e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(11); 1024-1041

Original Research Article

A Prospective Randomised Double-Blind Study Comparing the Analgesic Efficacy of Intrathecal Clonidine and Oral Clonidine in Parturients undergoing Caesarean Section under Subarachnoid Block

Vaishnavi B.R.[1], Vinayaka C.S.[2], Shruthi H.R.[3], Shashikala T.K.[4], Sinchana R.[5], Meghana R.[5]

[1,3,6]Department of Anaesthesia, MMCRI
[2]Assistant Professor, SJICSR, Mysuru
[4]Professor, Department of Anaesthesia, MMCRI
[5]YCMC., Department of OG, Pune

Received: 02-10-2022 / Revised: 30-10-2022 / Accepted: 20-11-2022
Corresponding author: Dr Vaishnavi B. R.
Conflict of interest: Nil

Abstract

Caesarean section is the most common surgical procedure which is performed in women of child bearing age. Subarachnoid block is the most commonly performed anaesthesia technique, it is easy. It provides prolonged post-operative analgesia.

Methods: Sixty parturients of age group between 19-35 years of ASA I & ASA II undergoing caesarean section are randomly allocated into two groups. Group OC received Tab. Clonidine 0.3mg orally 90mins before subarachnoid block (SAB) (1.8cc [9mg] of 0.5%hyperbaric bupivacaine + 0.5ml of Normal saline). Group ITC received(1.8cc[9mg] of 0.5% hyperbaric bupivacaine + 1mcg/kg intrathecal clonidine). Data collected are onset of motor and sensory block, duration of motor and sensory block, maximum level of sensory block, time of rescue analgesia, APGAR 1 and 5min and hemodynamic parameters (HR, MAP, SBP, DBP) and any adverse effects like bradycardia, hypotension, sedation, nausea, vomiting and shivering.

Results: Onset of motor and sensory block were early in group OC (2.37±0.26 v/s 3.55±0.52, 2.25±0.35 v/s 3.26±0.5 mins respectively) when compared group ITC, which is statistically highly significant (p=0.000). Total duration of sensory and motor block were less in group OC (164.87±6.03, 153.6±5.8 mins) when compared to group ITC (236.33±15.63, 219.93±14.84 mins) which is statistically highly significant (p=0.000). Time of rescue analgesia was prolonged in group ITC (255±18.77 mins) when compared with group OC (178.73±5.26mins) which is statistically highly significant(p=0.000). HR was significantly reduced at various intervals in group OC(p=0.000).

Conclusion: Intrathecal clonidine prolonged the duration of post-operative analgesia with better hemodynamic profile without any adverse effects when compared to oral clonidine.

Keywords: Subarachnoid block, caesarean section, oral clonidine, intrathecal clonidine.

Introduction

Caesarean section is the most common surgical procedure which is performed in women of child bearing age. Subarachnoid block is most commonly performed anaesthesia technique for caesarean section. There are several advantages of SAB over general anaesthesia in caesarean section. Firstly it is easy to perform, it provides quick and adequate anaesthesia and prolonged analgesia, avoiding polypharmacy, avoiding airway manipulation, which may be difficult in pregnant women, and early ambulation. All these can make a mother feed the baby at the earliest [1].

Post-operative pain has a major impact on the recovery process, it reduces the mobility of the patient, and increases the risk of thrombo-embolic events. The post-operative pain in the caesarean section is caused by big surgical incision and uterine contractions along with multiple mechanisms that lead to elevation of plasma catecholamine levels, which causes distress to every organ in the body [2]. Good control of post-operative pain will improve the mobility of the mother and reduce the risk of thrombo-embolic events [3].

However, in parturient, analgesia has to be balanced against known foetal and maternal effects including respiratory depression, hypotension, pruritis, postoperative nausea and vomiting. These adverse effects may hamper early post-operative recovery and quick breast feeding, infant rooming-in. Hence SAB can be accomplished by adding adjuvants to local anaesthetics. Most commonly used adjuvants in pregnancy are opioids like fentanyl, clonidine, neostigmine and melatonin. Fentanyl may cause adverse effects like pruritis, urinary retention, respiratory depression and severe nausea and vomiting with hemodynamic instability [4,5].

Clonidine is a heterocyclic imidazole derivative with molecular weight of 266.56. It is centrally acting alpha-2 adrenergic agonist. Clonidine is a selective partial agonist of alpha-2 receptors with aplha1 and 2 binding affinity of 220:1 respectively. It is used as an anti-hypertensive due to its sympatholytic action; it decreases sympathetic outflow from CNS. Unlike other sedative agents, clonidine does not appear to cause respiratory depression, its use is limited by its cardiovascular side-effects like hypotension, bradycardia. Clonidine has both centrally and peripherally mediated analgesic properties. It is often described as part of multimodal analgesia particularly in combination with opioids without any respiratory depression. Its analgesic effects is due to its action on postsynaptic alpha-2 receptors in substantia gelatinosa [6].

Clonidine may produce analgesia by inhibiting nor-epinephrine release from pre-junctional alpha-2 receptors, which triggers a sympatholytic effect. Oral dose of clonidine for premedication is 4mcg/kg body weight [6].

Objectives

This study is to compare the analgesic efficacy of oral and intrathecal clonidine and also reduce the rescue analgesics in first 24 hours in parturients coming for elective caesarean section under subarachnoid block.

Primary Objectives:

- Onset of sensory maximum, motor block (bromage 1), the time of maximum sensory block attained, time of two segment regression, total duration of sensory block, time of rescue analgesia, total duration of motor block, total consumption of analgesics Inj tramadol in 24 hrs
- Total analgesics consumption in first 24 hours.

Secondary Objectives:

- Changes in hemodynamic parameters; Heart rate (HR), Systolic blood

pressure(SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), at various intervals following subarachnoid block.
- APGAR score
- Adverse effects like bradycardia, hypotension, sedation, respiratory depression, post op nausea vomiting and shivering nausea, vomiting, shivering, urinary retention, sedation, pruritus and respiratory depression.

Materials and Methods

Sixty ASA I and II parturients between the age group of 19-35years were posted for caesarean section under subarachnoid block, without any comorbid diseases. After obtaining ethical and scientific committee clearance. Randomisation was done by using shuffled closed, opaque envelope technique. Parturients were allocated into two groups of 30 each.

1. Group OC received Tab. clonidine 0.3mg orally 90mins before SAB, SAB was done by using hyperbaric bupivacaine 0.5% 1.8cc (9mg) + 0.5ml NS (total 2.3ml).
2. Group ITC received 1.8cc (9mg) of 0.5% hyperbaric bupivacaine with 1mcg/kg of clonidine (total 2.3ml) for SAB.

