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Efficacy of Epidural Clonidine as an Adjuvant to Local Anesthetic in Lower Abdominal Surgeries: A Randomized Control Clinical Trail

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Abstract

Introduction: Management of both intraoperative anaesthesia and post operative pain by neuraxial block demands addition of additives which gives good and prolonged postoperative analgesia with minimal side effects. Among various choices of additives, alpha 2 agonists are one among the preferred drugs. *Aim of the Study:* To compare the efficacy of a mixture of 0.5% bupivacaine and clonidine 150 micrograms with 0.5% bupivacaine used alone in lumbar epidural anaesthesia for lower abdominal surgeries. *Materials and Methods:* Fifty patients belonging to ASA I or ASA II category were selected for the study. All patients were randomly divided into two groups of 25 each. Group I, the control group received 10-15 ml 0.5% of bupivacaine and 1 ml of normal saline and Group II. Clonidine group received 10-15 ml of 0.5% bupivacaine and 150µgm of clonidine. Onset and duration of sensory and motor block and duration of post-operative analgesia along with adverse effect were studied. Statistical analysis was performed using student unpaired t –test and chi- square test. *Results:* Epidural clonidine in the dose of 150 µgm combined with 0.5% bupivacaine produced an effective anaesthesia with rapid onset, intensified and prolong blockade and an extended duration of post operative analgesia with minimum side effects.

Keywords: Clonidine; Bupivacaine; Extradural; Analgesia.

Introduction

In the clinical situation of regional anaesthesia and postoperative pain management , neuraxial drugs with additives or synergistic interaction is more desirasble to improve anaesthesia and analgesia. Since the discovery of an adrenergic pain modulating system in the spinal canal, the extradural analgesic potential of alpha adrenergic agonist has been in the focus as an alternative to opioids [1]. Clonidine, apartial alpha 2 adrenergic agonist has been shown to produce analgesia of variable intensity and duration in both acute and chronic pain [2]. Clonidine exerts its analgesic effect through the activation of adrenergic receptors at the peripheral, spinal and brainstem sites.

Clonidine produces analgesia by activation of postsynaptic alpha 2 receptors in the spinal canal and exerts action on the descending inhibitory monoaminergic tracts, resulting in ant nociceptive effect. It also potentiate the effect of opioids and local anaesthetic agents [3,4].

The main side effect of extradural administration of clonidine are dose dependent hypotension, bradycardia, and sedation which are rarely severe and easily treated [3,5].

Main aim of the study is to compare the effects of extradurally administered clonidine and bupivacaine with those of extradural bupivacaine, with particular emphasis on postoperative pain and hemodynamic changes. The dose of extradural clonidine is chosen 150 µgms as this has been shown

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to produce significant analgesic benefit with minimal adverse effect [6].

Materials and Methods

After obtaining approval from the institutional ethics committee and written informed consent , fifty adult patients belonging to ASA I or II scheduled for lower abdominal procedure under lumbar epidural anaesthesia were included in the study.

Exclusion criteria included, patient refusal for regional anesthesia, patients with coagulopathy, obstetric patients, neurosurgical cases and patients with cardiac, kidney and liver pathology, history of hypersensitivity and patients belonging to ASA III and above.

All patients were randomly allocated in to two group of 25 each.

Meterial and Method

Group 1 Control group 10 to 15 ml of 0.5% bupivacaine and 1 ml of normal saline

Group 11 clonidine group 10– 15 ml of bupivacaine and 1 ml of clonidine [150 micro grams]

Details of the Parameters Studied

1. Sensory Blockade

Sensory blockade was assessed at 1 minute interval until peak effect, beginning from completion of epidural injection.

Assessment done by hollmens scale

Grade 0 normal sensation at pin prick

Grade 1- pinprick felt as sharp pointed but weaker as compared to same area in upper extremity.

Grade 3- pinprick recognized as touch with a blunt object.

Grade 4- no pinprick perception to touch.

2. Time of Onset of Sensory Analgesia at T 10.

Time of completion of epidural injection to the occurrence of grade 3 sensory block on hollmen scale at the level of umbilicus at T 10.

3. Duration of sensory blockade

The time from the maximum cephalad spread of analgesia to the time at which sensory block has regressed by two segments.

4. Motor Blockade

Motor blockade was assessed every minute till peak effect and every 5 minutes thereafter till complete motor blockade, by testing the power of a specific joint movement of both lower limbs which are regarded as equivalent to the corresponding myotomes using seow decimal score.

5. Time of Onset of Complete Motor Blockade

Time from completion of epidural injection to the time at which complete spread of motor blockade occurred.

