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Effects of Spinal Versus Intravenous Clonidine on Prolongation of Spinal Anaesthesia in Patients Undergoing LSCS

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Abstract: *The objective of the study was to evaluate the effect of intrathecal and intravenousclonidine on the duration of subarachnoid block in patients undergoing caesareansections under spinal anaesthesia. 63 patients undergoing elective caesareansections under spinal anaesthesia were randomized into three groups of 21 each. Group1 (intrathecal group) each patient received clonidine 30 μg (0.2 ml) and hyperbaric bupivacaine 9 mg.Group 2 (intravenous group)each patient received hyperbaric bupivacaine 9mg intrathecallyfollowed by intravenous clonidine 1μg /mg (0.2 ml)diluted to 10 ml of normal saline over 10 min.Group 3 (control group) each patient received hyperbaric bupivacaine 9mg intrathecally followed by 10 ml of normal saline over 10min. Time taken for regression to Modified Bromage Scale 0, two dermatomal regression of sensory blockade, duration of sensory block was higher in group 1 compared to group 2 (p values < 0.001). In conclusion intrathecal clonidine at low doses significantly prolongs the duration of sensory and motor block of bupivacaine spinal anaesthesia with good hemodynamic stability.*

Keywords: *bupivacaine,clonidine, Intrathecal,intravenous, Ramsay sedation scale, Spinal anaesthesia*

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I. Introduction

Caesarean section is one of the most common operation in the child bearing age of a woman. Safe and potent anaesthetic technique for patients undergoing caesarean section is Neuraxial blockade. Subarachnoid block for caesarean section is advantageous because of less neonatal exposure to depressant drugs ,decreased risk of maternal pulmonary aspiration and an awaken mother at the birth of her child [1](3).several adjuvants like epinephrine, phenylephrine, adenosine, magnesium sulphate, sodium bicarbonate, neostigmine and alpha$_2$ agonists like clonidine, dexmedetomidinehave been used intrathecally[2] andClonidine and dexmedetomidine are also used intravenously to prolong the duration of spinal block[3.]

Alpha-2 adrenergic agonists have both analgesic and sedative properties when used as adjuvants to regional anaesthesia. By action at the α_2-receptor in spinal and supraspinal sites, they

potentiate the effect of local anaesthetics and allow a decrease in the required doses.[4],[5] They produce sedation and anxiolysis by binding to pre synaptic alpha$_2$ receptors in locus coeruleus.

Locus coeruleus is among the one having highest densities of α2 receptors which is a predominant noradrenergic nucleus in the brain and an important modulator of vigilance. Activation of α2-adrenoceptor results in hypnotic and sedative effects in this site in the CNS. The locus coeruleus site for the descending medullospinal noradrenergic pathway is an important modulator of nociceptive neurotransmission. In this site, α2-adrenergic and opioidergic systems have common effector mechanisms.Prolongation of motor and sensory block with the use of α2 agonists occurs as a result of differential block of Aα and C fibers. Motor blocked by α2 agonists results from the direct inhibition of impulse transmission in large, myelinated Aα fibers. The EC 50 of α2 agonists is four fold less in large fibers compared to umyelinated C fibers. [6,7].This is probably the cause of increased sensory block leading to prolonged analgesia compared to motor block[8,9].

The intrathecal application of clonidine increases the duration of both sensory and motor block,[10-13] as well as postoperative analgesia.[14] The mechanism of clonidine in spinal anaesthesia is reported to be mediated by presynaptic (inhibition of transmitter release)[15] and postsynaptic (enhancing hyperpolarization)[16,17] effects.

Our study was undertaken to compare the effects of intrathecal and intravenous clonidine on duration of spinal anaesthesia in pregnant patients undergoing caesarean section and to evaluate its effects like sedation and hemodynamic stability.

II. Material and Methods

Source of data: The study was conducted in Government General Hospital, Government Medical College,Ongole, Prakasam District. 63 cases of ASA grade I-II undergoing caesarean section were included in this study. Patients were divided in to three groups each consisting of 21 patients. This study was done after obtaining informedwritten consent from the patients.