After getting written informed consent, a thorough pre anaesthetic evaluation was done. Parturients enrolled for the study were preloaded with Ringer lactate solution 15ml/kg and premedicated with inj rantidine 50mg+ inj. metoclopramide 10mg (as hospital protocol). Parturients were shifted to OT in the left lateral position. A Multiparameter monitor was connected (EDAN iM80). Under aseptic precaution lumbar puncture was done at L3-L4 level with 25G Quinke's spinal needle. After achieving free flow of CSF, 9mg of 0.5% hyperbaric bupivacaine + 1mcg/kg clonidine/0.5ml of NS, totalling 2.3ml was injected. Immediately after injection parturients are positioned in supine with 15degree wedge under the right buttock. The time of sensory onset was tested by pin prick method by using 25G hypodermic needle at T10 level. The time of motor onset was tested by using modified Bromage scale grade 1. The time of maximum sensory level was noted. The hemodynamic parameters like systolic, diastolic blood pressure and mean arterial pressure, heart rate, oxygen saturation were noted just before and after spinal anaesthesia, 3, 5, 10, 15mins after SAB, thereafter every 15mins till the end of surgery. APGAR score was recorded at 1 and 5 min after extraction of the baby. Time of two segment regression, total duration of sensory and motor block and time of rescue analgesia were recorded. Adverse effects like nausea, vomiting, bradycardia, hypotension, and sedation were recorded. Total analgesic consumption in the 1st 24hrs after surgery were also recorded.

Definitions

Sensory onset: time of spinal injection to loss of sensation at T10 level by pin prick method.

Motor onset: time of spinal injection to motor block of Bromage 1.

Maximum sensory level: time of spinal injection to maximum level of sensory loss.

Hypotension: it is defined as reduction in SBP of more than 20% below the base line or fall in SBP less than 90mmHg and it will be treated with increased rate of intravenous (IV) fluids and if needed inj.Mephentermine 3mg IV in incremental dose.

Bradycardia: it is defined as heart rate less than 50bpm and will be treated with injection Atropine 0.6mg IV in incremental dose.

Adverse effects: like nausea, vomiting, respiratory depression and hypotension, bradycardia, and shivering will be recorded.

Modified bromage scale:

1= complete motor blockade.

2=almost complete motor blockade, the patient is able to only move the feet.

3=partial motor blockade, the patient is able to move the knees.

4= detectable weakness of hip flexion, the patient is able to raise the leg but unable to keep it raised.

5=no detected weakness of hip flexion, the patient is able to keep the leg raised for at least 10 seconds.

6=no weakness at all, the patient is able to perform partial knee bend while supine.

Modified Ramsay sedation scale:

1=awake and alert, minimal or no cognitive impairment.

2=awake but tranquil, purposeful responses to verbal commands at conversation level.

3=appears asleep, purposeful responses to verbal commands at conversation level.

4= appears asleep, purposeful responses to verbal commands but at louder than usual conversation level or requiring light glabellar tap.

5=asleep, sluggish purposeful responses only to loud verbal commands or strong glabellar tap.

6= asleep, sluggish purposeful responses only to painful stimuli.

7= asleep, reflex withdrawal to pain stimuli only (no purposeful response).

8=unresponsive to external stimuli, including pain.

Results

Age group	Group		Total	p value
	Group Oral	Group Intrathecal		
25 to 26	6(20%)	5(16.67%)	11(18.33%)	0.740
27 to 28	13(43.33%)	16(53.33%)	29(48.33%)	
29 to 31	11(36.67%)	9(30%)	20(33.33%)	
Total	30(100%)	30(100%)	60(100%)	
Indication for CS	**Group**		**Total**	**p value**
	Group Oral	Group Intrathecal		
Breech presentation	8(26.67%)	9(30%)	17(28.33%)	0.684
CPD	3(10%)	5(16.67%)	8(13.33%)	
Failed induction	8(26.67%)	10(33.33%)	18(30%)	
Failure to progress	5(16.67%)	3(10%)	8(13.33%)	
Previous 2 LSCS	6(20%)	3(10%)	9(15%)	
Total	30(100%)	30(100%)	60(100%)	

Table 1

Group	GROUP OC	GROUP ITC	p value(student t test)
Age	27.97 ± 1.99	27.77 ± 1.63	0.672
Height	157.77 ± 3	157.9 ± 3.12	0.867
Weight	68.50 ± 0.73	67.90 ± 2.0	0.129
BMI	27.55 ± 1.12	27.26 ± 1.41	0.388

Sixty parturients of ASA grade I and II posted for caesarean section were randomly allocated into two groups. Group OC(n=30) received oral clonidine of 0.3mg, 90mins before section, group

ITC(n=30) received intrathecal clonidine 1mcg/kg along with 9mg of 0.5% bupivacaine. The demographic data of the study like age, sex, weight, height, BMI, and indication for surgery were not statistically significant.

