Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2018/253

Original Article

A Prospective, Double Blind, Randomized Study to Compare the Analgesic Effect of Oral Clonidine and Oral Pregabalin for Perioperative Pain in Lower Abdominal Surgeries

Veena Kachhwah[1], Sushant Rahal[2], Neeraj Narang[3]

[1]Associate Professor, Department of Anaesthesiology, Peoples College of Medical Sciences and Research Centre, Bhopal, Madhya Pradesh, India, [2]Postgraduate Student, Department of Anaesthesiology, Peoples College of Medical Sciences and Research Centre, Bhopal, Madhya Pradesh, India, [3]Assistant Professor, Department of Anaesthesiology, NSCB Medical College Jabalpur, Madhya Pradesh, India

Abstract

Background and Aims: The aim of this study is to compare the post-operative analgesic properties of oral clonidine versus oral pregabalin used preemptively.

Materials and Methods: Our study included 64 patients of both sex, aged between 18 and 50 years of ASA Grade I and II, scheduled for lower abdominal surgeries. Group A patients were provided with oral clonidine in a dose of 200 mcg 45 min before the scheduled operation. Group B patients were given oral pregabalin in a dose of 150 mg 45 min before the schedule time of operation. Various parameters were recorded such as intra- and post-operative hemodynamics, post-operative visual analog scale scores, time to first rescue analgesic, and mean doses of analgesic required in the post-operative period and the associated side effects of the drugs used in the study.

Results: Group A had least intraoperative cardiovascular stability and Group B had best intraoperative and post-operative cardiovascular stability. Group B patients showed maximum post-operative analgesia requirement. Overall, side effects were highest in Group B.

Conclusion: It could be concluded that the use of preemptive pregabalin provides excellent hemodynamic stability while superior analgesia, less post-operative analgesic requirement was observed with the preemptive use of oral clonidine.

Key words: Clonidine, Post-operative analgesia, Pregabalin

INTRODUCTION

Perioperative pain management is one of the major topics of interest for anesthesiologists. Post-operative pain has a direct relation with hospital stay that leads to more morbid complications and extra hospital costs. The cutting of the skin stimulates nerve fibers (myelinated A-delta and unmyelinated C fibers) which signal pain to the brain through the spinal cord. As the body begins to heal or the noxious stimulus is withdrawn, pain should decrease and eventually stop. Steps can be taken to minimize or eliminate pain.

A person's self-report is considered the most reliable measure of pain.[1] Many pain scoring systems have been formed for assessment of pain such as visual analog scale (VAS), verbal numerical scale, and word scale which employ scale from 0 (no pain at all) to 10 (worst pain ever felt).

Many drugs are used for pain management in perioperative period such as opioids (most commonly used), nonsteroidal anti-inflammatory drugs, selective cyclo-oxygenase-2 inhibitors, local anesthetics, alpha-2 adrenergic agonists, alpha-2 delta receptor modulators, N-methyl-D-aspartate

Access this article online

www.ijss-sn.com

Month of Submission : 07-2018
Month of Peer Review : 08-2018
Month of Acceptance : 09-2018
Month of Publishing : 09-2018

Corresponding Author: Dr. Neeraj Narang, Department of Anaesthesiology, N S C B Medical College Jabalpur, Madhya Pradesh, India. Phone: +91-9993217681. E-mail: nrang_neeraj@rediffmail.com

antagonists, and glucocorticoids.[2] Due to their side effects (when used alone or in higher doses), anesthesiologists are more inclined these days to employ multimodal analgesia technique using combination of different classes of analgesics with different mechanism of action and acting at different sites in the nervous system either central or peripheral, resulting in additive/synergistic analgesia with lowered side effects.[3] There had been a continuous search for newer and better drugs for the benefit and safety of the patient, surgeon, and anesthesiologist.

Clonidine is an imidazoline derivative having predominantly alpha-2 adrenergic activity. It is commonly used for its: (a) Anti-hypertensive and negative chronotropic effects, (b) sedative and anxiolytic properties, and (c) anesthetic and analgesic effects.[4]

Mechanism of Action

Drug being highly lipid soluble penetrates blood–brain barrier. Binding of the drug to the receptors is highest in the rostral ventrolateral medulla in the brain stem, which is the final common pathway for the sympathetic outflow, where it activates inhibitory neurons. The antihypertensive action is exhibited by binding of the drug to imidazoline receptors (non-adrenergic) in brain. Analgesic effect is mediated by blocking nociceptive transmission through pre- and post-synaptic alpha-2 adrenergic receptors. Overall effect (a) decreased sympathetic activity, (b) enhanced parasympathetic tone, and (c) reduced circulating catecholamines.[5]

Clonidine is available in various forms for oral, intramuscular, intravenous, intrathecal, epidural, and transdermal patch use. Oral dose: 3–5 μg/kg, onset: 30–60 min, duration of action: 8–12 h, bioavailability: 95%, urinary excretion: 62%, and plasma bound: 20%.[6]

Side Effects

A. More common: Sedation, dizziness, bradycardia, dry mouth, and hypotension.
B. Less common: Anxiety, nausea/vomiting, diarrhea, erectile dysfunction, weight gain/loss, and rash.
C. Uncommon: Hallucination, paraesthesia, itching, and nightmares.
D. Rare: Gynecomastia, alopecia, and hyperglycemia.