Inclusion Criteria:

1) Age 20--30 years
2) No association with co morbid conditions like diabetes, hypertension, asthma, anaemia
3) elective caesarean sections

Exclusion Criteria:

1. Patient refusal
2. Short stature (height less than 145 cm)
3. Uncooperative patients
4. Patients with hypersensitivity to local anaesthetics.
5. Infection over the site of injection.
6. Bleeding diathesis

After securing IV (18G) access and monitoring as per ASA standards, patients are preloaded with 20 ml/kg of Ringer's lactate solution over 10min. A baseline recording of heart rate, NIBP, SP02 were recorded. After ensuring the table in horizontal position thepatient turned in lateral position with neck flexed and knees drawn up as far as possible. Under strict aseptic precautions in group(1) 9mg of 0.5% hyperbaric bupivacaineand *30 μg* of clonidine (0.2ml)making a total volume of 2 ml is injected in the L3-L4 interspace with 23/ 25G quinke's spinal needle. In group 2 patients 9mg of 0.5% hyperbaric bupivacaine + 0.2 ml of normal saline making a total volume of 2ml injected in the L3-L4 interspace with 23/25 G quinke's spinal needle. immediately after shifting patient in to

supine position group 2 patients received *1 μg*/kg of clonidine diluted in 10ml of normal saline and given intravenously over 10 min. In group 3 patients 9mg of 0.5% hyperbaric bupivacaine + 0.2 ml of normal saline making a total volume of 2ml injected in the L3-L4 interspace with 23/25 G quinke's spinal needle. immediately after shifting patient in to supine position group 3 patients received 10ml of normal saline intravenously.Onset of peak sensory level and motor blockade are noted.NIBP, Heart rate & oxygen saturation are recorded immediately and after 5, 10, 15, 20 min & so on.

Sensory blockade will be checked with hypodermic needle in mid axillary line and the time taken for thehighest level of sensory blockade, two dermatomal regression from the maximum level and regression to S1 level will be noted. Sensory blockade will be assessed every 2 mins for the first 10 mins and thereafter every 15 mins during surgery and postoperatively. All the durations will be calculated considering the time of spinal injection as time 0. Motor blockade will be assessed by Modified Bromage Scale. Time taken for motor blockade to reach Modified Bromage Scale 3 and regression of motor blockade to Modified Bromage Scale 0 will be noted. Motor blockade will be assessed every 2 mins before the onset of the surgery and every 15 min in PACU.Hypotension (systolic blood pressure less than 90 mm Hg or more than 20% fall from base line value then treated with inj. mephentermine) & bradycardia(heart Rate<50/min , treated with inj. atropine) and post operative complications like nausea and vomiting will be noted and treated appropriately

The level of sedation was evaluated both intra operatively and post operatively every 15 mins using Ramsay Level of Sedation Scale till the patient is discharged from PACU. Excessive sedation was defined as score greater than 4/6.

Table 1: Modified Bromage scale

Grade	Criteria	Degree of block
0	Able to move the hip, knee and ankle	None
1	Unable to move the hip, but is able to move the knee and ankle	Partial 33%
2	Unable to move the hip and knee, but is able to move the ankle	Partial 66%
3	Unable to move the hip, knee and ankle	Complete paralysis

The level of sedation was evaluated using Ramsay Level of Sedation Scale [9].

Table 2: Ramsay sadation score

Scale	Level of sedation
1	Patient anxious, agitated, or restless
2	Patient cooperative, oriented, and tranquil alert
3	Patient responds to commands
4	Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep, no response

III. Observations and Results

The study was carried out on a total number of 63 patients operated under spinal anaesthesia. Demographic data, intraoperative and postoperative hemodynamics, Respiratory rate, Ramsay sedation score and side effects were compared between groups

Statistical analysis

The data obtained was entered in to Microsoft excel spreadsheet. The data was expressed in terms of percentages, mean and standard deviation (SD). The data was analysed by Annova test and paired ttest. A probability (p) value of less than or equal to 0.05 was considered as statistically significant.

Demographic data:

Age:

The mean age in the Group 1 was 21.95 ±2.13Yrs. as compared to21.81±1.99 years in the Group 2and 21.57±2.36 years in group 2 patients and the difference was statistically no significant (P value- 0.847537769). There was statistically no significant difference in age distribution in both groups.

Weight:

The mean weight in the group 1was 50.05±4.87kgs as compared to 51.43±4.42 kgs in Group 2 and 53.33±5.65 kgs in group 3 patientsand the difference was statistically not significant (Pvalue-0.111170486). There was no statistically significantdifference in weight distribution in both groups.

Duration of surgery:

The mean duration of surgery in group 1 was 48.57±7.77 minutes as compared to 44.29±7.95minutes in group 2 and 48.10±8.29min in group 3 patients and the difference was statistically not significant (P value-0.172793129).