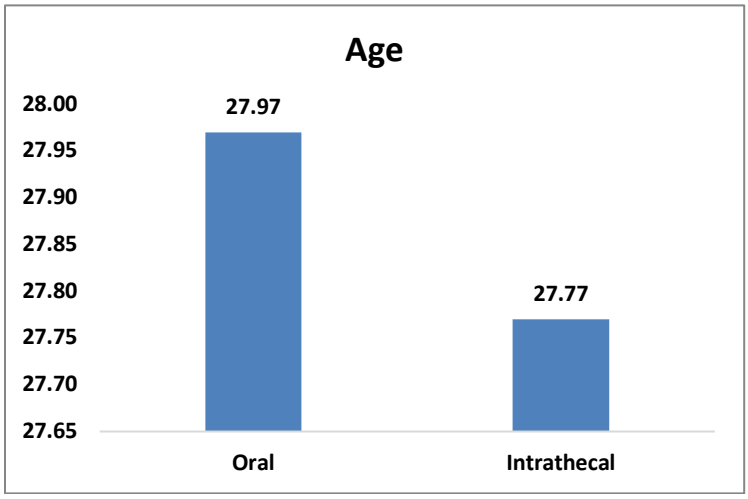

Figure 1

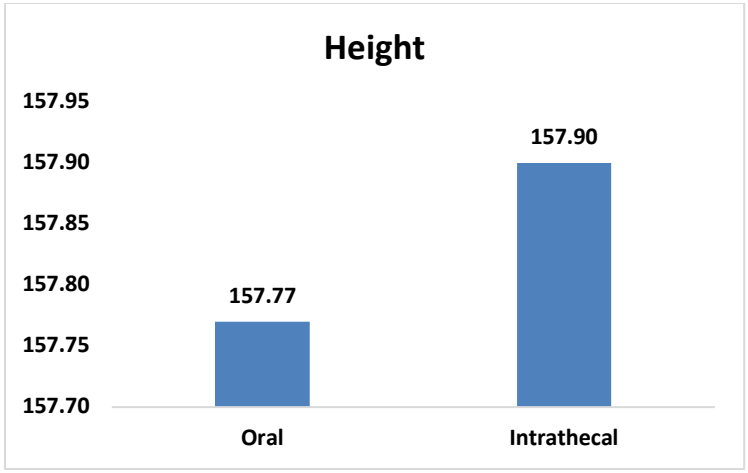

Figure 2

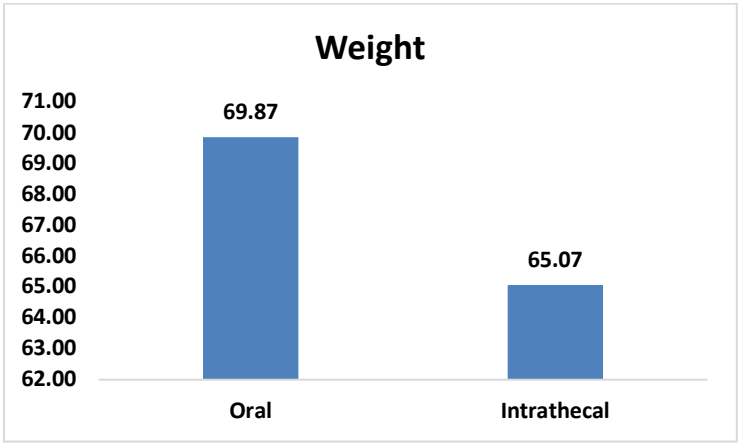

Figure 3

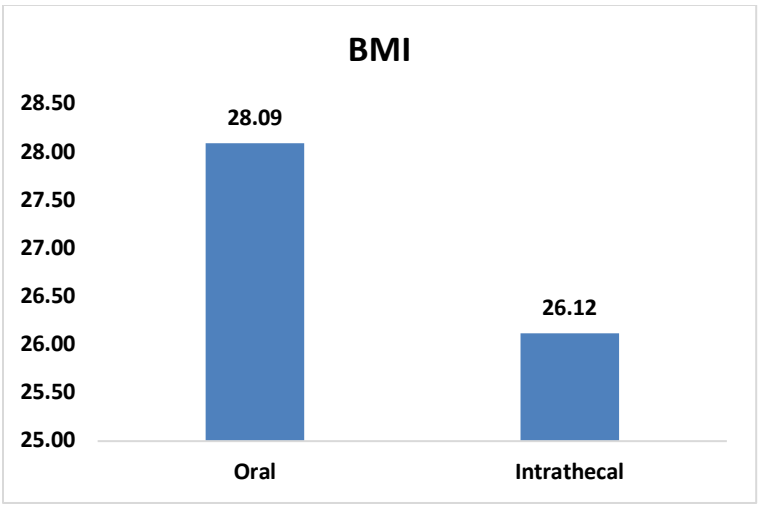

Figure 4

Group	Group Oral n=30	Group Intrathecal n=30	p value- Student t test
APGAR_1min	8.2±0.41	8.27±0.45	0.549
APGAR_5min	9.27±0.45	9.27±0.45	1.000

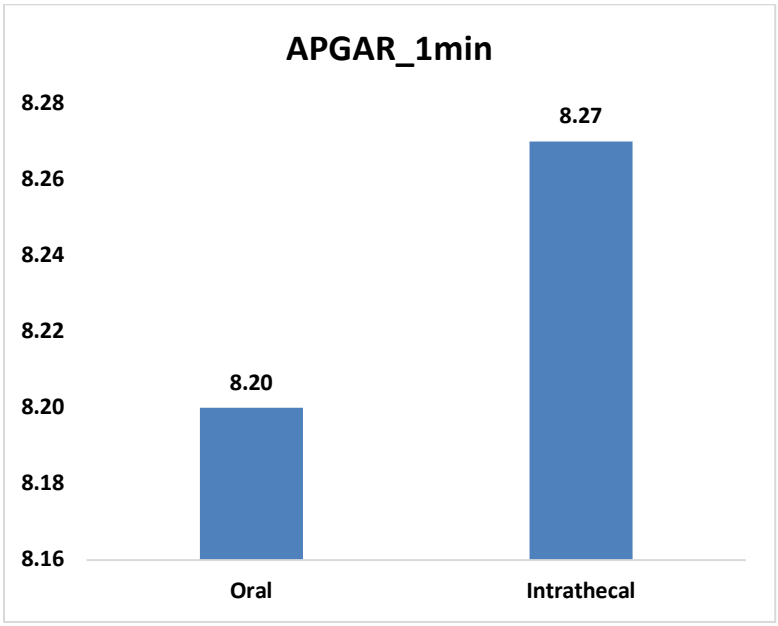

Figure 5

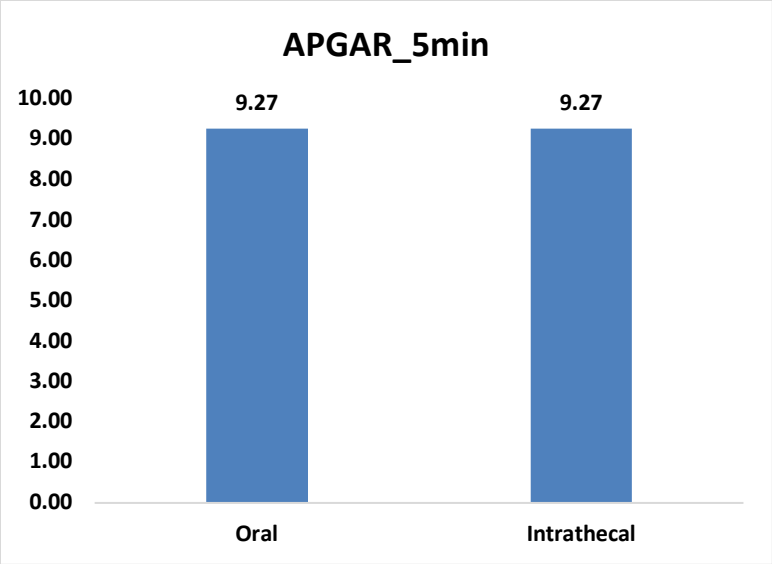

Figure 6

Group	Group Oral n=30	Group Intrathecal n=30	p value- Student t test
Time of onset of sensory block	2.25±0.35	3.26±0.5	***0.000***
Time for maximum sensory level attained	2.86±0.33	4.36±0.53	***0.000***
Time of 2 segment regression	43.4±4.01	196.13±11.03	***0.000***
Total duration of sensory block	164.87±6.03	236.33±15.63	***0.000***
Time of rescue analgesia	178.73±5.26	255±18.77	***0.000***
Time of onset of motor block	2.37±0.26	3.55±0.52	***0.000***
Time of duration of motor block	153.6±5.8	219.93±14.84	***0.000***

Time of onset of sensory block and time for maximum sensory level was early in group OC (2.25±0.35, 2.86±0.33 mins respectively) when compared to group ITC (3.26±0.5. 4.36±0.53 mins respectively) which is statistically highly significant(p=0.000). Time of two segment regression was early in group OC (43.4±4.01 mins) when compared to group ITC (196.13±11.03 mins) which is statistically highly significant (p=0.000). Total duration of sensory block was prolonged in group ITC (236.33±15.63 mins) when compared to group OC (164.87±6.03 mins) which is statistically highly significant(p=0.000). Time of rescue analgesia was significantly prolonged in group ITC (255±18.77 mins) when compared to group OC (178.73±5.26 mins), (p=0.000). Time of onset of motor block and motor regression was early in group OC (2.37±0.26, 163.6±5.8 mins respectively), when compared to group ITC (3.55±0.52, 219.93±14.84 mins respectively) which is statistically highly significant, (p=0.000). Total consumption of analgesics like Inj. Paracetamol IV and Inj. Tramadol IV in the first 24hrs after c-section was significantly high in group OC when compared to group ITC which is statistically highly significant p=0.000.