It is known to cross the placenta and has been kept in pregnancy category C. Caution has been warranted in breastfeeding women as it can pass into breast milk.[7]

Pregabalin is a lipophilic gamma aminobutyric acid (GABA) analog substituted at the 3'-position to facilitate diffusion across the blood–brain barrier. It was invented by medicinal chemist Richard Bruce Silverman at Northwestern University in the United States.[8]

Pregabalin is commonly used: (a) As an adjunct to the treatment of partial seizures, (b) for neuropathic pain management (diabetic peripheral neuropathy and postherpetic neuralgia), and (c) for anxiolysis and sleep modulation.

Mechanism of Action

It does not directly act on GABA receptors but modifies the synaptic and non-synaptic release of GABA by binding avidly to alpha-2 delta sub-unit of pre-synaptic voltage-gated Ca^{++} channels. Hence, it does not alter GABA uptake and degradation. This binding results in a reduction of the release of several neurotransmitters including glutamate, noradrenaline, serotonin, dopamine, and substance P.[9]

Pregabalin is not metabolized and is not bound to plasma proteins. Hence, virtually there is no drug–drug interaction. It is almost entirely (98%) excreted unchanged in urine. Pregabalin elimination is nearly proportional to creatinine clearance.

Oral dose: 150–600 mg/day in 2–3 divided doses, onset: 45–60 min, duration of action: 4.5–7.0 **h**, bioavailability: >90%, urinary excretion: 98%, plasma bound: Nil.[10]

Side effects: (a) Very common: Somnolence and dizziness, (b) common: Dry mouth, blurred vision/diplopia, peripheral edema, weight gain/increased appetite, and abnormal thinking, (c) in-frequent: Depression, lethargy, tachycardia, myoclonus, anorgasmia, agitation, and hallucinations, and (d) rare: Neutropenia, hypotension, and dysphagia.

It has been categorized as Schedule V controlled substance in the United States.[11]

The aims and objective of this study were to compare the analgesic effect of oral clonidine and oral pregabalin for perioperative pain in lower abdominal surgeries with the assessment of hemodynamic effects and compare the side effects of both the drugs.

MATERIALS AND METHODS

Study Design

This was a hospital-based, cross-sectional, and observational (comparative) study.

Study Area

The study is conducted in a tertiary care level institute in Peoples College of Medical Sciences and Research Centre (PCMS and RC), Bhopal.

Study Population
Patients posted for lower abdominal surgeries admitted at PCMS and RC, Bhopal.

Sample Size and Group Division
Sample size includes all the patients coming in the defined period and fulfilling the inclusion criteria ($n = 64$). Subjects are equally divided into 2 groups, i.e., Group A (clonidine) and Group B (pregabalin).

Inclusion Criteria
The following criteria were included in the study:
- All cases of ASA Grade 1 and 2.
- Age group 18–60 years.
- Weight 40–65 kg.
- Patients undergoing lower abdomen surgeries under spinal anesthesia.

Exclusion Criteria
The following criteria were excluded from the study:
- All cases of ASA Grades 3-6 and E.
- All patients who have contra-indication(s) to spinal anesthesia.
- Patients undergoing upper abdominal surgeries.
- Pregnant patients.
- Renal insufficiency patients.
- Surgeries performed under general anesthesia.

Premedication and Anesthetic Procedure
After complete pre-anesthetic check-up and obtaining valid written informed consent, the subjects went through the following.

In the Pre-operative Room
Recording the baseline vitals (pulse rate, blood pressure, respiratory rate, oxygen saturation, and cardiac rhythm).

Given oral drug with a sip of water 45 min before the commencement of surgery.
- Group A (pregabalin) received Cap. pregabalin 150 mg.
- Group B (clonidine) received Tab. clonidine 0.2 mg.

Pre-loading is done with 500 mL of ringer lactate after taking the vitals and giving the drug.

In the Operative Room
For pre-medication, injection ranitidine 50 mg and injection ondansetron 4 mg are given.

Undertaking all aseptic precautions, lumbar puncture is performed at L_3–L_4 level space using 25 G Quincke's needle, with the subject in sitting position. 3.5 mL injection bupivacaine (0.5%, hyperbaric) is injected intrathecally, and then the subject is turned supine for fixation of the drug. No intraoperative sedative or analgesic was given.

Intraoperative monitoring of pulse rate, blood pressure, electrocardiogram, and SPO_2 is done. For the first 15 min, the vitals are recorded after every 3 min, and after that, vitals are recorded after every 5 min until the surgery is over.

In the Surgical Intensive Care Unit
Post-operative on demand analgesia requirement is calculated in 24 h.

Injection diclofenac 75 mg (intravenous in 100 mL of normal saline) to be given on pain of grade more than 3 on VAS.

