonidine 30 µg is combined with Bupivacaine in spinal anesthesia to compare the onset and duration of block along with side effects and haemodynamic changes.

MATERIALS AND METHODS

This study was done at Meenakshi medical college hospital, Kanchipuram between January 2017 to September 2018 on 60 patients ranodomized into two groups ie, Group C and Group D of ASA physical status grade I and II undergoing infraumbilical surgeries. Institutional human Ethical committee approval was attained before study. Written informed consent was obtained from all patients selected in the study. Study design was Prospective double blinded randomized control manner. Patients allergic to study drugs**,** Patient on beta blocker or Clonidine therapy, patients with any other contraindication to SAB were excluded from the study.30 Patients in group C received 3 ml of 0.5% hyperbaric Bupivacaine with 30 µg Clonidine in preservative free Normal saline. 30 Patients in group D received 3 ml of 0.5% hyperbaric Bupivacaine with 3 µg of Dexmedetomidine in preservative free Normal saline Volume of drug solution was kept constant as 3.3 ml. A detailed preoperative assessment was done. Cases were randomized by lottery method. Emergency intubation cart with all needed equipment for airway management and emergency drugs were kept ready in OT. Premedication were not given before surgery. Table position was corrected to horizontal level and patient shifted to OT table. IV line was assessed and preloaded with 500 ml RL solution. Spo2, NIBP, monitors were connected. Preoperative vitals such as systolic and diastolic blood pressure, Spo2, pulserate, respiratory rate were recorded. After keeping the patient in right lateral decubitus position a midline lumbar puncture (LP) is given with 25GA quincke's spinal needle following strict asceptic conditions. First attempt of LP was successful in all patients. After injection of drug solution intrathecally patient was placed in supine position immediately. Vital signs were monitored and recorded. Every 5 min interval intraoperatively till end of the surgery and every 15 min postoperatively in recovery room vital signs were recorded. Assessment of motor block was done by Modified Bromage score[6]. (0- Patient can move hip,knee and ankle.,1- Patient cannot move hip but able to move knee and ankle,2- Patient cannot move hip and knee but able to move ankle,3- Patient unable to move hip ,knee and ankle). Assessment of sensory block is done by loss of pinprick sensation with 25 G needle along midclavicular line on both sides. Time taken to achieve Bromage score 3, time to achieve sensory block at T10 level, and peak level of sensory block were recorded. Duration of motor block is assessed as time to attain Bromage score0 and sensory block duration is taken as loss of pinprick sensation at heel of foot, which corresponds to S1 dermatome. Intraoperative complications such as nausea, additive analgesia, vomiting and sedation were recorded. Ramsay sedation score[7] (1- Anxious, restlessness, agitated,2- Cooperative, tranquil but alert, oriented ,3- Responds to command ,4- Asleep but brisk response to loud auditory stimuli or glabellar tap ,5- Asleep, slow response to auditory stimuli or glabellar tap ,6- Asleep, slow response to auditory stimuli or glabellar tap) was used to assess level of sedation, in which sedation score of ≥3 is considered significant. Postoperative assessment of vitals, sensory blockade, and motor Blockade were done every 15 min in recovery room and monitoring was continued till Bromage score becomes 0 and sensory regression to S1 dermatome is achieved. Afterwards patient was shifted to post-operative ward. Pain assessment was done by Visual analogue scale (0- no pain, 1-2 mild pain, annoying, 3-4 moderate pain, uncomfortable, nagging, 5-6 severe pain, distressing, 7-8 very severe pain, intense, horrible, 9-10 worst possible pain, unbearable, agonizing) in which VAS≥4 is considered significant. Effective analgesic duration was taken as time from onset of intrathecal injection and time to attain VAS ≥4 or whenever patient complaints of severe pain, inj. Diclofenac 75mg IM was given as the rescue analgesic and time of injection was noted. Monitoring was continued upto 24 hrs to determine occurrence of complications such as nausea, dry mouth, respiratory depression, vomiting. Symptoms of any transient neurological symptoms such as pain and paraesthesia in buttocks neck, leg or persisting pain which radiates to lower limb after recovery of SAB within 72 hrs were also enquired.

