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Research Paper

To evaluate and compare the effects of two different doses of clonidine (0.5 and 1 µg/kg bw) as an adjuvant to 15 mg hyperbaric bupivacaine in patients undergoing lower abdominal surgeries under spinal anesthesia

Medical Science

KEYWORDS : intrathecal ; clonidine;Bupivacaine ;postoperative pain; spinalanesthesia

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ABSTRACT

Clonidine is added to intrathecal Bupivacaine to improve intraoperative analgesia and to increase the duration of sensory and motor block.

This is study of 60 patients of either sex of ASA I & II status undergoing lower abdominal surgeries . They were randomly divided into three groups of 20 each. Group A patients received Bupivacaine heavy 0.5% 15mg + Clonidine 0.5 µg/kg Group B received Bupivacaine heavy 0.5% 15mg + Clonidine 1 µg/kg and Group C received Bupivacaine heavy 0.5% 15 mg.

. Intrathecal clonidine 0.5µg/kg and 1 µg/kg delayed the onset of sensory blockade by 197.8(+/-20.2)sec and 225.8(+/-22.1)sec respectively when compared to control group 179.8(+/- 17.01)sec. Similarly onset of motor blockade was also delayed by 257.3(+/-26.6) sec in Group A, 288 (+/-24.3)sec in Group B and 222.3(+/-20.03)sec in Group C.

there was statistically significant (P<0.05) decrease in mean pulse rate intraoperatively from 30 min upto 2 hours.

Fall in blood pressure was slightly greater in clonidine group (P<0.001) but was not severe.

Duration of post operative analgesia was very prolonged in group B:370(+/-39.95)min and group A:335(+/-33.32)min compared to group C: 235.5(+/-18.84)min which was highly significant. Adding clonidine 1 µg/kgbw to intrathecal Bupivacaine prolongs the duration of spinal anesthesia and postoperative analgesia without severe adverse effects

Introduction

Spinal anaesthesia have been shown to blunt the stress response to surgery, decrease intra operative blood loss, lowers the incidence of post operative thromboembolic events, possibly decreases morbidity in high risk surgical patients and also serves as a useful method to extend analgesia in the post operative period . For that purpose various adjuvant drugs have been used in combination with local anaesthetics, like Phenylephrine, Epinephrine, Neostigmine, Morphine, Buprenorphine, Fentanyl etc. Intrathecal clonidine as an adjuvant is extensively evaluated as an alternative to neuraxial opioids for control of pain and has proven to be a potent analgesic.

Clonidine was tried intrathecally by Gordh1 in 1983.It acts by activation of the $\alpha 2$ adrenoreceptor located post synaptically in the dorsal horn of spinal cord and substancia gelatinosa (supraspinal effect).Inhibitory action of clonidine on catecholaminergic area of the lower brainstem is responsible for its anxiolytic effect1.

Addition of intrathecal clonidine to Bupivacaine a local anaesthetic enhances its sensory effects and provides postoperative pain relief.

The aim of our study was to evaluate and compare the analgesic efficacy and common side effects of clonidine 0.5µg/kg and 1µg/kg along with bupivacaine0.5%heavy via intrathecal route in patients undergoing lower abdominal surgeries.

Materials and Method

The present study was carried out in 60 patients of ASA grade I and II physical status of either sex posted for lower abdominal surgeries . The patients were randomly allocated into three groups each having 20 patients.

Group A - Inj Bupivacaine heavy 0.5 % 3cc (15mg) + clonidine 0.5 µg/kg

Group B - Inj Bupivacaine heavy 0.5 % 3cc (15mg) + clonidine 1 µg/kg

Group C – Inj Bupivacaine heavy 0.5 % 3cc (15mg)

All patients were thoroughly examined on the previous day of the operation and again in pre anaesthetic room in the morning on the day of surgery. A history of any present or past illness and detailed general as well as systemic examination were done and investigations were checked. Visual analogue scale was shown to the patient and the procedure of post operative pain measurement was explained in detail. Base line vitals were noted and informed written consent was taken from patient and his or her close relative .

On the operative day Intravenous line was secured with a 20 G cannula and all the patients were preloaded with Ringer lactate solution at 20 ml/kg and Vitals like pulse, BP, RR and Spo2 were noted. Glycopyrrolate 4 µg/kg (0.2mg) was given intravenously.

Patients were positioned in the left lateral position and after aseptic precautions lumbar puncture was performed in L3-L4 inter vertebral space using midline approach with 25 G quincke's spinal needle. After ensuring free flow of CSF, intrathecal study drug was injected and patient was given supine position .The time at which the intrathecal injection was completed was considered Zero time. All the patients were monitored in the form of BP, Pulse, RR, ECG and Spo2 at 1 minute, 5 minute, 10 min, 15 min and then every 15 minute interval.