VAS Scale
- Grade 0: No pain
- Grade 1–3: Mild pain (can be ignored)
- Grade 3–5: Moderate pain (interferes with tasks)
- Grade 5–7: Moderate pain (interferes with concentration)
- Grade 7–9: Severe pain (interferes with basic needs)
- Grade 9–10: Worst pain possible (bed rest required).

Any side effects such as hypotension, bradycardia, nausea, vomiting, sedation, dry mouth and pruritis are noted.

Hypotension (fall in mean arterial pressure of more than 20% of pre-induction value) is treated by pushing intravenous fluids, and with an intravenous bolus of vasopressor drug (injection mephentermine 6 mg) if not manageable with fluids alone.

Any episode of bradycardia (heart rate <60/min) is treated with increments of 0.02 mg/kg of I.V. atropine.

All the drugs used in the study are sourced from the same manufacturer.

Statistical Analysis
Statistical analysis was performed using Statistical Package of he Social Sciences (SPSS Version 20.0; Chicago Inc., USA). Data comparison was done by applying specific statistical tests to find out the statistical significance of the comparisons. Quantitative variables were compared using mean values and qualitative variables using proportions. The significance level was fixed at $P \leq 0.05$.

RESULTS

Table 1 shows the demographic distribution of study subjects according to age and gender. The mean age in Group A is 34.25 years and Group B is 41.75 years. The average age of study group is 38 years.

Table 2 shows the distribution of study subjects according to type of surgery and mean duration of surgery in minutes. The subjects were distributed according to the type of surgery and crudely categorized into three types (Types 1–3) according to the pain felt in the surgery. In Type 1, mild pain surgeries such as hydrocoele and sinus tract surgeries were considered. Type 2 included moderate pain surgeries such as hernia, hemorrhoids, and fistula while Type 3 included severe pain surgeries such as hysterectomy, orchidectomy, and appendicectomy.

Type 1 surgery included 22 (34.4%) subjects among which 16 (50.0%) subjects were from Group A and the rest of the 6 (18.8%) subjects were from Group B. Similarly, Type 2 surgery included 26 (40.6%) subjects, 8 (25.0%) subjects from Group A, and 18 (56.2%) subjects from Group B. Type 3 surgery constituted 16 (25.0%) subjects in total and equal number of subjects from Groups A and B, i.e., 8 (25.0%) subjects each. On applying Chi-square test, value came out to be 8.392. The derived P = 0.015, which is significant.

Mean duration of surgery in Group A was 97.81 ± 41.23 min and Group B was 102.1 ± 40.99 min. The calculated *t* value came out to be 0.426. The calculated *P* value comes out to be 0.672 which is not significant.

Table 3 shows the demographic distribution of subjects under study according to type of pain and analgesic requirement. The pain intensity was assessed using a 10-cm VAS. VAS = 1–3 denoting mild pain, VAS = 3–5 denoting moderate pain (interferes with task), and VAS = 5–7 denoting moderate pain (interferes with concentration). In a total of 64, 16 (25%) subjects experienced mild pain, 40 (62.5%) subjects experienced moderate pain (interferes with task) while only 8 (12.5%) subjects experienced severe pain (interferes with concentration). It is observed that the moderate pain (interferes with task) was experienced by the highest number of subjects followed by the subjects who experienced mild pain while moderate pain (interferes with concentration) was observed in the least number of subjects.

Among the 50% subjects of Group A 12 subjects experienced mild pain, 18 subjects experienced moderate pain (interferes with task) and only 2 subjects experienced moderate pain (interferes with concentration) while in

Table 1: Demographic distribution of study subjects according to age and gender

Gender	Group A clonidine *n* (%)	Group B pregabalin *n* (%)	Total *n* (%)	Chi-square value	*P* value
Male	22 (68.8)	16 (50.0)	38 (59.4)	2.332	0.127 (NS)
Female	10 (31.2)	16 (50.0)	26 (40.6)		
Age (year)					
18–40 years	26 (81.2)	16 (50.0)	42 (65.6)	6.926	0.008 (S)
41–60 years	6 (18.8)	16 (50.0)	22 (34.4)		
Total	32	32			
Mean age	34.25 years	41.75 years			
Total mean age	38.0 years				

Table 2: Distribution of study subjects according to type of surgery and mean duration of surgery in minutes

Type of surgery	Group A clonidine *n* (%)	Group B pregabalin *n* (%)	Total *n* (%)	Chi-square value	*P* value
Type 1	16 (50.0)	6 (18.8)	22 (34.4)	8.392	0.015(S)
Type 2	8 (25.0)	18 (56.2)	26 (40.6)		
Type 3	8 (25.0)	8 (25.0)	16 (25.0)		
Duration of surgery (minutes)					
Mean ± SD	97.81±41.23	102.1 ± 40.99			
Student *t*-test	0.426				
P value	0.672 (NS)				

Table 3: Type of pain and analgesic requirement among Group A and B

Type of pain	Group A clonidine *n* (%)	Group B pregabalin *n* (%)	Total *n* (%)	Chi-square value	*P* value
Mild pain (VAS=1–3)	12 (37.5)	4 (12.5)	16 (25.0)	6.400	0.041 (S)
Moderate pain (VAS=3–5)	18 (56.2)	22 (68.8)	40 (62.5)		
Severe pain (VAS=5–7)	2 (6.2)	6 (18.8)	8 (12.5)		
Analgesic requirement					
Yes	20 (62.5)	28 (87.5)	48 (75.0)	5.333	0.021 (S)
No	12 (37.5)	4 (12.5)	16 (25.0)		

VAS: Visual analog scale

the Group B there were only 4 subjects who experienced mild pain, 22 subjects who experienced moderate pain (interferes with task) and 6 subjects experienced moderate pain (interferes with concentration).