The demographic data was summarized in Table3

Table3: Demographic data in both groups

Patient's Demographic Data				
Demographic	**Intrathecal(N=21)**	**Intravenous(N=21)**	**Control(N=21)**	**P value**
Age (Years)	21.95+2.13	21.81+1.99	21.57+2.36	0.8475
Weight (kg)	50.05+4.87	51.43+4.42	53.33+5.65	0.1112
Height(cm)	154.47±5.32	154.43±4.62	154.04±4.9	0.9544
Duration of Surgery (In Min)	48.57+7.77	44.28+7.95	48.09+8.29	0.1728
Data represented as Mean; p>0.05 is considered statistically non-significant compared with other two groups				

Duration of sensory block in the groups

The mean duration of sensory block in the group 1 was193.67±43.16
minutes as compared to 189.85 ± 29.144minutes in group 2 and 167.04± 36.88 min in group 3 patients. Between the groups the p values are

Between group 1 and group 2---- the p value is 0.3478(insignificant)

Between group 1 and group 3---0.0269 (significant)

Between group 2 and group 3--- 0.0390(significant)

The duration of sensory block in both the groups is summarized in the table below

Duration of motor block in both the groups

The mean duration of motor block in the group 1was 165.38± 35.71 minutes as compared to 148.81±30.43minutes in group 2 and 128.33±13.07 min in group 3 patients.Between the groups the p values are

between group 1 and group 2---- the p value is 0.0630(insignificant)

between group 1 and group 3---0.000127(significant)

between group 2 and group 3--- 0.00690(significant)

The duration of motor block in both the groups is summarized in Table±

Duration of two segment regression in both the groups

The mean duration of two segment regression in the group 1 was 144.048±30.11 minutes as compared to 134.38± 26.45minutes in group 2 and 108.43±20.49min in group 3.Between the groups the p values are

between group 1 and group 2---- the p value is 0.0857(insignificant)

between group 1 and group 3---0.00064(significant)

between group 2 and group 3--- 0.00145(significant)

The duration of two segment regression in both the groups is summarized in Table4

Table4: comparison of outcome variables between the groups

	Group 1	**Group 2**	**Group 3**	**Gr1 vsGr2 p values**	**Gr1 vs Gr3 pvalues**	**Gr2 vsGr3 pvalues**
Time to reach T6 sensory level (min)	3.24±1.179	3.05±0.804	3.14±0.35	0.25914	0.35244	0.28819
Time to reach motor blocked bromage 3 (min)	5.38±1.63	5.28±1.55	5.62±0.49	0.41463	0.25676	0.14249
Two segment regression time (min)	144.04±30.11	134.38±26.45	108.42±20.49	0.08572	0.00064	0.00145
Sensory recovery time (min)	193.67±43.16	189.85±29.144	167.04±36.88	0.34786	0.02697	0.03907
Motor recovery time (min)	165.38±35.71	148.81±30.43	128.33±13.07	0.06304	0.00012	0.00690
Data represented as Mean; $p<0.05$ is considered statically significant compared with other two groups						

As regard HR comparison between groups in baseline, 5 min 15min, 30 min and 45 min showed that in group 1 there was decrease in mean value of heart rate at 5min, 15min,30min,and 45min from 91.8,91.2,88.75,86.21 beats per min and also in group 2 there was decrease in mean value of HR at 5 min,15min,30 min and 45 min from 82.1.81.6,81,79.18 beats per min. and the decrease was statistically significant between the groups. In group 3 patients also the mean value of HR decreases from base lime to 45 minas 85 ,79.1,76.3,78,78.5,74.72.

But the number of patients requiring atropine for management of bradycardia was higher in group 1(14%) as compared to group 2 9.5% andin group 3 no patients require atropine for management of bradycardia.