Evaluation:

i Onset of sensory blockade was tested by Time required in seconds to produce loss of pin prick sensation bilaterally at shin of tibia .(L4 Dermatome)

ii Onset of motor blockade :

Bromage criteria 45		
Scale	Criteria	Degree of block
0	Free movement of legs and feets with ability to raise extended legs	None
1	Inability to raise extended leg, knee flexion decresed but full flexion at ankle and feet present	33 %
2	Inability to raise legs or flex knee , flexion at ankle and feet present	66%

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3	Inability to raise legs,flexion knee or ankle or move toes	Complete Paralysis

iii Sedation

Sedation score- chenik44	
Score	Response
0	Awake
1	Sleeping comfortably but easily arousable
2	Deep sleep but arousable
3	Deep sleep but not arousable

iv Status of the tongue was checked for the assessment of dryness of mouth, after asking the patient to protrude the tongue.It was graded as dry or moist.

v Side effects

1	Nausea
2	vomiting
3	Bradycardia > 30% fall in pulse
4	Hypotension > 30 % fall in BP
5	Respiratory Depression < 10 breaths/ min
6	Sedation
7	Dryness of mouth

After surgery was over , patients were shifted to the recovery room and temperature , pulse rate , blood pressure , respiratory rate , Spo2 and visual analogue scale (VAS) were measured every 3 hourly for 12 hours and then 6 hourly intervals upto 24hrs .

Time of regression of analgesia to pin prick below T- 10 dermatome was considered as duration of anaesthesia. Supplemental analgesia was administrated in the form of inj Diclofenac sodium 75 mg IM when VAS was >5 and it was considered as duration of post operative analgesia. Duration, intensity and number of episodes of nausea, vomiting bradycardia, hypotension, and respiratory depression were assessed. For comparison of three groups, the student T- test was used.

Results

There was no significant difference in demographic characteristics .

TABLE 1
ONSET OF SENSORY BLOCKADE IN SECONDS

Time in seconds	Group A	Group B	Group C
151-180	4(20%)	-	13(65%)
181-210	12(60%)	7(35%)	7(35%)
211-240	3(15%)	10(50%)	-
241-270	1(5%)	2(10%)	-
271-300	-	1(5%)	-
Minimum time	170	190	155
Maximum time	250	280	210
Mean time	197.8	225.8	179.8
SD	20.23	22.14	17.01

Group A Vs Group C P = <0.001

Inf = H.S

Group B Vs Group C P = <0.001

Inf = H.S

Group A Vs Group B P = <0.001

Inf = H.S

Table1 analyzes the onset of sensory blockade in seconds as judged by loss of pinprick sensation, bilaterally at shin of tibia. The mean time in seconds in Group A, B and C was 197.8+/-20.23, 225.8+/-22.14 and 179.8+/- 17.01 respectively. Comparison of the three groups is highly significant (H.S) (P < 0.001).

These findings suggest that the delay in the onset of sensory blockade was observed in clonidine groups.

TABLE 2
ONSET OF MOTOR BLOCKADE IN SECONDS

Time in seconds	GroupA	Group B	Group C
181-210	1(5%)	-	6(30%)
211-240	6(30%)	-	13(65%)
241-270	10(50%)	7(35%)	1(5%)
271-300	2(10%)	7(35%)	-
301-330	1(5%)	6(30%)	-
331-360	-	-	-
Minimum time	205	250	190
Maximum time	320	330	270
Mean time	257.3	288	222.3
SD	26.63	24.3	20.03

Group A Vs Group C P = <0.001 Inf = H.S

Group B Vs Group C P = <0.001 Inf = H.S

Group A Vs Group B P = <0.001 Inf = HS

Analysis of onset of motor blockade in seconds is according to modified bromage criteria. The mean time of onset of motor blockade in seconds was 257.3(+/-26.6) in Group A, 288 (+/-24.3) in Group B and 222.3(+/-20.03) in Group C. There was statistically highly significant difference between the three groups. The delay in onset of motor blockade was due to addition of clonidine in Group A and Group B.

Mean pulse rate was statistically not significant preoperatively and intraoperatively upto 10 minutes after subarachnoid block, there after there was significant difference upto 2 hours . At 60 min intraoperative we observed maximum decrease in heart rate. The mean pulse rate per minute was 71.6(+/-3.28),70.3(+/-3.04) and 76(+/-5.2) for Group A, B and C respectively. These findings was highly significant (P<0.001), and it remained significant upto 2 hours .There after it was not significant.

