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Original article

Study of effect of epidural clonidine alone as an adjuvant on sensory characteristics of intrathecal bupivacaine in the patients undergoing infraumbilical surgeries

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Abstract:

Introduction: Both epidural and spinal anaesthesia produce what is known as a neuraxial block. Deposition of local anaesthetic into the spinal space produces blockade of conduction much more rapidly, as the meninges do not need to be traversed in order to reach the site of action. A smaller dose of local anaesthetic is required as it rapidly diffuses through the cerebrospinal fluid to produce sensory blockade. The anaesthetic and the analgesic requirement get reduced to a huge extent by the adjuvant like clonidine because of its analgesic properties and augmentation of local anaesthetic effects.

Material and methods: It was an observational longitudinal study of 124 enrolled patients conducted during 2 years period from October 2016 in the Department of Anaesthesiology & Critical Care, Pravara Rural Hospital (PRH) Loni. A total of 124 enrolled patients belonging to American Society of Anaesthesiologists Physical Status grade I and II undergoing infraumbilical procedures were allocated into group C (Control) and group S (Study) of 62 patients each. Group C included patients who had received SAB (Sub Arachnoid Block) bupivacaine 0.5%, 15 mg (3 ml) intrathecally. Group S included patients who had received injection clonidine 150 µg, diluted to 5 ml in normal saline (NS) via epidural catheter 10 min before SAB. All statistical analyses were performed using IBM Statistical Package for the Social Sciences 22

Results: Epidural clonidine produced faster ($p<0.05$) onset (mean=37.29 sec in group S compared to mean=51.39 sec in group C) of sensory blockade. The time for two segment regression was greater in study ($p<0.05$) group (192.81 min) compared to control group (107.82 min). The total duration of analgesia was greater ($p<0.05$) in study group (302.60 min) compared to control group (154.74 mins).

Conclusion: From this study, we conclude that, the epidural administration of clonidine prior to SAB has an adjuvant effects like faster onset and greater duration of sensory blockade along with prolonged duration of analgesia.

Introduction:

Both epidural and spinal anaesthesia produce what is known as a neuraxial block. Deposition of local anaesthetic into the spinal space produces blockade of conduction much more rapidly, as the meninges do not need to be traversed in order to reach the site of action. A smaller dose of local anaesthetic is required as it rapidly diffuses through the cerebrospinal fluid to produce sensory and motor blockade.

Combined spinal–epidural (CSE) anaesthesia offers a safe and inexpensive technique with the advantage of both spinal and epidural anaesthesia. It provides faster onset of surgical anaesthesia and prolongs the duration of post-operative pain relief. Various adjuvants further increase its efficacy[1].

The addition of opioid does provide a dose sparing effect of local anaesthetic and superior analgesia but there is always a possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting and respiratory depression[2,3].

Our aim was to study and evaluate the onset and duration of sensory blockade and further study the total duration of analgesia with epidural adjuvant clonidine .

Material and methods:

An observational longitudinal study of 124 enrolled patients was conducted during 2 years period from October 2016 in the Department of Anaesthesiology & Critical Care, Pravara Rural Hospital (PRH) Loni. A total of 124 enrolled patients belonging to American Society of Anaesthesiologists Physical Status grade I and II undergoing infraumbilical procedures were allocated into group C (Control) and group S (Study) of 62 patients each. Group C included patients who had received SAB (Sub Arachnoid Block) bupivacaine 0.5%, 15 mg (3 ml) intrathecally. Group S included patients who had received injection clonidine 150 µg, diluted to 5 ml in normal saline (NS) via epidural catheter 10 min before SAB. All drugs were administered by consultant anaesthesiologist who was not involved in the study. Characteristic of sensory blockade and total duration of analgesia were observed. All statistical analyses were performed using SPSS statistical software.

Patient Inclusion criteria:

a) Patients from age range 18 – 60 years.
b) ASA grade I and II, without any co-morbid disease.
c) Patients willing for the study and giving written informed consent.