6. Intensity of Motor Blockade

Number of myotomes blocked, expressed as myotome score on *Seow decimal score.*

Table 1:

	Right	Left
Hip flexion [L2]	1	1
Knee extension [L3]	1	1
Ankle dorsiflexion[L4]	1	1
Great toe dorsiflexion[L5]	1	1
Plantar flexion[s1]	1	1
	5	5=10

7. Duration of Motor Blockade

Time from complete motor blockade to the recovery of complete power of all joint movements.

Intraoperatively blood pressure and pulse rate were recorded every two minute for first 30 minutes and every 5 minutes thereafter till the end of procedure. Any complications like adverse reactions and failure of analgesia were noted.

In the post operative ward the patient were monitored for haemodynamic changes.

8. Duration of Analgesia

The intensity of pain was charted on visual analogue scale every hour and the duration to reach a visual analogue score of 4 cm was noted for patients in both the groups.

Time taken for VAS to reach 4 from the time of injection of drug or for the patients request for analgesia from the time of injection of drug is taken as duration of analgesia for that particular group. Top up of 0.125% bupivacaine 5-8 ml was administered for analgesia

8. Sedation RAMSAY SEDATION SCORE was used

1. Anxious, agitated and restless
2. Awake, cooperative, oriented and tranquil
3. Semi asleep but responds to commands
4. Asleep with response to stimuli
5. Asleep with sluggish response to stimuli
6. No response

Statistical Analysis was performed using students unpaired t test for mean age, height, weight distribution, haemodynamic variables. Time of onset of sensory block, motor block, duration of sensory and motor blockadeand duration of analgesia. *Chi – square test* was used for analysis of intra operative adverse effects. p< 0.005 suggest statistically significant .

Results

I. Onset Time

Mean onset time of sensory block at T10 in control group was 9.6+3.09 mins and in clonidine group was 6.16+2.59, which was statistically highly significant.

Complete motor blockade was not achieved in 2 patients in clonidine group and in control group out of 25 patients in each group. Mean time for onset of complex motor block was 22.82+4.22 compared to 17.39+5.44 in control group, which was statistically highly significant.

II. Duration Time

The mean time of duration of sensory blockade was 102.26+10.89 mins in control group in comparison to 145.86+22.31 in clonidine group, which was highly significant.

Table 2: Mean time of onset of sensory and motor blockade

Parameter	Group	N	Mean	SD	t
Sensory	Control	25	9.60	3.095	4.258
Blockade (T_{10})	Clonidine	25	6.16	2.592	P=0.001 vhs
Motor	Control	23	22.82	4.228	3.782
Blockade	Clonidine	23	17.39	5.441	P=0.001 vhs

Table 3: Mean time of duration of sensory and motor blockade

Parameter	Group	N	Mean	SD	t
Sensory	Control	23	102.26	10.897	8.421
Blockade (T_{10})	Clonidine	23	145.86	22.316	P=0.001 vhs
Motor	Control	22	204.27	23.417	16.205
Blockade	Clonidine	25	366.48	41.456	P=0.001 vhs

Table 4: Myotome Score

Parameter	Group	N	Mean mins	SD	t
2 (L_2)	Control	25	6.160	2.426	0.14300
	Clonidine	25	6.040	3.421	P>0.05 ns
4(L_3)	Control	25	10.720	3.482	1.631
	Clonidine	25	17.39	5.441	P>0.05 ns
6 (L_4)	Control	25	14.880	3.844	2.545
	Clonidine	25	11.960	4.257	P<0.05 sig
8 (L_5)	Control	25	18.360	3.795	3.457
	Clonidine	25	14.240	4.594	P<0.001vhs
10 (S_1)	Control	23	22.826	4.228	3.782
	Clonidine	23	17.391	5.441	P<0.001vhs

The mean time of duration of motor blockade was 204.27+ 23.41 in control group in comparison to 366.48+41.45 in clonidine group, which was highly significant.

III. Intensity of Motor Blockade

No significant difference was observed between the two groups in the time to attain myotome score 2 and 4. The time to attain the particular myotome score, thereafter was significantly shorter in the clonidine group compared to the control group.

IV. Sedation

Patients in clonidine group had higher sedation score 3 or above in comparison to the control group and was statistically significant. Onset of sedation noticed within 30 minutes of administration and was observed throughout the intraoperative period. Patients were easily arousable and responded to verbal commands.

There was no depression in ventilation as evidenced by pulse oximetry. One patient in clonidine group had snoring and drop in oxygen saturation from 100% to 96% .