Mean arterial pressure was statistically not significant preoperatively and intraoperatively upto 10 minutes after subarachnoid block, but there was significant difference upto next 90 minutes. (P=<0.001). There after MAP was not significant (p>0.05) again at 30 minutes intraoperatively we observed maximum fall in MAP. It was 78.3(+/-3.4.7),73.8(+/-4.7) and 83.6(+/-3.8) mm Hg for Group A, B and C respectively. The fall in MAP was highly significant in Group B.

TABLE 3
DURATION OF ANAESTHESIA

Time in minutes	GroupA	Group B	Group C
101-150	2(10%)	-	17(85%)
151-200	15(75%)	13(65%)	3(15%)
201-250	3(15%)	7(35%)	-
Minimum time	145	160	105
Maximum time	210	220	160
Mean time	176	192	130
SD	17.7	17	14.7

Group A Vs Group C P = <0.001 Inf = H.S

Group B Vs Group C P = <0.001 Inf = H.S

Group A Vs Group B P = <0.001 Inf = H.S

The mean duration of sensory anaesthesia in minutes was 176(+/-17.7), 192(+/-17) and 130(+/-14.7) in Group A, B and C respectively The prolongation of duration of anaesthesia was highly significant in three groups.

Table iv
DURATION OF POST OPERATIVE ANALGESIA IN MINUTES

Time in seconds	Group A	Group B	Group C
201-250	1(5%)	-	17(85%)
251-300	2(10%)	2(10%)	3(15%)
301-350	13(65%)	2(10%)	-
351-400	4(20%)	14(80%)	-
401-450	-	1	-
451-500	-	1	-
Minimum time	250	290	210
Maximum time	400	460	280
Mean time	335	370	235.5
SD	33.32	39.95	18.84

Group A Vs Group C P = <0.001 Inf = H.S

Group B Vs Group C P = <0.001 Inf = H.S

Group A Vs Group B P = <0.001 Inf = H.S

Duration of post operative analgesia in minutes was illustrated in table iv. The mean duration of postoperative analgesia in minutes was 335(+/-33.32), 370(+/-39.95) and 235.5(+/-18.84) in Group A, B and C respectively. There was a highly significant difference in the mean duration of analgesia between the three groups.

Table v
SIDE EFFECTS

	Group A	Group B	Group C
Headache	1(5%)	2(10%)	2(10%)
Nausea	2(10%)	2(10%)	2(10%)
Vomiting	1(5%)	1(5%)	-
Hypotension	3(15%)	4(20%)	2(10%)
Bradycardia	-	1(5%)	-
Dryness of mouth	4(20%)	7(35%)	3(15%)
Respiratory Depression	-	-	-

Incidence of headache nausea and vomiting are almost equal in three groups.

Incidence of hypotension was higher in patients in group A(15%) and B (20%)as compared to group C. Incidence of dryness of mouth was also higher in group A (15%) and group B (35%) as compared with group C(10 %).Respiratory depression and significant bradycardia was not observed in any of the groups.

Table vi
SEDATION SCORE

Score	Group A	Group B	Group C
0	14(70%)	11(55%)	17(85%)
1	5(25%)	6(30%)	3(15%)
2	1(5%)	3(15%)	-
3	-	-	-

14 patients (70%)in group A, 11 patients(55%) in group B and 17 patients(85%) in groupC remain awake in the intraoperative period.5 patients (25%) in group A, 6 patients(30%) in group B and 3 patients(15%) in groupC were sleepy but easily arousable. 1 patients (5%) in group A, 3 patients(15%) in group B were in deep sleep but arousable, while none in group C.

Discussion

Intrathecal opiod are synergistic with local anaesthetics that intensify the sensory block without increasing the sympathetic block. Clonidine is a good adjuvant in this regard with some acceptable side effects. Clonidine is a selective partial α 2 agonist . It is known to increase both the sensory and motor blockade of local anesthetics.The analgesic effect following its intrathecal administration is mediated spinally through activation of postsynaptic α 2 receptors in substantial relations of spinal cord. 2-6 Neverless less clonidine is needed intrathecally than epidurally to produce nearly same analgesic effect with fewer side effects as shown by Filos et al 19922.