Patient Exclusion criteria:

a) Patients with known coagulopathy or patients on anti coagulants
b) Patients with known hypersensitivity to study drugs.
c) Infection at the site of combined spinal epidural block.
d) Patients with neurological or psychiatric disorders.

Fischer exact test and Chi-Square test were applied for nominal data. Student's *t* test was used for parametric data. $P < 0.05$ considered statistically significant. All statistical analyses were performed using IBM Statistical Package for the Social Sciences 22 (SPSS Inc. Chicago, IL, USA) statistical software.

Sensory block:

Sensory block was assessed as loss of pin prick sensation using the blunt needle. Sensory block was graded as –

- Grade 0: Sharp prick felt at L1 dermatome.
- Grade 1: Analgesia, dull sensation felt at L1 dermatome.
- Grade 2: Anaesthesia, no sensation felt at L1 dermatome.

Duration of sensory blockade: Duration of sensory blockade was the time from the onset of sensory blockade to return of dull pain and VAS > 5. Surgery commenced after sensory block at T_6 dermatome was attained.

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Observations & Results:

The present observational prospective longitudinal study was undertaken to compare adjuvant epidural clonidine with hyperbaric bupivacaine SAB and plain hyperbaric bupivacaine SAB in infraumbilical surgeries.

Table.1a, 1b and 1 c shows the demographics of age, gender and ASA grades between the control and study groups.

Table. 1a Age demographics

Age demographics					
	Group	**N**	**Mean**	**Std. Deviation**	**P Value**
Age	**Control**	62	42.32	13.58	>0.05
	Study	62	42.82	12.94	>0.05

Table 1b. Gender demographics

Gender *(p>0.05)*			
	Male n (%)	**Female n (%)**	**Total**
Control	46 (74.19%)	16 (25.80%)	62
Study	36 (58.06%)	26 (41.93%)	62

Table. 1c ASA grades

ASA grades *(p>0.05)*				
	ASA grade I n (%)	**ASA grade II n (%)**	**P Value**	**Total**
Control	44 (70.96%)	18 (29.03%)	> 0.05	62
Study	38 (61.29%)	24 (38.70%)	> 0.05	62

The statistical analysis with Chi Square test showed no significant difference between age, gender and ASA grades of Control and Study groups.

The Chi Square and Student T test showed significant difference ($p<0.05$) between control and study group with respect to various parameters shown in Table.2. Graph.1 shows the bar diagram.

The statistical tests for Visual Analogue Scale (VAS) was carried out in control and study group at 30 min, 60 min, 120 min, 180 min, 240 min, 300 min and 360 min was carried out. The Chi Square and Fischer Exact test showed significant difference ($p<0.05$) between the study and control groups. Graph.2 shows the line diagram for pain score.