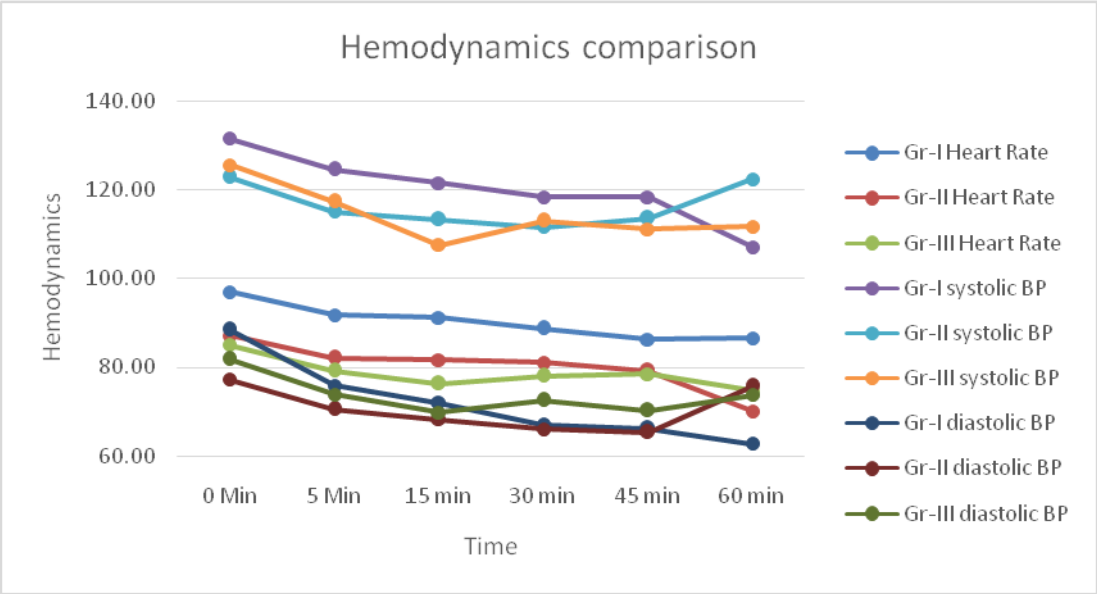

Fig1: comparison of hemodynamic between the groups

As regard systolic BP comparison between groups in base line ,5 min,15 min,30 min and 45 min showed that in group 1 there was decrease in mean value of SBP AT 5 min,15 min ,30 min and 45 min from 125,121.5,118.4.119.3 mm Hg and also in group 2 there was decrease in mean SBP from 115,113.2,111.6,113.5 mmHg . and in group 3 patients the mean SBP from baseline to 45 min are as 125.6,117,107.6,113,111.1 and 111.6 mmHG .and the decrease in SBP between the groups was statistically not significant.

As regard diastolic BP comparison between groups in baseline ,5 15,30,45 min showed that in group 1 there was decrease in mean value of DBP at 5 ,15,30 and 45 min from 75.9,72,67.1,66.11 mmHg and in group 2 there was decrease in mean DBP from 70.5,68.25,66.05,65.29 mmHg. In group 3 patients the mean value of DBP was 81.7,73.8,69.75,72.55,70.167,73.72 from baseline to 60 min and there was no significant decrease in DBP between the groups. The number of patients requiring vasopressor for management of hypotension was higher in 1 group (33%) as compared to group 2 and 3 (28% and 14% respectively.)

Hypotension and bradycardia are the most commonly reported adverse events in women undergoing LSCS with the use of intrathecalclonidine. But we have successfully managed them by using Inj.Mephentermine and Inj, atropine.

As regards spo2 values there was no significant difference between groups throughout the period. There was no significant difference in sedation scores between the groups.

APGAR score a predictor of foetal wellbeing was found to be good in both groups. APGAR scoring system is specific but not verysensitive and fail to detect small foetal effect of maternal arterial hypotension.[18,19,20]

Table5: Comparison of sedation score ,spo2 and APGAR data in between the groups

	Group 1	**Group 2**	**Group 3**
sedation score	2	2	2
apgar score	10	10	10
spo2	99.63±0.76	99.47±0.90	99.63±0.76

IV. Discussion

Different drugs like epinephrine, phenylephrine, adenosine, magnesium sulphate, sodium bicarbonate, neostigmine and alpha2 agonists like clonidine, dexmedetomidine have been used as adjuvants to local anaesthetics to prolong the duration of spinal anaesthesia. Among them clonindine an alpha2 agonist is widely used by oral, intrathecal and intravenous routes as an adjuvant to prolong spinal anaesthesia. Alpha 2 adrenoreceptor agoists act by bindig to the presyaptic C fibers and post synaptic dorsal horn neurons.they produce analgesia by depressing the release of C fiber transmitters and by hyperpolarisation of post synaptic dorsal horn neurons.[3,23,24].The complimentary action of local anesthetics and alpha 2 adrenoreceptor agonists accounts for their profound analgesic properties.the prolongatio of motor block of spinal anesthetics may be the result of binding of alpha 2 adrenoreceptor agonists to the motor neurons in the dorsal horn.[3,23]Clonidine is a selective partial agonist for α-2 adrenergic receptors; the analgesic effect following its intrathecal administration is mediated spinally through the activation of postsynaptic α-2 receptors in substantia gelatinase of the spinal cord[(21,22)]The drug acts at locus ceruleus and dorsal raphe nucleus to produce sedation and analgesia.