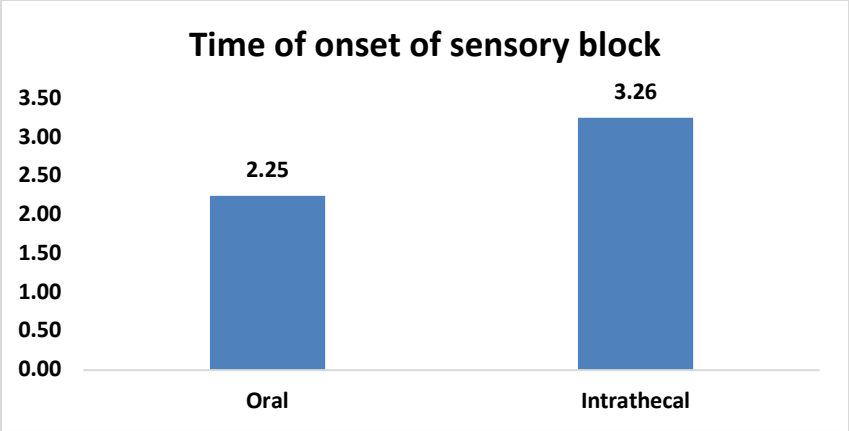

Figure 7

Maximum sensory level attained	Group		Total	p value
	Group Oral	Group Intrathecal		
T4	17(56.67%)	12(40%)	29(48.33%)	0.196
T6	13(43.33%)	18(60%)	31(51.67%)	
Total	30(100%)	30(100%)	60(100%)	

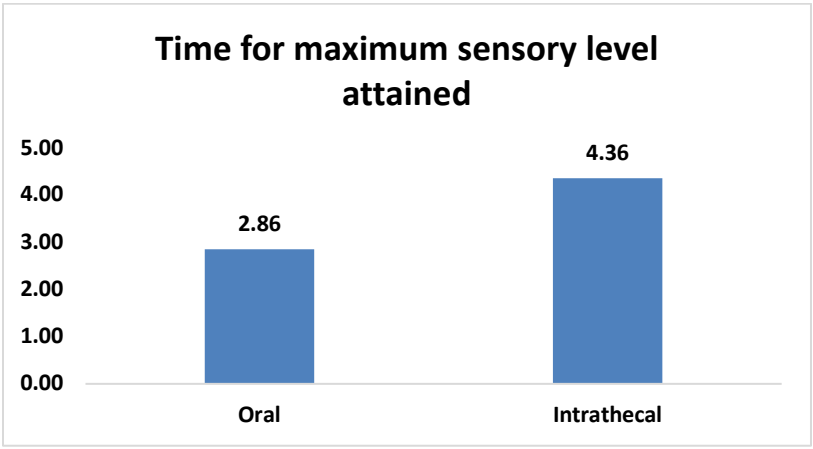

Figure 8

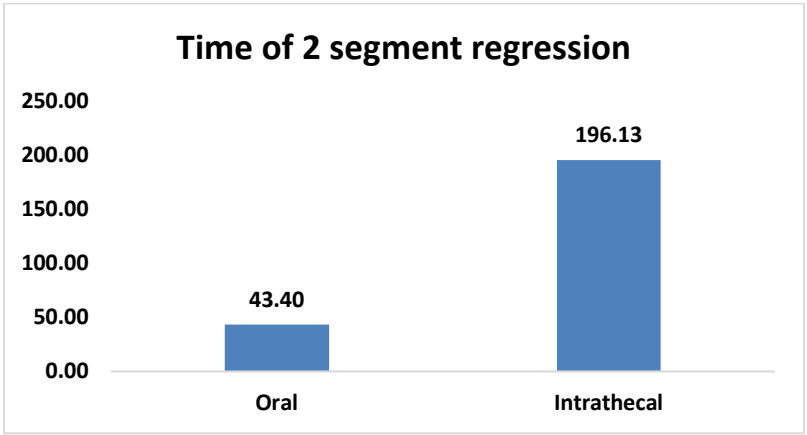

Figure 9

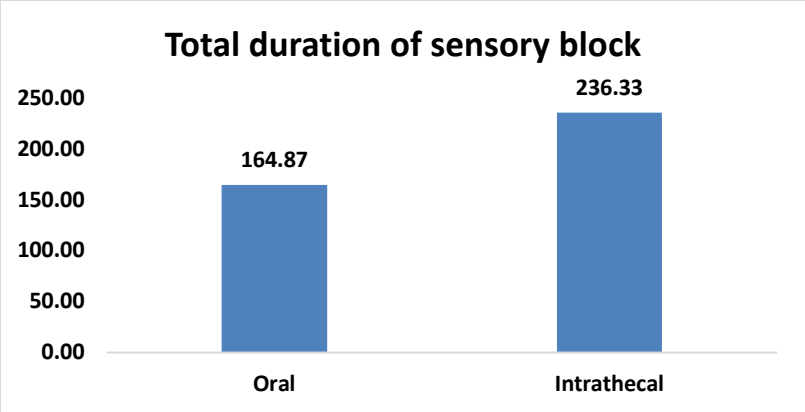

Figure 10

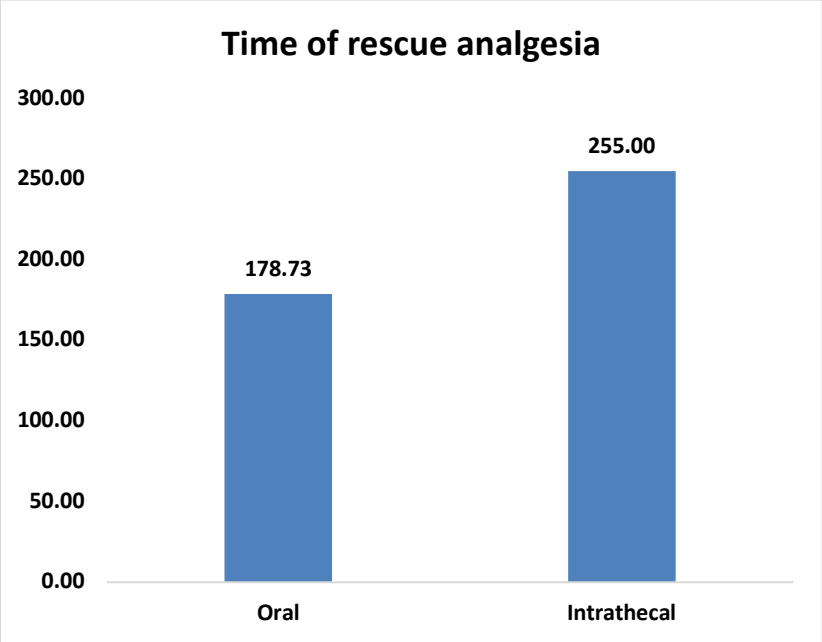

Figure 11

PCT(g)	Group		Total	p value
	Group Oral	Group Intrathecal		
nil	16(53.33%)	12(40%)	28(46.67%)	
1	8(26.67%)	18(60%)	26(43.33%)	0.005
2	6(20%)	0(0%)	6(10%)	
Total	30(100%)	30(100%)	60(100%)	
Tramadol(mg)	**Group**		**Total**	**p value**
	Group Oral	Group Intrathecal		
nil	8(26.67%)	18(60%)	26(43.33%)	
100	8(26.67%)	12(40%)	20(33.33%)	0.000
200	14(46.67%)	0(0%)	14(23.33%)	
Total	30(100%)	30(100%)	60(100%)	