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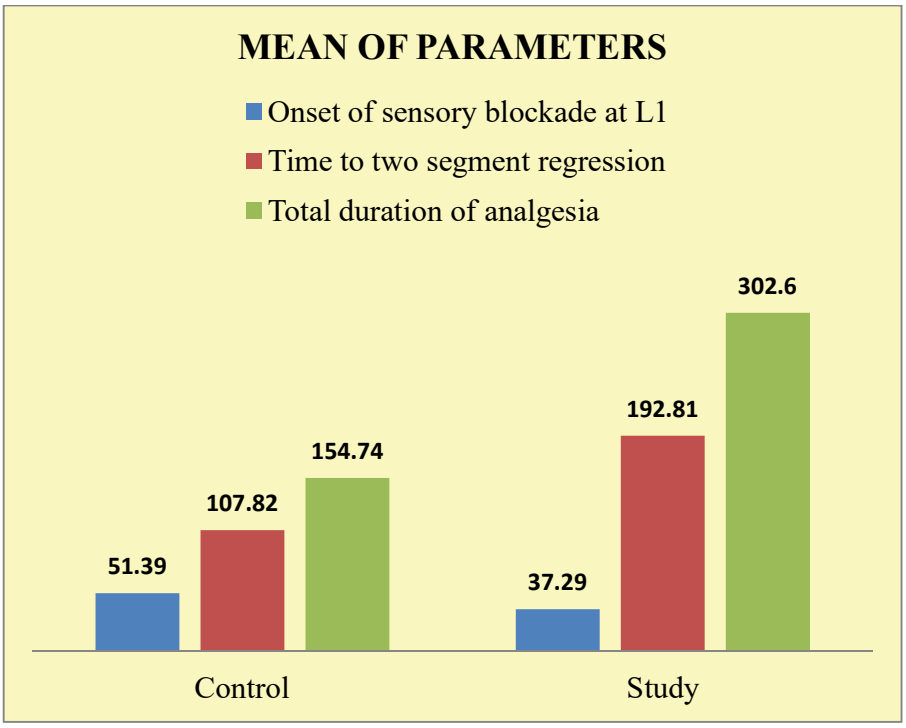
Table.2 Comparison of parameters between Control and Study groups.

Parameters between study and control groups				
	Group	**N**	**Mean ± SD**	**P value**
Onset of sensory blockade at L1 (seconds)	**Control**	62	51.39 ± 2.26	<0.05
	Study	62	37.29 ± 3.61	
Time to two segment regression (minutes)	**Control**	62	107.82 ± 5.21	<0.05
	Study	62	192.81 ± 6.26	
Total duration of analgesia (minutes)	**Control**	62	154.74 ± 7.89	<0.05
	Study	62	302.60 ± 12.98	



Graph.1 Mean of parameters of groups

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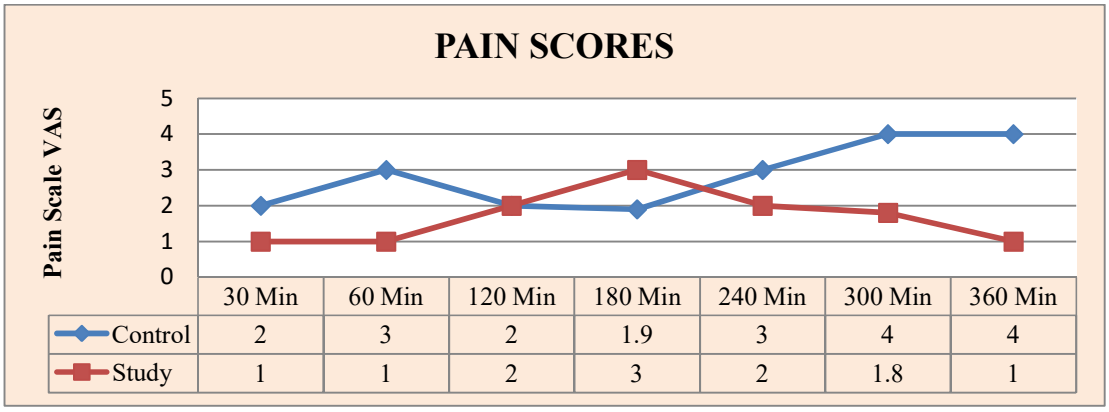

Graph.2 Pain scores

Discussion:

The use of neuraxial opioids is associated with quite a few side effects, so various options including α-2 agonists are being extensively evaluated as an alternative with emphasis on opioid-related side effects such as respiratory depression, nausea, urinary retention and pruritis[3-5]. The pharmacologic properties of α-2 agonists have been extensively studied and have been employed clinically to achieve the desired effects in regional anaesthesia[6-9].

We had a faster onset of sensory blocakade (37.29 ± 3.61sec), higher time for two segment sensory regressions (192.81 ± 6.26 min) and prolonged duration of analgesia (302.60 ± 12.98) in the Group S (clonidine).