The calculated Chi-square value is 6.400 and *P* value came out to be 0.041 which significant.

Out of total 64 subjects, the analgesia was given in only 48 (75%) subjects while no requirement of analgesia was found in the remaining 16 (25%) subjects. The cumulative analgesic requirement was statistically significantly less for Group A than Group B. From Group A; there were 20 subjects who were given analgesia while 28 subjects were given analgesia in Group B. Furthermore, the subjects with analgesic requirement are far more than those without it. In Group A, there is no significant difference in the subjects with and without analgesic request. On the contrary, major portion of the population from Group B required analgesia leaving just 4 subjects in which no analgesia was given. It can be said that the requirement of analgesia is high in pregabalin group. The calculated Chi-square value is 5.333 and *P* value came out to be 0.021 which is highly significant.

Table 4 shows mean VAS, mean time to 1st dose of analgesic, and mean required total dose of analgesic among Groups A and B. It was observed that the mean VAS score for Group A was 4.13 ± 1.008 and the mean time to 1st dose analgesic was 375 ± 233.84 min with required 84.38 ± 80.25 mg total dose of analgesic. On the other hand, the mean VAS score for Group B was 4.81 ± 0.089. The mean time to 1st dose of analgesic with 117.19 ± 71.11 mg required a total dose of analgesic was 316.25 ± 285.33 min.

Demographic Distribution of Subjects Under Study According to Side Effects in Perioperative Period among Groups A and B

The side effects such as bradycardia, hypotension, sedation, and dry mouth were observed in the perioperative period. Among 64 subjects, bradycardia was observed in 22 (20%) subjects, hypotension was observed in 28 (25%) subjects, sedation was observed in 38 (35%) subjects, and dry mouth was observed in 22 (20%) subjects. It is clear that the overall incidence of sedation is highest, followed by hypotension, whereas the incidence of bradycardia and dry mouth is least.

It can be seen that the incidence of side effects is more in Group A as compared to Group B. Among Group A, bradycardia was observed in 20 subjects, hypotension was observed in 22 subjects, sedation was observed in 18 subjects, and dry mouth was observed in 6 subjects. Furthermore, the incidence of hypotension was highest in Group A, followed by bradycardia, sedation, and incidence of dry mouth was least in Group A. On the other hand, 2, 6, 20, and 16 subjects from Group B had side effects of bradycardia, hypotension, sedation, and dry mouth, respectively. It was observed that the incidence of bradycardia was least, followed by hypotension, dry mouth, and sedation. The incidence of sedation was highest in Group B [Table 5].

The incidence of bradycardia was observed in 20 (62.5%) subjects from Group A and 2 (6.2%) subjects from Group B. Among Group A, mean baseline heart rate was 74.56 ± 7.474 and mean last heart rate was 60.31 ± 5.025. For Group B, the noted value of mean baseline heart rate was 78.69 ± 8.014 and that of mean last heart rate was 70.00 ± 7.397. The calculated Chi-square value is 22.442 and the calculated P = 0.001 which is highly significant [Table 6].

Table 4: Mean VAS, mean time to 1st dose of analgesic and mean required total dose of analgesic among Groups A and B

Group	VAS (0–10)	Time to 1st dose of analgesic (min)	Required total dose of analgesic (mg)
	Mean±SD	Mean±SD	Mean±SD
Group A clonidine	4.13±1.008	375.00±233.84	84.38±80.25
Group B pregabalin	4.81±0.896	316.25±285.33	117.19±71.11
Student *t*-test	2.884	0.901	1.731
P value	0.005 (HS)	0.371 (NS)	0.058 (S)

VAS: Visual analog scale

Table 5: Bradycardia among Groups A and B

Group	Baseline heart rate	Last heart rate	Bradycardia *n* (%)		Chi-square value	*P* value
	Mean ± SD	Mean ± SD	Yes	No		
Group A clonidine	74.56 ± 7.474	60.31 ± 5.025	20 (62.5)	12 (37.5)	22.442	0.001 (HS)
Group B pregabalin	78.69 ± 8.014	70.00 ± 7.397	2 (6.2)	30 (93.8)		
Student *t*-test	2.129	6.128				
P value	0.037 (S)	0.001 (HS)				