Studies have shown the efficacy of both intrathecal and intravenous clonidine in prolonging spinal anaesthesia . our study is designed to compare intrathecal and intravenous routs of clonidie on duration of spinal aesthesia in patients undergoing LSCS . our study results are compared with the previous study Namrata Ranganath et al[(25)·]They compared intathecal cloidine 75µgms groupA with intravenous clonidine 3µgms/kg group B in patients undergoing infraumblical surgeries.

In our study the duration of sensory blockade i.e. time for regression to S1 dermatome was significantly prolonged in group 1[193.67min±36.88] compared to group 3 control group[167.04min ± 36.88] (p value 0.00269) and significant prolongation was also seen in group 2 intravenous compared to group 3 control[189.85min± 29.144 min and 167.04±36.88minrespectively] (P value <0.0390) . Similar results were also reported by Namrata Ranganath et al [25] 2016 a) Group A- 286± 74.51min, b) Group B- 231 ± 43.13min, c) Group C- 194 ± 21.87min [in intrathecal, intravenous and control group respectively] with p valuesbetween group A and Cwas< 0.004 and between group B and C was 0.006. but in contrast to our results between group 1 and group 2(p value 0.3478) Namrata Ranganath et al[25] reported a significant prolongation between group A and group Balso (p value 0.004). Mean total duration of sensory block was highest in intrathecal clonidine group.Sukhmider Jit Sigh Bajwa et al[26]2018 was also reported a significant dose dependent prolongation of mean duration of sensory blockadewith intrathecal clonidine 30µgms ,37.5 µgms and 45µgms as 168.2±9.4, 184.8±10.6 and 186.2±11.8respectively and contorl132.4±7.6(p value 0.010).and, by Ruchee Arora et al [27]140.40±43.05 ,175.20±37.43 vs 128.40±33.00 15µgms ,30µgms and control respectively. Significant prolongation in mean duration of sensory blockade in intravenous group when compared with control group was also reported by others like Pranav Jetley et al [28](2017) reported a significantly longer duration of analgesia with intravenous clonidine at 1.2µgms/kg dose in their study with levobupivacaine. And Dr. Prerana N.Shah et al [29]2014 also reported similar prolongation with intravenous clonidine 3µgms/kg [206.20 ± 19.155 vs 136.20 ± 15.104 intravenous and control group respectively p value0.000].

The regression time to reach the modified Bromage Scale 0 was significantly prolonged in group 1 [165.38± 35.71mins] compared to group 3 [128.33 min±13.07](p value 0.00690)and significant prolongation was also seen in group 2 compared to group 3 [148.81 min±30.43 vs128.33 min±13.07 with p value 0.00012]. But between group 1 and 2 there no significant prolongation in motor blocked [165.38± 35.71minsvs148.81 min±30.43 with p value 0.0630] Mean total duration of motor block was highest in intrathecal clonidine group .Delay in motor block regression to Bromage

Scale 0 was also reported in previous study.NamrataRanganath et al[25]2016 observed the results[a) group A 269.50±64.17 min b) group B patients 234.75±52.45min and c) group C patients190.50±27.24 min.] which are similar to our study. Mean total duration of motor block was highest in intrathecal clonidine group. [the p value group A vs group B 0.083 ,group B vs group C 0.020 and group A vs group C 0.001]Sukhmider Jit Sigh Bajwa et al[26] 2018 was also reported a significant dose dependent prolongation of mean duration of motor blockade with intrathecal clonidine 30µgms ,37.5 µgms and 45µgms as 186.6±10.8, 192.2±9.6and 196.8±10.8respectively and contorl174.4±12.6.(p value 0.042). and also by Ruchee Arora et al [27]2018171.60 ±38.20 vs 113.20±35.79 intrathecal 30µgmsvs control group but between intrathecal 15 µgms vs control group there was no difference 115.20±38.41 vs113.20±35.79 Significant prolongation in mean duration of motor blockade in intravenous group when compared with control group was also reported by Dr.Prerana N.Shah et al [29] 2014[157.60±14.365 vs 129.60 ±14.422 p value 0.000] . In contrast to this Pranav Jetley et al [28](2017) reported no prolongation in mean duration of motor blocked.

V. Conclusion

From the present study we concluded that intravenous clonidine after bupivacaine spinal anesthesia has characteristics similar to and comparable with intrathecal clonidine with bupivacaine in terms of duration of motor block; Duration of analgesia; and Hemodynamic stability.

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