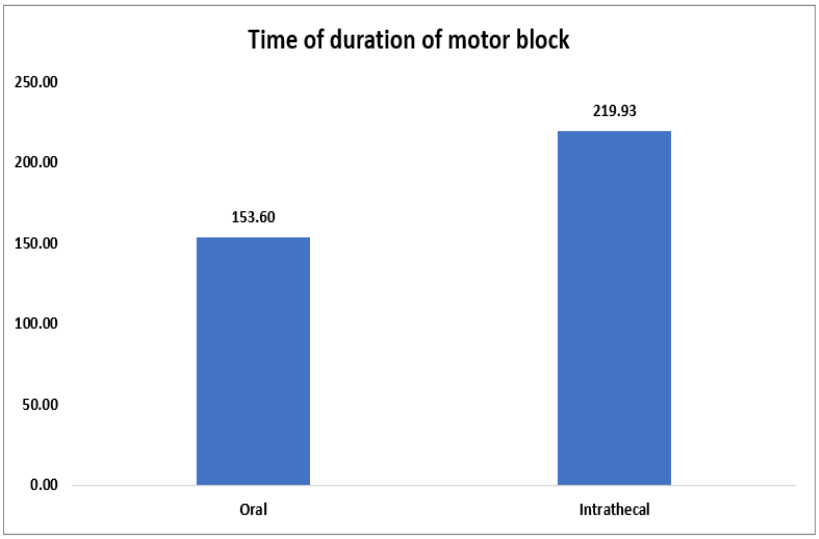

Figure 12

Hemodynamic characters like SBP, DBP, and MAP were not altered significantly in either groups except in a few time intervals .

Group	Group Oral n=30	Group Intrathecal n=30	p value- Student t test
SBP_Basal	110.8±5.36	112.7±11.58	0.418
SBP_Immediately after SAB	110.3±5.07	108.57±8.35	0.335
SBP_2min	110.93±4.67	115.4±15.11	0.127
SBP_4min	110.13±4.62	110.07±11.46	0.977
SBP_6min	111.53±4.61	115.8±15.15	0.145
SBP_8min	111.7±5.29	118.9±17.26	***0.033***
SBP_10min	111.2±5.6	117.57±13.48	***0.020***
SBP_20min	111.43±2.91	111.93±12.07	0.826
SBP_30min	111.4±4.65	115.33±13.52	0.137
SBP_45min	109.33±4.47	114.83±12.43	***0.026***
SBP_60min	111±5.52	112.13±11.48	0.628
SBP_90min	111.3±6.39	112.83±13.67	0.580
SBP_120min	110.9±3.45	111.47±11.51	0.797