Table 6: Mean systolic and diastolic blood pressure among Group A and B

Group	Baseline systolic BP	Last systolic BP	Baseline diastolic BP	Last diastolic BP
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Group A clonidine	115.13 ± 6.84	101.31 ± 7.315	73.94 ± 5.886	62.25 ± 4.745
Group B pregabalin	125.50 ± 11.37	111.31 ± 8.775	81.75 ± 8.948	68.94 ± 7.286
Student *t*-test	4.422	4.952	4.126	4.351
P value	0.001 (HS)	0.001 (HS)	0.001 (HS)	0.001 (HS)

Table 7: Hypotension and bradycardia among Groups A and B

Group	Hypotension *n* (%)		Bradycardia *n* (%)	
	Yes	No	Yes	No
Group A clonidine	22 (68.8)	10 (31.2)	20 (62.5)	12 (37.5)
Group B pregabalin	6 (18.8)	26 (81.2)	2 (6.2)	30 (93.8)
Total	28 (43.8)	36 (56.2)	22 (34.37)	42 (65.63)
Chi-square value	16.254		22.442	
P value	0.001 (HS)		0.001 (HS)	

Table 8: Sedation and dry mouth in perioperative period among Groups A and B

Group	Sedation *n* (%)		Dry mouth *n* (%)	
	Yes	No	Yes	No
Group A clonidine	18 (56.2)	14 (43.8)	6 (18.8)	26 (81.2)
Group B pregabalin	20 (62.5)	12 (37.5)	16 (50.0)	16 (50.0)
Total	38 (59.4)	26 (40.6)		
Chi-square value	0.259		6.926	
P value	0.611 (NS)		0.008 (S)	

The incidence of hypotension was observed in 25% subjects. The values for BP are high for Group B in comparison to Group A. The calculated P value in all the cases was 0.001 which is highly significant [Table 7].

On comparing the occurrence of bradycardia and hypotension, it was observed that the incidence of both is high in Group A than Group B. Among Group A, both the incidences are approximately same but in Group B, the incidence of bradycardia is more than hypotension [Table 8].

The remaining side effects with the equal incidence of 20% were sedation and dry mouth. The incidence of both the side effects is high in Group B with 20 (62.5%) subjects suffering sedation and 16 (50.0%) subjects having problem of dry mouth. It can also be observed that there is no significant difference in the number of subjects with sedation among both the groups [Figures 1-11].

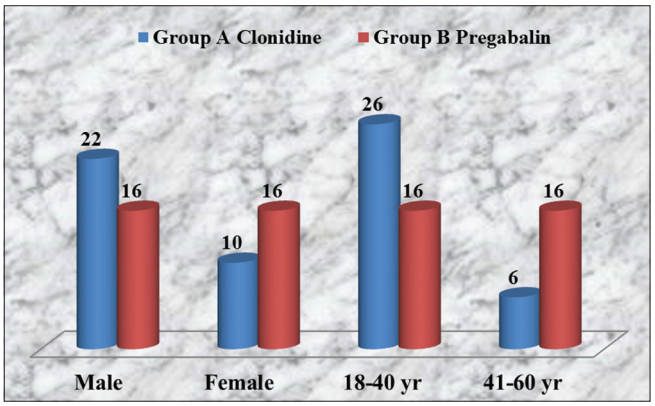

Figure 1: Demographic distribution of study subjects according to age and gender

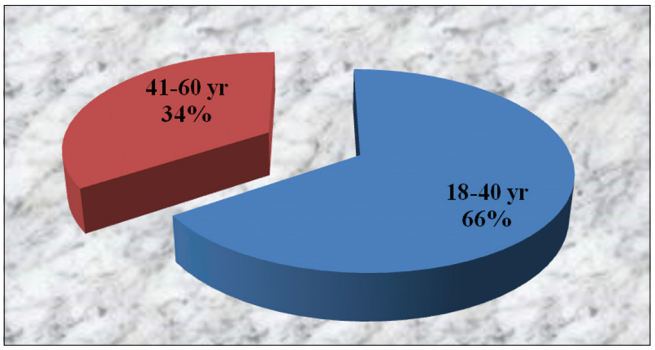

Figure 2: Demographic distribution of study subjects according to age

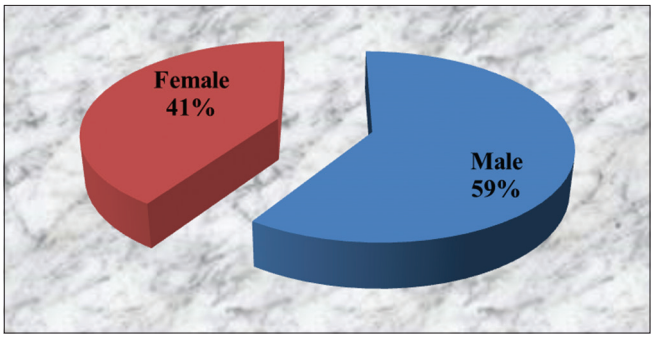

Figure 3: Demographic distribution of study subjects according to gender

DISCUSSION

Clonidine is an α_2 adrenergic agonist that produces dose-dependent analgesia at spinal and supraspinal sites. Oral clonidine is almost completely absorbed, and peak plasma concentration is reached after 1–3 h of administration. It is highly lipid soluble and crosses the blood–brain barrier