Clonidine has been used intrathecally in different doses like 150 µg, 75 µg 37.5 µg. We compared two different doses 1 and 0.5 µg/kg similar to Kaabachi O et al 2002 7 and Thakur Anil et al. 20138

The mean onset of sensory blockade in seconds was 197.8+/-20.23, 225.8+/-22.14 and 179.8+/- 17.01 in Group A, B and C respectively in our study.. Similarly the mean time for onset of motor blockade in seconds was 257.3(+/-26.6) in Group A, 288 (+/-24.3) in Group B and 222.3(+/-20.03) in Group C respectively . On comparison the delay in onset of sensory and motor blockade was statistically highly significant(p<0.001) correlating with the study of Arun Vyas 1992.9

At 60 min intraoperative we observed maximum decrease in heart rate. The mean pulse rate per minute was 71.6(+/-3.28),70.3(+/-3.04) and 76(+/-5.2) for Group A, B and C respectively. These findings was highly significant (P<0.001), and it remain significant upto 2 hour .There after it was not significant results co related to F Bonnet et al.12 1992 observed 24.8+/-10.4% decrease in heart rate in a group of patients receiving clonidine 150µg intrathecally compared to 19.6+/- 4.8% in control group,receiving plain bupivacaine. In our study,one patient in clonidine group B (1 µg/kg) developed bradycardia which was successfully treated with inj Atropine 0.6mg iv suggesting fall in pulse rate was dose dependent.

L Neimi 199411 observed significant decrease in pulse rate when using 3 µg/kg clonidine intrathecally. Similarly to our study Dobrydnojov et al.3 in 2003 studied (15 µg,30 µg) of clonidine with bupivacaine and observed small dose clonidine will not lead to significant bradycardia.

Mean arterial pressure

Mean arterial pressure was statistically not significant preoperatively and intraoperatively upto 10 minutes after subarachnoid block, but there was significant difference in next 90 minutes. (P=<0.001). There after MAP was not significant (p>0.05). At 30 minutes intraoperatively we observed maximum fall in MAP. It was 78.3(+/-3.4.7),73.8(+/-4.7) and 83.6(+/-3.8) mmHg for Group A, B and C respectively. The fall in MAP was highly significant in Group B. comparable with the studies of Dobrydnojv I et al3, Stephan Strebel 200412 and B S Sethi 2007. 13

There was no significant changes observed in the respiratatory rate or Spo2 ,intraoperative and post operative in the three groups of our study which was comparable to study observed by B S Sethi et al13 in 2007 and Dobrydnojv and colleagues3 in 2003 .

14 patients (70%)in group A, 11 patients(55%) in group B and 17 patients(85%) in groupC remain awake in the intraoperative period. 5 patients (25%) in group A, 6 patients(30%) in group B and 3 patients(15%) in groupC were sleepy but easily arousable. 1 patient (5%) in group A, 3 patients(15%) in group B were in deep sleep but arousable, while none in group C.comparable to Thakur anil et al 20138 where as Niemi L 199411had recorded in his study that patients receiving intrathecal clonidine 3 µg/kg mixed with bupivacaine remained sedated for 3-6 hours compared to control group. Sedation due to clonidine is dose dependent.

The mean duration of anaesthesia (until regression of block below T 12) in minutes was 176(+/-17.7), 192(+/-17) and 130(+/-14.7) in Group A, B and C respectively. On comparison the duration of anaesthesia was statistically highly significant(p<0.001).which was Similar to study of B S Sethi13 in 2007,Neimi L199411 , F Bonnet199210 and . Stephen Strebel12 et al in 2004 noted dose dependant prolongation of time in regression of spinal anesthesia below L1 , when using intrathecal clonidine.

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The mean duration of postoperative analgesia in minutes was 335(+/-33.32), 370(+/-39.95) and 235.5(+/-18.84) in Group A, B and C respectively.The mean duration of analgesia between the three groups(P<0.001)was highly significantsimilar to studies of B S Sethi200713 ,Neimi L199411,. Strebel S 200412 et al observed that duration of pain relief from intrathecal clonidine until the first request for supplemental analgesia was significantly prolonged.

1(5%) Patient in group A, 2(10%) in groupB and 2(10%) in group C developed headache in 24 hours that was not significant and possibly due to dural puncture and was treated with analgesics and fluids.

There was no significant incidence of nausea and vomiting, , dryness of mouth and respiratory depression correlating with almost all the studies. Though heart rate started dropping in clonidine more in 1µg/kg group after 20 min maximum at 60 minutes but bradycardia was never severe to be a cause for concern .in conclusion that adding clonidine 1µg/kg to Intrathecal bupivacaine 0.5% heavy 15mg prolongs the spinal anaesthesia and duration of post operative analgesia.It is safe and effective witout severe adverse effects.

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