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Original Research Article

Efficacy of pregabalin premedication prior to surgery in attenuating the adverse hemodynamic response to laryngoscopy and tracheal intubation

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ABSTRACT

Background: In general pregabalin is used in patients with normal blood pressure undergoing operation for controlling the response of the pressor in nature. There are few studies which have been carried out to study efficacy of pregabalin in controlling responses to instrumentation of the airway in patients with controlled hypertension. Objective was to study efficacy of pregabalin premedication 90min prior to surgery in attenuating the adverse hemodynamic response to laryngoscopy and tracheal intubation.
Methods: Hospital based randomized comparative trial was conducted. 100 patients of ASA I and II physical status aged 18-60 yrs scheduled to undergo elective surgery like orthopaedic, spine, otorhinolaryngeal, gynaecological and general surgical procedures. Patients were randomly divided into 2 groups of 50 each. Randomization was done by computer generated table. Group "P" received- 150mg pregabalin. Group "C" received-200µg clonidine.
Results: The patients in clonidine group documented the heart rate as more compared to the patients in the pregabalin group at various time intervals. The patients in clonidine group documented the mean systolic blood pressure as more compared to the patients in the pregabalin group at various time intervals. The patients in clonidine group documented the mean diastolic blood pressure as more compared to the patients in the pregabalin group at various time intervals.
Conclusions: We concluded that use of pregabalin is more effective in comparison to use of clonidine in terms of controlling the hemodynamic parameters. But it has been found that bradycardia may not be properly attenuated with the use of pregabalin.

Keywords: Clonidine, Efficacy, Pregabalin, Premedication, Surgery

INTRODUCTION

Airway instrumentation which includes direct laryngoscopy and tracheal intubation form an integral part of an anaesthesiologist armament in anaesthetic care. General anesthesia is associated with depression of airway, respiratory, and cardiovascular functions.[1]

After intubation many patients may not show adverse effects. But in some normal patients and all patients with pre-existing disease condition, it may show adverse effects. There is increase in the heart rate for short time. There is increase in blood pressure for short time. But this can be dangerous for patients with pre-existing disease conditions. These patients can develop complications.[2]

The catecholamines in the plasma increase as a response to intubation and laryngoscopy. This leads to the ischemia of the myocardium and can also result in the bleeding in the brain especially in patients who are susceptible to such incidents.[3]

There are many drugs available to overcome the above mentioned problem related to the intubation and laryngoscopy. But not a single drug can be considered as 100% ideal or effective.[4]

What is ideal anesthetic agent? It should have been tolerated by the patient after absorption. It should have less adverse effects. There should be minimum drug interactions, easily eliminated out of the body. It should not be a narcotic agent. It should be easy to give to the patients.[5]

Clonidine and pregabalin are such two drugs which are closer to be ideal. Clonidine is an alpha 2 adrenergic agonist. Initially it was used for controlling high blood pressure. It can be used as for analgesia. It reduces pain in the patients. Pregabalin is a Gabapentinoid compound. It reduces anxiety. It can act as an analgesic.[6]

The present study was being done to study efficacy of Pregabalin premedication 90min prior to surgery in attenuating the adverse hemodynamic response to laryngoscopy and tracheal intubation.

METHODS

This was a hospital based randomized comparative trial study. Hospital ethics committee clearance was obtained for this study. Informed consent was taken from all the patients. Patients who denied participation in study were treated by routine protocol of anesthesia with dignity. This study was conducted at care hospital, Banjara Hills, Hyderabad, India.

All the patients of ASA I and II physical status aged 18-60 yrs scheduled to undergo elective surgery like orthopaedic, spine, otorhinolaryngeal, gynaecological and general surgical procedures.

This study has been conducted over a time frame of one year (01/05/2016 to 31/05/ 2017). The sample size was calculated based on the previous studies, and using the formula as below:

$n = 2\sigma 2\ (Z\beta + Z\alpha/2)^2\ (\text{Difference})^2$

Where,

- n = Sample size in each group (assumes equal sized groups),
- σ = Standard deviation of the outcome,
- Zβ = Represents desired power,
- Zα/2 = Represents the desired level of statistical significance (typically 1.96),
- Difference = effect size (the difference in means).