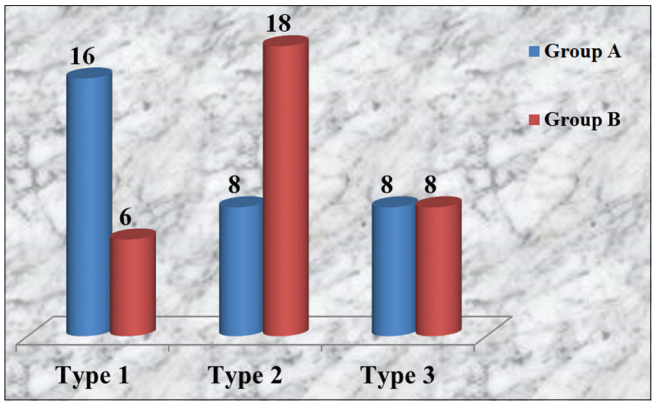

Figure 4: Distribution of study subjects according to type of surgery

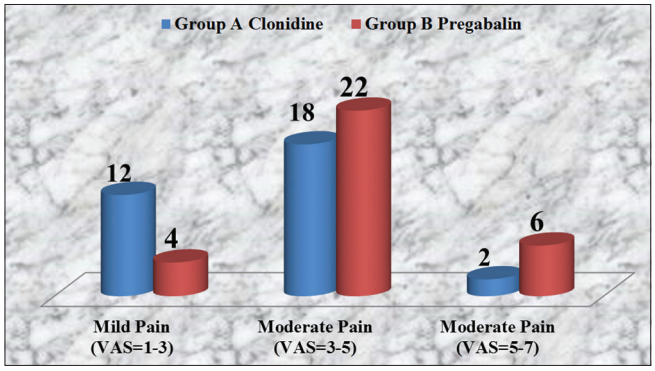

Figure 5: Distribution according to type of pain

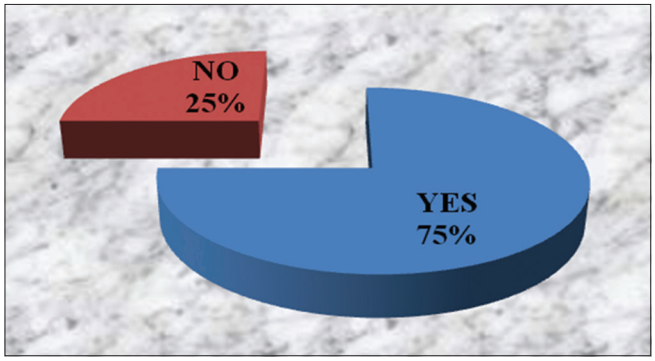

Figure 6: Analgesic requirement among Groups A and B

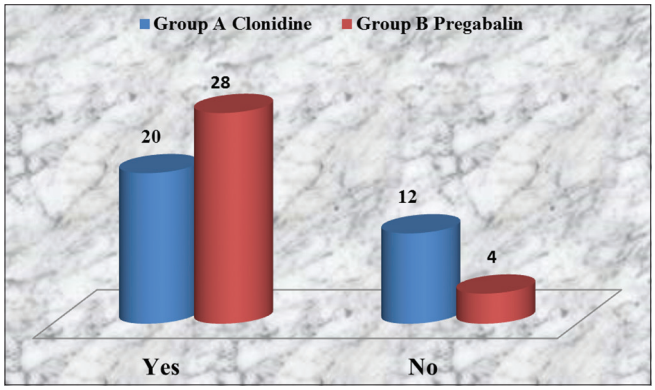

Figure 7: Analgesic requirement among Groups A and B

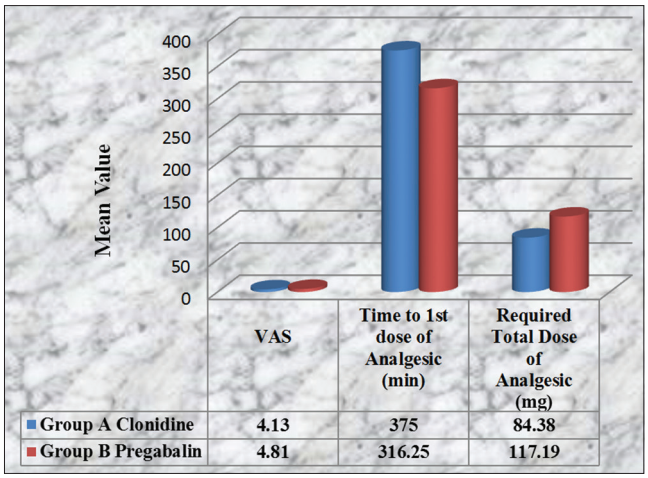

Figure 8: Mean visual analog scale, mean time to 1st dose of analgesic and mean required total dose of analgesic among Groups A and B