Statistical analysis: In this study all recorded data were entered in MS Excel software and statistical significance were determined using SPSS version 16 software. Results of study were entered as standard deviations, means, medians, ranges, numbers or percentages. Normal distribution of continuous variables among different

groups were done by using one way analysis of variance and if possible followed by Bonferronis test for post hoc analysis. Chi square test or Fishers exact test were used to compare nominal categorical data between groups. Mann-Whitney U-test were used to compare ordinal categorical variables and continuous variables which are non-normally distributed.

OBSERVATION AND RESULTS

One way ANOVA and t test proves that demographic variables like height, weight and age are statistically not significant between two groups.(Table 1)

Table 1: Demographic distribution

		N	Mean	S.D	Significance
Age (yrs)	Clonidine	30	41.20	8.75	P<0.70
	Dexmedetomidine	30	43.28	12.175	
	Total	60	42.41	10.173	
Weight (yrs)	Clonidine	30	54	7.330	P<0.653
	Dexmedetomidine	30	55.6	10.760	
	Total	60	55.12	8.680	
Height (cms)	Clonidine	30	158.40	7.044	P<0.122
	Dexmedetomidine	30	161.85	6.823	
	Total	60	160.25	6.652	

As per Pearsons chi X^2 square test distribution of ASA pysical status and sex between both groups gives a P value 0.532 and 0.832 respectively which suggests comparability between both groups.(Table 2)

Table 2: Distribution of sex and ASA status among groups

Group	FEMALE: MALE	ASA 1:2	Total
CLONIDINE	8:22	20:10	30
	26%:73.3%	63.6%:36.4%	100%
DEXMEDETOMIDINE	7:23	18:12	30
	23.4%:76.6%	61.8%:38.2%	100%
TOTAL	13:47	38:22	60
	21.6%:78.4%	63.33%:36.66%	100%

Eventhough mean duration of surgery is more in group Clonidine group(100.8 min) and compared to Dexmedetomidine group (91.9min), it is statistically insignificant**.** (P=0.37) (Table 3)

Table 3: Duration of surgery (Mins)

Parameters	Group C	Group D	ANOVA
No.of cases	30	30	P=0.37
Mean duration(mins)± S.D	100.8±32.5	91.9±28.36	

Pearsons chiX^2 square test (p<0.80), shows no statistical significant difference in surgeries performed in both groups. (Table 4)

Table 4: Type of surgery by groups

SURGERY	Group C	Group D
Inguinal hernia repair	14	15
	46.67%	50%
Appendicectomy	3	5
	10%	16.67%
Totalabdominal hysterectomy	6	5
	20%	16.67%
Hydrocele	3	2
	10%	6.667%
Incisional hernia repair	1	1
	3.33%	3.33%
Varicose vein surgery	3	2
	10%	6.667%

Mean onset of sensory block is 3.34 min in group D compared to 4.032 min group C (Table 5, fig 1). Mean onset of motor blockade is 3.27min in group D compared to 3.8min in group C. Rapid onset of sensory and motor blockade is seen in group D than group C, in which its statistical significance is confirmed by post Hoc test (Bonferronis test) (p<0.0001).

Table 5: Distribution of mean onset of sensory and motor block(mins)

PARAMETERS	Group C	Group D	ANOVA
No.of cases	30	30	
Onset of sensory block Mean (Mins)± SD	4.032±43.54	3.34±32.235	P<0.0001
Onset of motor block Mean (mins)±SD	3.8±1.041	3.27±1.1108	<0.0001