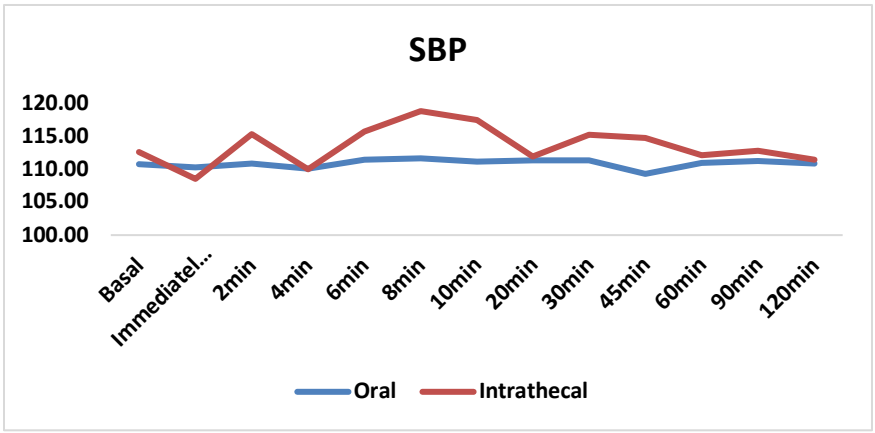

Figure 13

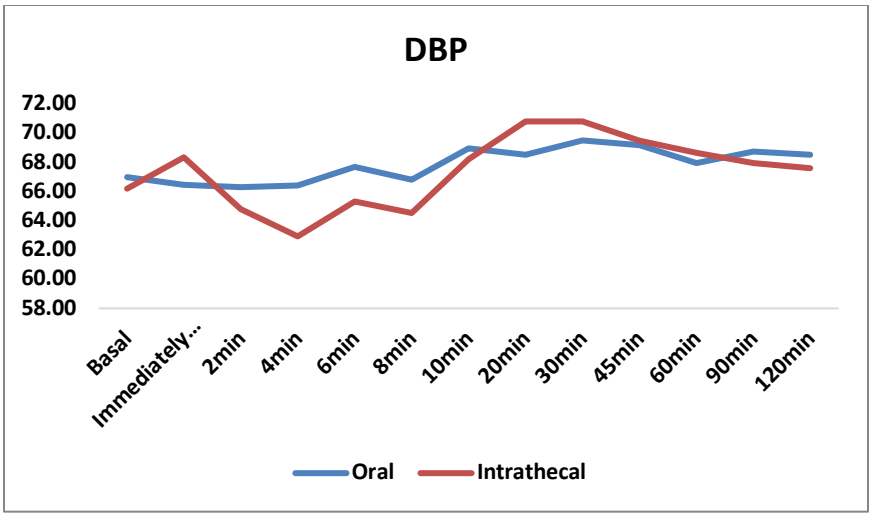

Figure 14

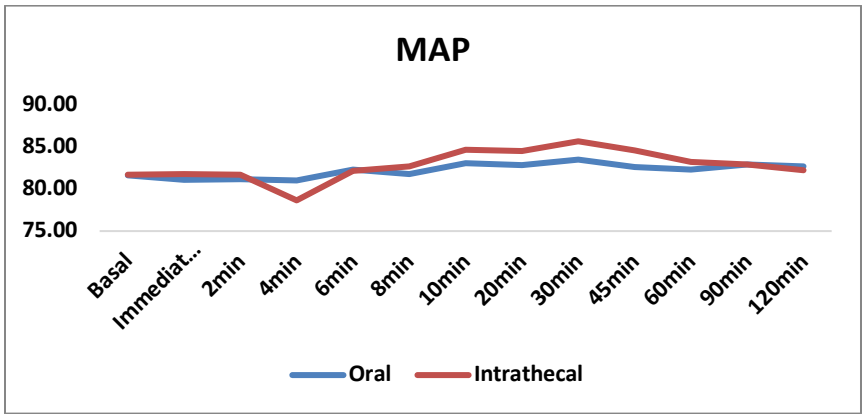

Figure 15

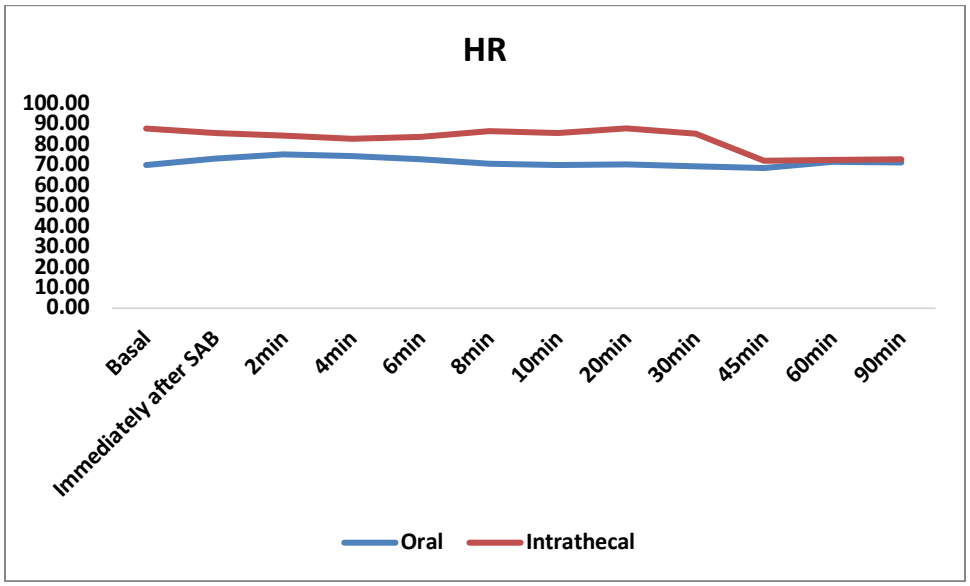

Figure 16

Group	Group Oral n=30	Group Intrathecal n=30	p value- Student t test
DBP_Basal	67±4.11	66.2±3.2	0.404
DBP_Immediately after SAB	66.47±4.06	68.33±2.77	***0.042***
DBP_2min	66.3±4.32	64.8±3.43	0.142
DBP_4min	66.43±4.14	62.93±1.68	***0.000***
DBP_6min	67.67±4.86	65.33±3.84	***0.043***
DBP_8min	66.83±4.3	64.53±4.45	***0.046***
DBP_10min	68.97±3.64	68.2±3.62	0.417
DBP_20min	68.5±3.94	70.8±1.06	***0.003***
DBP_30min	69.5±3.56	70.8±1.71	0.077
DBP_45min	69.17±2.74	69.47±2.9	0.682
DBP_60min	67.93±3.89	68.67±3.65	0.454
DBP_90min	68.73±2.84	67.93±2.45	0.247
DBP_120min	68.5±3.88	67.6±4.25	0.395
Group	**Group Oral n=30**	**Group Intrathecal n=30**	**p value- Student t test**
MAP_Basal	81.6±3.22	81.7±4.05	0.916
MAP_Immediately after SAB	81.08±3.33	81.74±3.02	0.420
MAP_2min	81.18±3.66	81.67±6	0.705
MAP_4min	81±2.89	78.64±3.57	***0.007***
MAP_6min	82.29±3.86	82.16±5.92	0.918
MAP_8min	81.79±3.49	82.66±6.55	0.525
MAP_10min	83.04±3.05	84.66±5.24	0.151
MAP_20min	82.81±2.64	84.51±4.18	0.065
MAP_30min	83.47±2.7	85.64±4.56	***0.028***
MAP_45min	82.56±2.5	84.59±4.44	***0.033***
MAP_60min	82.29±3.72	83.16±4.4	0.413
MAP_90min	82.92±2.74	82.9±4.89	0.983
MAP_120min	82.63±3.11	82.22±5.15	0.709

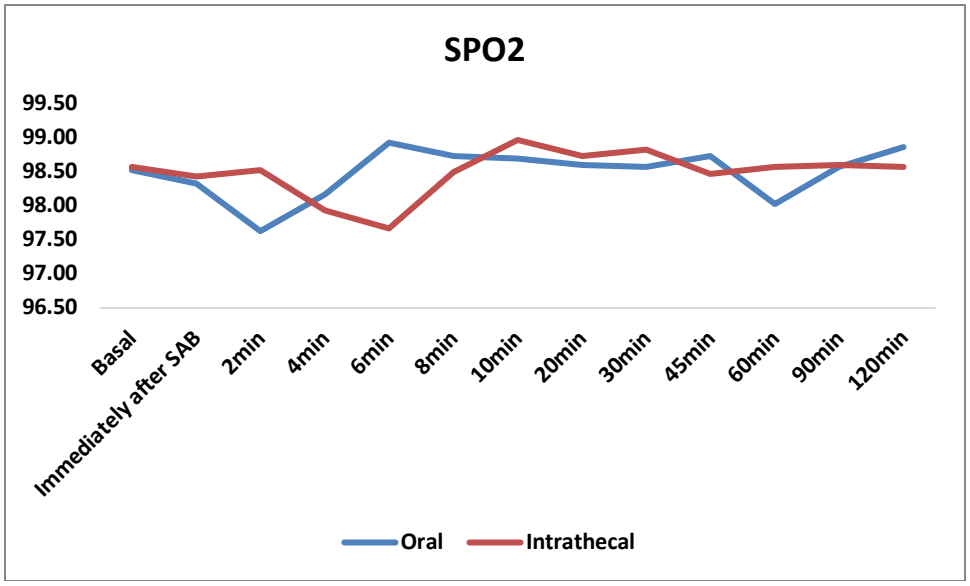

Figure 17

Table 2

Group	Group Oral (n=30)	Group Intrathecal (n=30)	p value- Student t test
HR_Basal	70±2.63	88±6.93	***0.000***
HR_Immediately after SAB	73.2±3.96	85.67±8.64	***0.000***
HR_2min	75.37±5.23	84.6±7.88	***0.000***
HR_4min	74.6±5.3	82.9±8.71	***0.000***
HR_6min	72.9±5.96	84±7.36	***0.000***
HR_8min	70.63±3.83	86.67±9.36	***0.000***
HR_10min	70.2±2.87	85.93±5.67	***0.000***
HR_20min	70.37±3.42	88.1±9.3	***0.000***
HR_30min	69.53±4.62	85.43±7.49	***0.000***
HR_45min	68.67±4.4	72.23±3.38	***0.001***
HR_60min	71.8±4.33	72.73±3.31	0.352
HR_90min	71.37±3.87	72.93±3.11	0.089
HR_120min	74.4±6.67	73.3±2.2	0.395
Group	**Group Oral (n=30)**	**Group Intrathecal (n=30)**	**p value- Student t test**
SPO2_Basal	98.53±0.63	98.57±0.57	0.830
SPO2_Immediately after SAB	98.33±0.99	98.43±0.68	0.651
SPO2_2min	97.63±1.07	98.53±0.73	***0.000***
SPO2_4min	98.17±1.18	97.93±1.11	0.433
SPO2_6min	98.93±0.74	97.67±1.09	***0.000***
SPO2_8min	98.73±0.64	98.5±1.17	0.341
SPO2_10min	98.7±1.02	98.97±0.76	0.257
SPO2_20min	98.6±1.16	98.73±0.78	0.605
SPO2_30min	98.57±1.01	98.83±0.87	0.278
SPO2_45min	98.73±0.74	98.47±1.25	0.319
SPO2_60min	98.03±1.1	98.57±1.07	0.062
SPO2_90min	98.57±0.94	98.6±0.97	0.893
SPO2_120min	98.87±0.97	98.57±0.94	0.228