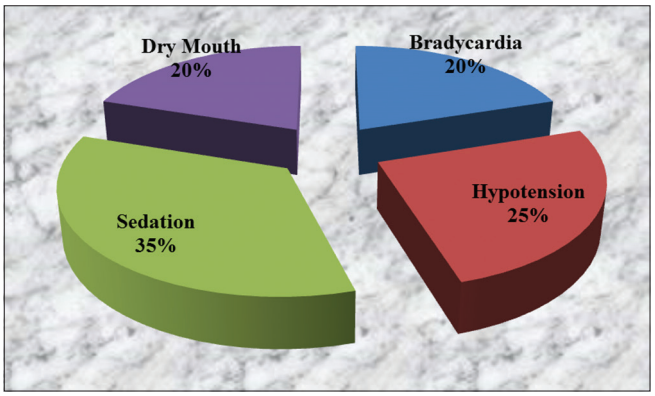

Figure 9: Incidence of side effects in peri-operative period

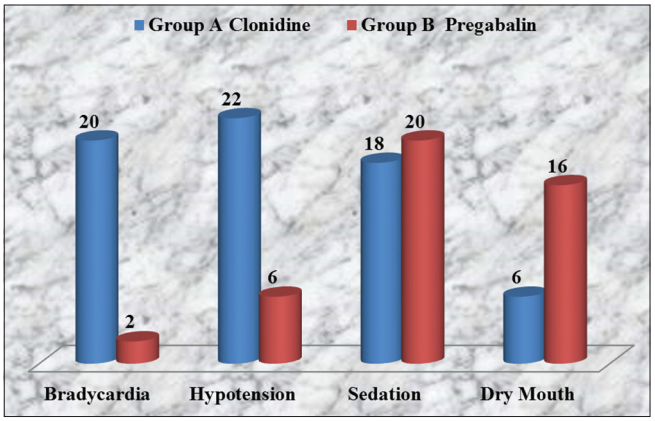

Figure 10: Side effects in perioperative period among Groups A and B

easily. It is an imidazoline derivative commonly used as antihypertensive, sedative, anxiolytic, and analgesic. Clonidine is licensed for the treatment of hypertension, migraine, and menopausal flushing.[12] Analgesic effect of clonidine is mediated by blocking nociceptive transmission through pre- and post-synaptic α_2 adrenergic receptors. It is

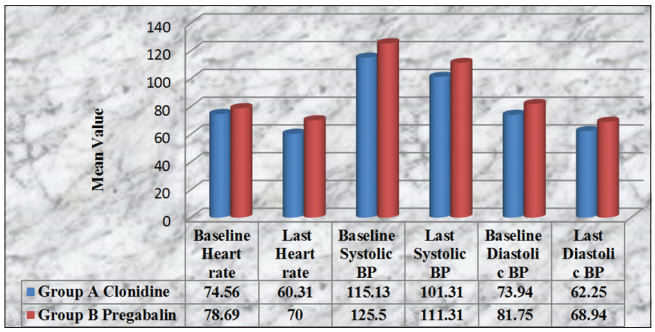

Figure 11: Mean systolic and diastolic blood pressure among Groups A and B

metabolized in the liver and excreted by kidneys. Clonidine used in the study was through the oral route with dose 0.2 mg (200 μg).

Pregabalin is a lipophilic GABA analog substituted at the 3'-position to facilitate diffusion across the blood–brain barrier. Pregabalin is used for partial seizures and as an anxiolytic. Pregabalin was shown to be effective in neuropathic pain, incisional injury, and inflammatory injury.[13] It modifies the synaptic and non-synaptic release of GABA by binding to α_2 δ subunit of pre-synaptic voltage-gated Ca++ channels. It is almost entirely excreted unchanged in urine. The oral dose used is 150–600 mg.

The rationale for the dose selection (150 mg for pregabalin and 0.2 mg for clonidine) is that it adequately sedates the patient and the hemodynamic stability is maintained. When individually concerned, pregabalin attenuates the pressor response to tracheal intubation in adults if given 1 h before surgery.[14] Clonidine at its low dose results in less bradycardia and hypotension during spinal anesthesia. A test dose of 150 mg of oral pregabalin was based on the studies where such a dose produced no acute hemodynamic alterations as well as sedation.[15]

In our study, 0.2 mg of oral clonidine and 150 mg of oral pregabalin were given 45 min before the commencement of surgery which prolonged the duration of analgesia. On pain of VAS >3, rescue analgesia (injection diclofenac 75 mg i.v. in 100 mL of normal saline) was given.

This study was a prospective study where total 64 subjects were divided into two groups, i.e., Group A where oral clonidine was used and Group B in which oral pregabalin was used in the subjects.

There was no significant difference found in the demographic distribution of study subjects according to age and gender. However, there was statistically significant result in analgesic requirement and side effects of the drug in the mentioned study groups.

Analgesic Effect of the Drug on Subjects in Both the Groups

In this study, as far as the analgesic effect of oral clonidine and pregabalin taken to an account, *P* value came out as 0.015 which is significant. In a study conducted by Bafna *et al.*[16] where oral pregabalin was used for post-operative analgesia in gynecological surgeries, the results came as significant with $P < 0.001$ hence, showing longer mean duration and effective analgesic property of both the drugs.