Table 11: Intraoperative sedation score

Time	Group	N	Mean	SD	T
30	Control	25	2.00	0	12.970
	Clonidine	25	3.52	5859	P=0.001 vhs
60	Control	25	2.00	0	15.087
	Clonidine	25	3.68	5567	P=0.001 vhs
90	Control	25	1.96	2000	14.241
	Clonidine	25	3.52	5099	P=0.001 vhs

V. Duration of Analgesia

Duration of analgesia was significantly increased in the clonidine group (598.68+110.91 mins) compared to the control group as they required additional 0.5% bupivacaine in the intropeative period.

Group	N	Mean	SD	T
Control	22	270.636	36.350	13.245
Clonidine	25	598.680	110.916	P=0.001

VI. Visual Analogue Scale

Table 13: Vas Score

Time (hrs)	Group	N	Mean	SD	T
½	Control	22	0.272	455	2.996
	Clonidine	25	.0	.0	P=0.001vhs
1	Control	22	1.636	.847	9.666
	Clonidine	25	.0	.0	P=0.001 vhs
2	Control	22	3.636	1.093	16.659
	Clonidine	25	.0	.0	P=0.001vhs
3	Control	16	5.187	.655	28.551
	Clonidine	25	0.160	.472	P=0.001 vhs
4	Control	2	6.0	.0	-
	Clonidine	25	0.480	.714	
5	Control	0	-	-	-
	Clonidine	25	1.320	1.030	
6	Control	0	-	-	-
	Clonidine	25	2.210	1.103	
7	Control	0	-	-	-
	Clonidine	25	2.850	1.387	
8	Control	0	-	-	-
	Clonidine	25	3.500	1.095	
9	Control	0	-	-	-
	Clonidine	25	4.330	1.303	
10	Control	0	-	-	-
	Clonidine	25	4.500	1.915	

Discussion

For Post operative pain control various adjuvants like opioids, neostigmine, clonidine, midazolam, ketamine etc has been tried with local anesthesia to potentiate its action. Alpha agonists like Clonidine is in focus when we think about any alternative to opioids. Enough evidences exists to implicate the role of clonidine in the inhibition of nociceptive transmission when administered epidurally in humans [1,3].

Our study demonstrated that epidural clonidine when administered with bupivacaine produced effective anaesthesia with a rapid onset of action of both sensory and motor blockade, with a prolonged and intensified block. T zeng et al reported that epidural clonidine when administered with lidocaine produces effective anaesthesia with a rapid onset, longer duration of action and more profound block [7].

On the other hand previous studies by Engel et al reported no change in the onset of sensory and motor blockade by epidural clonidine. Only difference between their and our results might be because their study used Ropivacaine, which has a slower onset and shorter duration of action than bupivacaine.

Our study demonstrates prolonged analgesia with almost 2 fold increase in the duration of analgesia with administration of clonidine [598±110.91 compared to 290.63±36.35 in control]. Previous studies show similar prolonged analgesia with use of epidural clonidine. Engel et al reported analgesia of 513±92 minutes duration and it is shorter than our study as Ropivacaine was used in their study.

Studies by Kalia et al, Carabine et al, O Meara et al, Tzeng et al, all demonstrated similar findings. The duration of analgesia obtained in their studies were shorter due to the use of lower concentration or lesser volume of bupivacaine or lidocaine in comparison with our study [6,9,10].

VAS scores were lower with epidural administration of clonidine and complete relief was observed in the initial four hours of postoperative period, providing satisfactory analgesia. Studies by Carabine et al, O Meara et al, Anzai et al reported lower pain scores and satisfactory analgesia with epidural administration of clonidine [6,10,11].

In our study, no significant difference was observed in the incidence of hypotension, bradycardia, with epidural administration of clonidine. However mean arterial pressure were lower with the use of clonidine than with plain bupivacaine. Also in the postoperative period, patients who received clonidine showed a lower mean arterial pressure and lower heart rate. This might be either due to the central effect of clonidine on sympathetic outflow or due to decreased analgesia in the patients receiving plain bupivacaine.

In our study, sedation was observed following epidural clonidine and the onset was observed within 30 minutes. All previous studies on clonidine have shown that it produces sedation with minor or no effect on ventilation. By a central neuraxial blockade, sedation may be a desired action as it reduces the need of any other sedatives and anxiolytics. Incidence of shivering was lower significantly with the use of clonidine. Studies done by Zhao et al have demonstrated that clonidine possess anti shivering properties and has been used clinically in the prevention of shivering [12].

Conclusion

Epidural clonidine in the dose of 150 µgm combined with 0.5% bupivacaine produced an effective anaesthesia with rapid onset, intensified and prolonged blockade and an extended duration of post operative analgesia with minimum side effects.

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