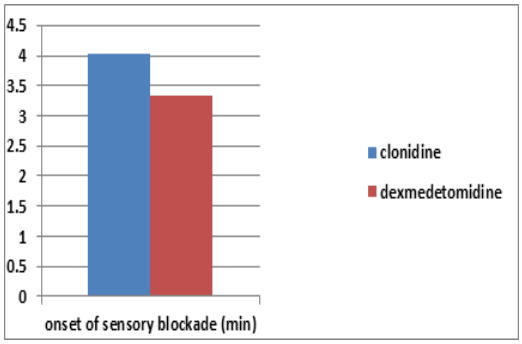

Figure 1: Mean onset of sensory block in mins

Maximum sensory block level achieved were T4 in both groups. 70% of patients in group D achieved peak sensory block of T4 level while only 40% in group C achieved same level of block. Hence group D provides more higher sensory block compared to group C which is statistically significant. (Non-parametric test-Kruskal wallis rank test P=0.002). Both the groups provided maximum motor blockade of Bromage score3 which is statistically insignificant. Mean duration of two segmental regression in Group D(136.54min) were prolonged compared to group C (99.54min) is statistically significant by ANOVA and Bonferronis test (P<0.001)(Table 6,fig. 2).

Table 6. Characteristics of spinal block in both groups

PARAMETERS	Group C	Group D	ANOVA
No.cases	30	30	
Duration of two seg reression Mean(Mins)±S.D	99.54± 16.7	136.54± 11.7	P<0.001
Duration of motor block Mean(min)± S.D	205.8± 12.903	262.42± 12.903	P<0.001
Duration of sensory block Mean(min)± S.D	265.46± 17.27	337.98± 22.46	P<0.001
Duration of Analgesia Mean(min)± S.D	305.7± 17.342	366.0± 28.634	P<0.001

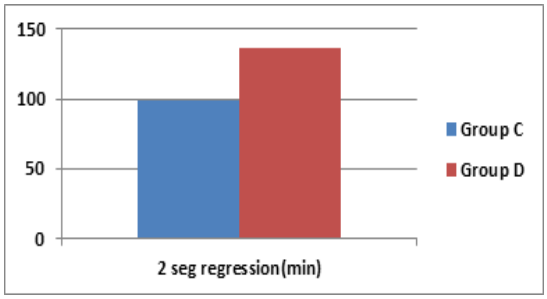

Figure 2: Two segmental regression (mins) by groups

Mean duration of motor blockade is much prolonged in group D(262.42min) compared to group C (205.8min) which is statistically significant by ANOVA and bonferronis test(P<0.001). (fig 3)

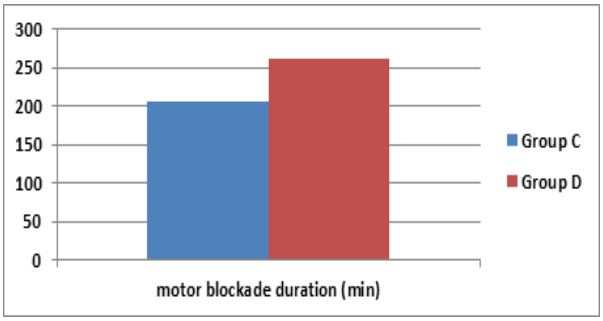

Figure 3: Distribution of mean duration of motor block (mins) by groups

Duration of sensory block is very much prolonged in group D(337.98min) compared to group C(265.46min) which is statistically significant by ANOVA and Bonferronis post hoc-P<0.001. (fig 4).

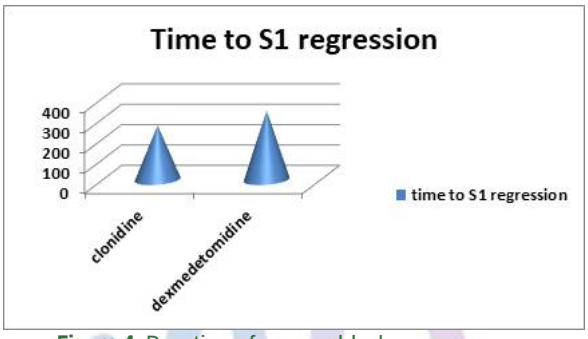

Figure 4: Duration of sensory block among groups

Duration of effective analgesia is much higher in group D(366.0min) compared to group C (305.7min) which is statistically significant(P<0.001). (fig 5)