Additional Analgesic Requirement

In the study Group A, 48 (75.0%) required whereas 16 (25.0%) do not required any additional analgesia. In the study conducted by Kolarkar *et al.*, it was concluded that pregabalin proved to have a better analgesic effect, reducing the total consumption of post-operative analgesia as compared to the placebo group.[17] There was a meta-analysis evaluating the addition of α_2 agonist on post-operative pain following surgery by Blaudszun *et al.* This review concluded that perioperative clonidine use decreases the post-operative opioid consumption, pain intensity, and nausea without prolonging the recovery times.[18] In our study, the requirement of post-operative analgesia is slightly more in pregabalin group which may explain as it was used in low dose and its better effect on mild pain as compared to moderate or severe pain on VAS.

Drugs Side Effects

On observing both drug groups, the study came out with the result that side effects such as sedation found in (35%) followed by hypotension (25%) and dry mouth, and bradycardia (20%) each with maximum subjects included in the Group A, i.e., in clonidine group. In Group A (clonidine), bradycardia and hypotension were observed in the majority of subjects while side effects such as sedation and dry mouth in Group B (pregabalin) subjects. Common side effects of both the drugs include dizziness and dry mouth. Sedation and bradycardia are usually more seen with clonidine while somnolence and disturbed vision is with pregabalin. Gupta *et al.*[14] studied the side effects of oral pregabalin and oral clonidine where she concluded that there is an increased incidence of intra- and post-operative bradycardia with oral clonidine. However, clonidine is still considered superior to pregabalin for attenuation of hemodynamic responses. Prasad *et al.* concluded in her study that oral pregabalin 150 mg prolong the post-operative pain relief after spinal anesthesia but produces less sedation as compared with oral clonidine.[15]

Hemodynamic Response of the Drug

As far as blood pressure was concerned, clonidine group showed 22 cases of hypotension and pregabalin with 6 cases which proved that oral clonidine causes more decrease in blood pressure as compared to oral pregabalin. In the study conducted by Gupta *et al.* where 150 mg of

oral pregabalin and 0.2 mg of oral clonidine were used, it concluded that clonidine was superior to pregabalin for attenuation of the hemodynamic responses to surgery, without prolongation of recovery times and side effects.

Thus, overall; oral clonidine and oral pregabalin prolong the time period for the first dose of analgesic requirement, in lower abdominal surgeries conducted under the subarachnoid block.

CONCLUSION

This study was a hospital-based, cross-sectional, and observational (comparative) study. 64 subjects of ASA physical status 1 and 2, between the age of 18 and 60 **year**s were divided into two groups of 32 subjects each. Group A (clonidine) received tab. Clonidine 200 μg and Group B (pregabalin) received cap. Pregabalin 150 mg orally, with a sip of water, approximately 45 min before the surgery (after recording the baseline vitals). Time for the first dose of analgesia and total analgesic requirement in the 24 h was recorded, and hemodynamic stability and side effects of the drugs were also observed.

Both groups were comparable with respect to the demographic distribution of age and gender. Type and duration of surgery, type of pain (based on VAS), analgesic requirement, and adverse effects of the drugs were also comparable.

On the basis of age, the subjects recruited in our study were of age between 18 and 60 years. The mean age of total, Group A and B subjects came out to be 38.0, 34.25, and 41.75 years, respectively, which is highly significant for age in two study groups. There was no statistical significance of gender in both the study groups.

Mean duration of surgery in the two study groups was slightly prolonged in Group B (approximately 4 min) but not statistically significant.

Out of total 64 subjects, rescue analgesia was required in 48 subjects. The cumulative analgesic requirement was statistically significantly less for Group A (20 subjects) than Group B (28 subjects). The requirement of analgesia was high in G**rou**p B as major portion of the population required analgesia leaving just 4 subjects in which no analgesia was given, which is highly significant.

The pain intensity was assessed using a 10-cm VAS. The statistical data suggest that pain felt by subjects of Group A was of lower intensity as compared to that of Group B and total requirement of analgesia was more in the latter.

The side effects such as bradycardia, hypotension, sedation, and dry mouth were observed in the perioperative period. It is clear that the overall incidence of sedation is highest, followed by hypotension, whereas the incidence of bradycardia and dry mouth is least. It can be seen that the incidence of side effects is more in Group A as compared to Group B. The incidence of hypotension was highest in Group A, followed by bradycardia, sedation, and incidence of dry mouth was least in Group A. On the other hand, incidence of bradycardia was least, followed by hypotension, dry mouth, and sedation. The incidence of sedation was highest in Group B.

To conclude, both drugs lowered the analgesic requirement in the perioperative period in lower abdominal surgeries conducted under the subarachnoid block, oral pregabalin providing better hemodynamic stability with lesser side effects but with more sedation.

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How to cite this article: Kachhwah V, Rahal S, Narang N. A Prospective, Double Blind, Randomized Study to Compare the Analgesic Effect of Oral Clonidine and Oral Pregabalin for Perioperative Pain in Lower Abdominal Surgeries. Int J Sci Stud 2018;6(6):81-90.

Source of Support: Nil, **Conflict of Interest:** None declared.