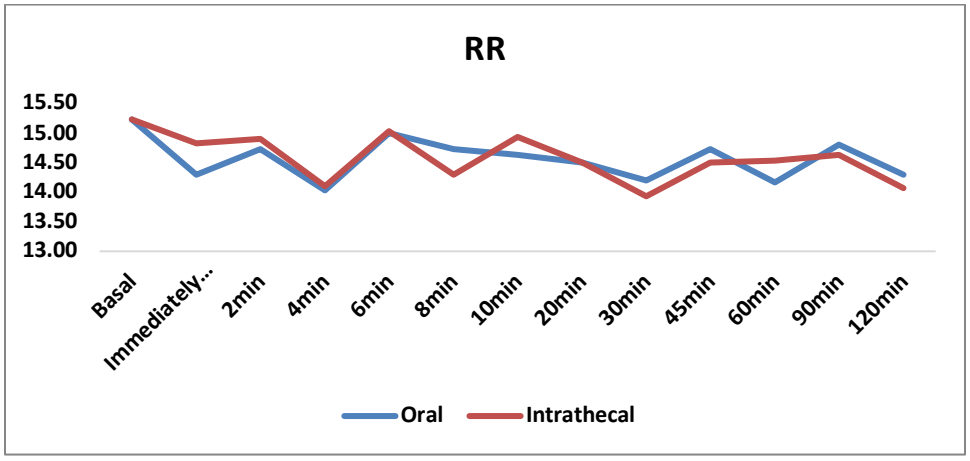

Figure 18

Group	Group Oral (n=30)	Group Intrathecal (n=30)	p value- Student t test
RR_Basal	15.23±1.17	15.23±1.19	1.000
RR_Immediately after SAB	14.3±1.12	14.83±1.23	0.085
RR_2min	14.73±1.28	14.9±1.09	0.591
RR_4min	14.03±0.76	14.1±1.18	0.797
RR_6min	15±1.17	15.03±1.1	0.910
RR_8min	14.73±0.94	14.3±0.92	0.076
RR_10min	14.63±1.5	14.93±1.23	0.400
RR_20min	14.5±1.22	14.5±1.22	1.000
RR_30min	14.2±1.03	13.93±0.91	0.292
RR_45min	14.73±1.14	14.5±1.04	0.412
RR_60min	14.17±1.09	14.53±1.01	0.180
RR_90min	14.8±1	14.63±1.16	0.553
RR_120min	14.3±1.18	14.07±0.69	0.354

Heart rate at various interval in group OC was significantly reduced upto 45mins after SAB, when compared to group ITC (p=0.000). Spo2 and respiratory rate was not statistically significant in either group (p>0.05).

Adverse effects	Group		Total	p value
	Group Oral	Group Intrathecal		
None	24(80%)	26(86.67%)	50(83.33%)	
Bradycardia	1(3.33%)	0(0%)	1(1.67%)	0.314
Hypotension	2(6.67%)	0(0%)	2(3.33%)	
Hypotension & sedated	1(3.33%)	0(0%)	1(1.67%)	
Sedation	2(6.67%)	4(13.33%)	6(10%)	
Total	30(100%)	30(100%)	60(100%)	
Drugs given	**Group**		**Total**	**p value**
	Group Oral	Group Intrathecal		
None	26(86.67%)	30(100%)	56(93.33%)	
inj. Atropine 0.6mg	1(3.33%)	0(0%)	1(1.67%)	0.117
inj. Ephedrine 6mg bolus	3(10%)	0(0%)	3(5%)	
Total	30(100%)	30(100%)	60(100%)	

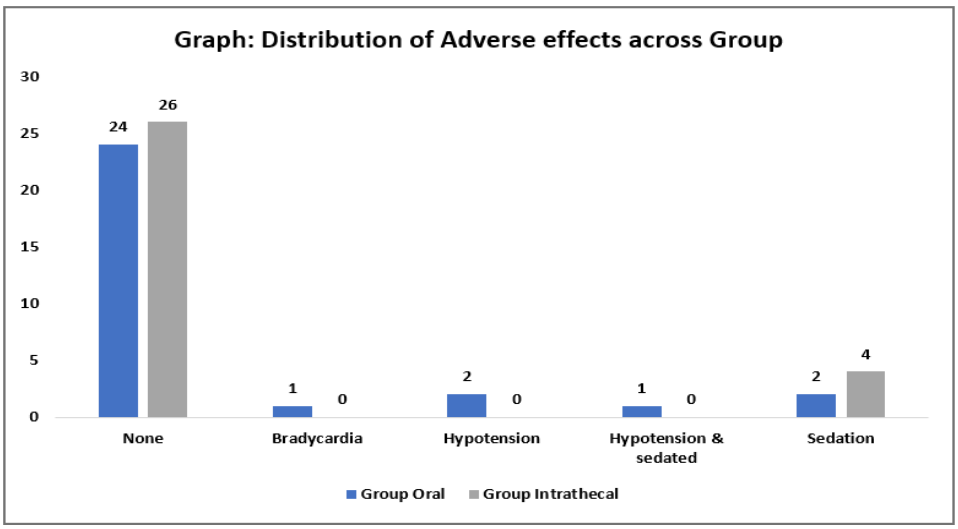

Figure 19

Adverse effects like bradycardia, hypotension, and sedation was not significantly seen in either group ($p>0.05$).

Discussion

Clonidine is centrally acting alpha-2 agonist, the analgesic effect of intrathecal clonidine is mediated spinally through activation of postsynaptic alpha-2 receptors in substantia gelatinosa [7,8].

The rationale behind intrathecal administration of clonidine is to achieve high drug concentration in the vicinity of alpha-2 receptors which are present in the spinal cord, and intensify the conduction block of local anaesthetics. Many clinical trials provide evidence that less dose of clonidine is needed intrathecally than epidural to produce the same amount of analgesics effects with minimal side effects.[9] Oral administration of clonidine results in virtually complete absorption and peak plasma concentration within 1-3 hours after oral administration [10]. The drug is highly lipid soluble and easily crosses the blood-brain barrier, and interacts with alpha adrenergic receptors at spinal and supra spinal levels.[11] Several studies have been done to evaluate the effect of oral clonidine when used as a premedicant before SAB [12-16]. The aim of our study is to evaluate the analgesic efficacy of oral clonidine v/s intrathecal clonidine on SAB, in parturients coming for caesarean section.

The study conducted in sixty ASA I and II parturients of age group of 19-35years coming for caesarean section were randomly allocated into two groups. Group OC received 0.3mg of oral clonidine 90mins before SAB, group ITC received 1mcg/kg of intrathecal clonidine along with local anaesthetics. In both the group's total volume was 2.3 ml.

The demographic characters like age, height, weight, BMI were not statistically significant in both the groups.