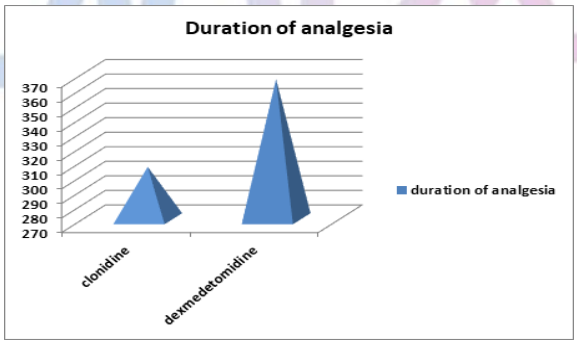

Figure 5: Distribution of mean duration of analgesia among groups

Hypotension, bradycardia and sedation, dryness of mouth were observed in both the groups (Table 7, Fig 6). But increased incidence of hypotension and bradycardia was seen in Clonidine group (p<0.001), whereas profound sedation of RSS≥ 3 was seen in Dexmedetomidine group (p<0.0001) which is statistically significant

Table 7: Distribution of side effects

EFFECTS	GROUP C		GROUP D	
	NO	%	NO	%
Hypotension	12	40	4	13.3
Bradycardia	10	33.3	4	13.3
Sedation	16	53.33	24	80
Dryness of mouth	0	0	3	10