Our results are comparable to the results by Prasad et al[10], Satheesa et al[11] and and Shobhana et al[12].

Clonidine is a centrally acting partial α_2 adrenoceptor agonist with selectivity ratio of 200:1. Its analgesic effect is mediated by binding to postsynaptic α_2 receptors (G-protein coupled inhibitory receptors) in the dorsal horn of the spinal cord. This mimics the effects of noradrenaline which is released from the descending inhibitory pathways in the central nervous system. Thus, decreased activity of the second-order neurons and wide dynamic range neurons in the dorsal horn occurs which in turn attenuates the input from peripheral nociceptive A_δ and C fibres. Studies in rats show that clonidine partially inhibits voltage-gated sodium and potassium channels and suppresses generation of action potentials in tonic firing spinal dorsal horn neuron[13]. As clonidine-induced analgesia is mediated by activation of adrenergic receptors on the dorsal horn of the spinal cord, intrathecal or epidural administration of the drug close to its action site seems to be logical.

Agarwal et al[14] studied clonidine as an adjuvant to hyperbaric bupivacaine for spinal anesthesia in 60 elderly patients undergoing lower limb orthopedic surgeries. Clonidine facilitated the ascent of sensory level block to higher dermatomes for a longer time.

Clonidine, a α-2 agonist agent, is causing analgesia with a non-opioid mechanism as an alternative agent to opioid[6]. Alpha-2 agonists when used as adjuvant in central neuraxial blockade produce significantly lower post-operative pain scores without any of these opioid-related side effects[4,5]. As side effects, such as sedation, hypotension or bradycardia, are at least partly related to systemic absorption, the route that provides the best balance between analgesia and side effects is more acceptable.

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When given by epidural route with local anesthetics, it increases analgesia potency. However, it is also true that it causes side effects like hypotension, bradycardia and sedation[7].

This has been demonstrated in a variety of clinical settings[15,16,17,18]and has shown to result in the prolongation of the sensory blockade and a reduction in the amount or the concentration of local anesthetic required to produce postoperative analgesia. Previous work with epidural infusions has shown that 150 µg of clonidine, when added to bupivacaine 0.25% approximately doubled the duration of the analgesia produced[17].

Studies comparing effects of the two α_2 agonists – dexmedetomidine and clonidine on spinal and epidural anaesthesia – have found that both produce a similar prolongation in the duration of the motor and sensory block with preserved haemodynamic stability and sedation[5].

Additive effect of clonidine to local anesthetics can be explained by various mechanisms. Alpha-2 agonists form their antinociceptive effects probably by affecting descending noradrenergic tract in spinal cord that plays an important role in pain modulation by a non-opioid mechanism[5]. Noradrenergic ganglions in pons and medulla cannot be activated by opioid or noxious stimulus that causes nor epinephrine secretion at dorsal horn of spinal cord[2,3]. When molecular weight, lipid solubility and cerebrospinal fluid pharmacokinetics of clonidine are taken into consideration, start of its analgesic effect and duration of analgesia can be expected to be similar to Fentanyl but analgesic effect of Fentanyl starts faster and lasts longer[8,9].

Alpha-2 adrenergic agonists are known to have spinal and epidural antinociceptive effect via alpha-2 receptor sub types. Clonidine, a well-known alpha-2 adrenergic agonist, produces a synergistic antinociceptive effect with opioids. Several studies have been published in the last decades describing the anesthetic sparing effects and analgesic property of epidural clonidine[1-3]. It was stated that clonidine neither affects proprioception like local anesthetics nor causes respiratory depression, itching, nausea and vomiting like opioids, but, when given by epidural route with local anesthetics, it increase analgesia potency.

Conclusion:

From this study, we conclude that, the epidural administration of clonidine prior to SAB has an adjuvant effects like faster onset and greater duration of sensory blockade along with prolonged duration of analgesia.

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