In the present study time of onset of sensory block was early in group OC (2.25 ± 0.35 mins) when compared to group ITC (3.26 ± 0.5 mins) which is statistically highly significant($p=0.000$). Our study can be comparable with MB Adegboye et.al study, they have compared two different doses of oral clonidine (100mcg, 200mcg), patients who received 200mcg of oral clonidine had almost similar results of sensory onset time as that of ours. It is also comparable with Anjali Teresa MO et.al study, they also got

similar results. Time of onset of motor block in our study was early in group OC(2.37±0.26mins) when compared to group ITC (3.55±0.52 mins) which is statistically highly significant(p=0.000). Our study cannot be comparable with any other study because they used different dosages of oral clonidine. And, they have early motor onset in intrathecal group than oral clonidine group. In our study time of two segment regression, total duration of sensory and motor block, time of rescue analgesia was early in group OC (43.4±4.01, 164.87±6.03, 153.6±5.8, 178.73±5.26mins respectively) when compared group ITC (196.13±11.03, 236.33±15.63, 219.93±14.84, 255±18.77 mins respectively) all these characters were statistically highly significant, (p=0.000). Total duration of sensory and motor block of group OC of our study can be comparable with MB Adegboye et.al study of group C (100mcg of oral clonidine) duration of sensory and motor block of their study with almost similar results as that of ours. Our study is also comparable with Sudar codi et.al study, they also got similar results of duration of motor block. Duration of rescue analgesia of our study cannot be comparable with any of the above-mentioned studies, because of usage of different dosages of oral clonidine, in different set of patients. Though I.Van Tuijl et.al used similar dosage of intrathecal clonidine in similar set of patients our study cannot be comparable with this study, because their primary outcome was total morphine consumption in 24hrs, so in their study duration of rescue analgesia was 129mins in-spite of same dosage of intrathecal clonidine. Anjali Teresa MO et.al have done comparative study between oral clonidine(2.5mcg/kg) versus intrathecal clonidine(75mcg) with hyperbaric 0.5%bupivacaine(15mg) in orthopaedic cases, so their results were prolonged when compared to ours.

Hemodynamic characters of our study like SBP, DBP and MAP at various time intervals, were not significantly altered between group OC and group ITC except in few time intervals, but MAP was maintained at all time intervals. Bradycardia and hypotension was noticed in 3 patients belonging to group OC which was treated by inj. atropine (0.6mg) and inj. ephedrine (6mg bolus). Hemodynamic parameters of our study in group OC were comparable with

MB Adegboye et.al, they also noticed changes in SBP, DBP and MAP at various intervals, but MAP was maintained at all time intervals. Hemodynamic characters in group ITC of our study can be comparable with B.S. Sethi *et al* study, they also got similar results that of ours. Our study can also be comparable with I.Van Tuijl et.al study. Heart rate in our study in both the group at various interval are comparable. Upto 45mins of interval heart rate was significantly reduced in group OC when compared to group ITC(p=0.00). Our study group OC can be comparable with MB Adegboye et.al study they also got similar results in oral clonidine groups. APGAR score at 1 and 5mins of our study in both the groups were not statistically significant. Our study can also be comparable with I.Van. Tuijl study. In our study adverse effects like bradycardia, hypotension and sedation was noticed in group OC {1(3.33%), 2(6.67%), 2(6.67%) respectively}. In group ITC only 4 patients (13.33%) had sedation, none of them had bradycardia and hypotension. Similar adverse effects were noticed in oral clonidine group of Sudar codi.et.al study. Total analgesic consumption in first 24hrs in our study, patient received inj. Paracetamol(1g IV) if the pain persist patient received 100mg Inj. Tramadol(BD). Highest dosage of paracetamol received was 2g(IV) and 200mg tramadol (IV) in first 24hrs in group OC (2g- 6 patients; 200mg- 14 patients) respectively,

which is statistically highly significant, (p=0.000).

Conclusion

Intrathecal clonidine with hyperbaric bupivacaine provides better post-operative analgesia with better hemodynamic stability with less consumption of immediate post-operative analgesics when compared to oral clonidine.

References

1. Kallapur, Basavaraj et al. Clinical Study to Determine the Efficacy of Clonidine as an Adjuvant to Intrathecal Bupivacaine in Patients Undergoing Cesarean Section. Anesthesia, essays and researches. 2017; 11(4): 946-951.
2. Breivik H, Stubhaug A. Management of acute postoperative pain: still a long way to go! Pain. 2008 Jul 15;137(2):233-234.
3. Gadsden, Jeff C. et al. Post-Cesarean Delivery Analgesia. Anesthesia & Analgesia. 2005;101: S62-S69.
4. Etches, Richard C. et al. Respiratory depression and spinal opioids. Canadian Journal of Anaesthesia. 1989;36: 165-185.
5. Bajwa SJ, Bajwa SK, Kaur J, et al. Prevention of hypotension and prolongation of postoperative analgesia in emergency cesarean sections: A randomized study with intrathecal clonidine. International Journal of Critical Illness and Injury Science. 2012 May;2(2):63-69.
6. Veeralakshmanan, Pushpa et al. Clonidine and Anaesthesia. 2019.
7. Reddy SVR, Yaksh TL, Spinal noradrenergic terminal system mediates antinociception. Brain Res 1980; 189: 391-401.
8. Brandt SA, Livingston A. Receptor changes in spinal cord of sheep associated with exposure to chronic pain. Pain 1990; 42:323-9.
9. Filos KS, Goudas LC, Patroni O, Polyzou V. Intrathecal clonidine as a sole analgesic for pain relief after caesarean section. Anesthesiology 1992; 77: 267-74.
10. Liu, Spencer, Andrew A., Neal, Joseph M., Randal L., et al. Oral Clonidine Prolongs Spinal Anaesthesia in Human Volunteers. Anesthesiology. 1993; 86: 1353-1359.
11. Timmermans PB, Brands A, Van Zwietan PA. Lipophilicity and brain disposition of clonidine and structurally related imidazolidines. Naunyn-Schmiedergs Arch Phamacol. 1977;300:217-226.
12. AftabBeighAkhtar N, Farooq A K. Haemodynamic and analgesic effects of oral clonidine on sub-arachnoid block with lidocaine. J Anaesthclin.Pharmacol. 2003; 19:389-393.
13. Pouttu J, Tuominen M, Scheinin M, Rosenbert PH. Effects of oral pre-medication on concentrations of cortisol and monoamine neurotransmitters and their metabolites in cerebrospinal fluid and plasma. ActaAnaesthscand. 1989;33:137-141.
14. Ota, Namiki A, Iwasaki H, Takahashi I. Dose-related prolongation of spinal anaesthesia in humans. Anesthesiology. 1995;82:1353-1359.
15. Bonnet F, Brun Buisson V, Francois Y. Effects of oral and sub-arachnoid clonidine on spinal anaesthesia with bupivacaine. Reg Anesth. 1990;15:2.
16. Sudor CR, Selyarajan N, Manimekalai K, Kartik JS. Effects of oral clonidine pre-medication on the duration of analgesia produced by spinal Bupivacaine. Int J Pham Bio Sci.2013;4:1017-1024.
17. Adegboye MB, Kolawole IK, Bolaji BO. Dose related effects of oral clonidine pre-medication on bupivacaine spinal anaesthesia. Afri Health Sci. 2018;18(4): 1283-1291.

18. Teresa Mathew Ollapally, Anjali. Effect of oral and intrathecal clonidine on spinal anaesthesia. International Journal of Advanced Research. 2019.
19. Codi, R. Sudar et al. Effect Of Oral Clonidine Premedication On The Duration Of Analgesia Produced By Spinal Bupivacaine. International journal of pharma and bio sciences. 2013.
20. Van Tuijl I, van Klei WA, van der Werff DB, Kalkman CJ. The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after Caesarean section: a randomized controlled trial. Br J Anaesth. 2006 Sep;97(3):365-70.
21. Sethi, B et al. Efficacy of Analgesic Effects of Low Dose Intrathecal Clonidine as Adjuvant to Bupivacaine. Indian Journal of Anaesthesia. 2007;51: 415.