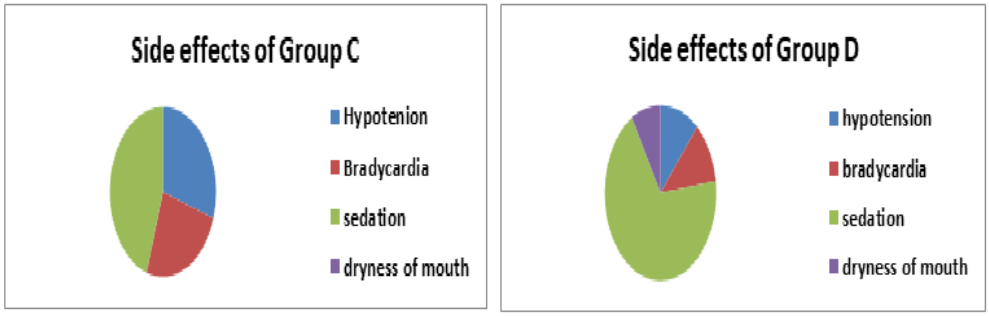

Figure 6: Distribution of side effects in group C and group D

DISCUSSION

α2 agonist drugs, Clonidine and Dexmedetomidine when used as adjuvants added to LA intrathecal injection in SAB provide effective surgical anesthesia. In this study, mean time to sensory block onset was4.03 in group C and 3.34 min in group D. When compared to group C rapid onset of sensory block is seen in group D. According to Al Mustafa *Et al*[8,9] intrathecal injection of 5 µg Dexmedetomidine with 0.5% Bupivacaine 12.5mg vs Bupivacaine 12.5mg alone. Sensory block onset time were 6.3and 9.5 mins respectively. It shows rapid onset of sensory block is seen in Dexmedetomidine group which is similar to our study. Mean time of onset of motor block was 3.8min in group C and 3.27 min in group D. Dexmedetomidine fasten the onset of motor block when compared to Clonidine which is statistically significant(post hoc analysis give difference between group C and D which is Bonferroni –P<0.001).Al Mustafa etal[8,9] , gives similar values in his study ,group C -13 min ,and group D -10min in which onset of motor block is delayed in group C. Maximum sensory block achieved in both groups were T4 level. In this study70% of patients among Dexmedetomidine group had peak level of sensory block of T4 level wheras its only 40% among Clonidine group. As Dexmedetomidine has higher level of sensory blockade regular usage of Dexmedetomidine for supraumbilical surgeries should be studied even more. Kanazi *et al*[10], found that use of intrathecal Clonidine 30 µg and Dexmedetomidine 3 µg along with 0.75% Bupivacaine gives lower peak sensory level block in group C T6.5 (T3-T9) compared to T5 in group D, which is similar to our study. Using modified Bromage score, median of maximum motor block achieved was grade 3 in both groups which is not statistically significant. As per klimscha *et al*[11] intrathecal Clonidine 150 µg along with 0.5% Bupivacaine resulted in significant increase in degree of motor block. According to Bonnet *et al*[12,13] both intensity and duration of motor block was prolonged with increased dose of Clonidine from 75 µg to 150 µg along with 0.5% Tetracaine 15 mg I n our study mean time for two segmental regression was less in group C (99.54min) compared to group D (136.54min) which was statistically significant in group D. Same result seen in studies of Al Mustafa *et al*[8,9] and kanazi *et al*[10]. In our study mean duration of motor block is prolonged in group D (264.42mins) compared to group C (205.8mins) which is statistically significant. As per kanazi *et al*[10] mean duration of motor block by clonidine and Dexmedetomidine is 216min and 215min respectively. Al Mustafa *et al* also demonstrated motor block duration of 246 min using Dexmedetomidine which correlates approximaltely to our study. The maen time for sensory regression to S1 dermatome was 265.46 mins in group C 337.98 min in group D in this study which is statistically significant. Kanazi *et al*[10] demonstrated significant difference in duration of sensory block between Clonidine (272min) and Dexmedetomidine (303min) groups which correlates well with result of our study. According to Debrydnjov *et al*[14], addition of Clonidine along with Bupivacaine for inguinal hernioraphy surgeries had increased duration of analgesia than control group. As per gautier *et al*[15], Clonidine added with Sufentanil for first stage of labour prolonged the duration of analgesia than with addition of Sufentanil alone. Mercier *et al*[16]also demonstrated increased duration of effective analgesia by addition of Clonidine along with Sufentanil intrathecally. Pulse rate, SBP, DBP was decreased after addition of Clonidine and Dexmedetomidine. But group C shows sustained and significant lowering in SBP and DBP for a prolonged duration. In our study hypotension was seen in 40% of patients who received Clonidine. Hypotension and bradycaridia was treated by Ephedrine and Atropine respectively. Hence we recommend not to use higher dose of Clonidine. As per chiari Astrid *et al*[17], usage of Clonidine intrathecally as a sole analgesic agent in first stage of labour demonstrated that increased incidence of hypotension was associated with increased doses of Clonidine. Fibs kriton *et al*[18], in his study found increased and profound hypotension associated with Clonidine use. In this study, RSS value of ≥3 were observed in 80% of patients in Dexmedetomidine group, whereas it's only 53.3% in Clonidine group. Hence patients who received Dexmedetomidine had deeper level of sedation with mean

Ramsay sedation score of 3.3, when compared to patients recieved Clonidine, which did not need any active intervention. As per Nawaz Ahmed *et al*[19], mean sedation scores were significantly higher in Dexmedetomidine ($p<0.0001$) compared to Clonidine when administered intrathecally along with Bupivacaine. Patients with RSS >3 were 68% in group D and 24% in group C which is similar to our study results.

CONCLUSION

Addition of Clonidine and Dexmedetomidine as adjuvants with 0.5% Bupivacaine Heavy intrathecally in SAB provides rapid onset and prolonged duration of both motor and sensory blockade. Addition of 3 µg Dexmedetomidine along with 0.5% Bupivacaine Heavy in SAB is more potent, which provides rapid onset and increased duration of sensory and motor block with prolonged postoperative analgesia, in comparison with addition of 30 µg Clonidine. In most of the cases lowering of HR and BP by Dexmedetomidine were not severe enough to demand an active intervention but the same fact cannot be said in use of higher doses of Clonidine.

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