Inclusion criteria

- ASA Grade 1 and 2 aged 18-60 years,
- Patients willing for the study.

Exclusion criteria

- Patients with hypertension, diabetes mellitus, coronary artery disease,
- Renal, hepatic or cerebral insufficiency,
- Asthma,
- Allergy to pregabalin or clonidine,
- Patients with coagulopathies or receiving drugs influencing blood coagulation,
- Anticipated difficult intubation,
- Morbid obesity and history of taking antihypertensive, beta blockers, antidepressants, anxiolytic, anticonvulsants and antipsychotics.

Methodology

After obtaining informed written consent, patients were randomly divided into 2 groups of 50 each. Randomization was done by computer generated table.

- Group "P" received- 150mg Pregabalin.
- Group "C" received -200µg Clonidine.

Data Collection

Data was collected by using pre-designed and pre-tested questionnaire. All study subjects were assessed through pre-anesthetic check-up a day prior to surgery. The procedure of general anaesthesia and study protocol was explained to the patient. A written consent was obtained for participation in this study after explaining study protocol and risk and benefits of experiment to the all the participants. Preparation included overnight fasting. Pre-anesthesia check-up and preparation protocol was followed. On the day of surgery, systolic and diastolic blood pressures and heart rate were measured before premedication. Socio-demographic Information like name, age, sex, residence, other information like type of surgery and vitals were recorded after obtaining consent. The drug either pregabalin or clonidine was given to the patient by ward nurse with sips of water 90min prior to surgery. Pulse rate, systolic blood pressure, and diastolic blood pressure mean arterial pressure and rate pressure product which is a product of heart rate and systolic blood pressure were recorded at baseline and post induction at 1, 3, 5 and 10min.

Statistical analysis

Student t-test (two tailed, independent) was used to find the difference in means of the two groups. P value if found less than 0.05 as usual was taken as a mark of statistical significance.

RESULTS

Table 1 shows comparison of baseline characteristics between the two groups. Mean age of oral pregabalin and oral clonidine groups is statistically insignificant with a p-value of 0.609. There is no significant difference in the

sex distribution of the patients between the groups (P>0.05). There is no significant difference in the weight distribution of oral pregabalin and oral clonidine groups. P-value of weight distribution is >0.05.

Table 1: Comparison of baseline characteristics between the two groups.

Baseline characteristics		Group P	Group C	P value
Age (years)		31.66±10.6	30.58±10.42	0.609
Weight (kg)		57.4±6.09	56.94±6.8	0.789
Sex	Male	36%	60%	0.0901
	Female	64%	40%	

Pregabalin group showed a mean baseline heart rate and standard deviation of 82.52±6.30. At 1 minute, 3 minute, 5 minute and 10 minute interval the increase in mean heart rate were 92.06±6.32, 88.88±6.83, 82.06±5.47 and 77.58±4.99 respectively. Clonidine group showed a mean baseline heart rate and standard deviation of 79.54±6.34. At 1 minute, 3 minute, 5 minute and 10 minute interval the mean heart rate were 87.78±6.04, 86.68±6.53, 79.20±6.49 and 76.46±5.94 respectively. At baseline, 1 min, 3 min and 5 mins, heart rate response to laryngoscopy and intubation in the clonidine group is clinically lesser than Pregabalin group and statistically significant (p<0.05). Values were insignificant at 10 minutes (p>0.05). Clonidine better attenuates tachycardia response (Table 2).

Table 2: Heart rate at different recording interval.

Heart rate (bpm)	Group P	Group C	P value
Baseline	82.52±6.30	79.54±6.34	0.020
1 minute	92.06±6.32	87.78±6.04	0.001
3 minutes	88.88±6.83	86.68±6.53	0.004
5 minutes	82.06±5.47	79.20±6.49	0.019
10 minutes	77.58±4.99	76.46±5.94	0.310

Table 3: Systolic blood pressure at different recording intervals.

SBP (mm Hg)	Group P	Group C	P value
Baseline	128.76±11.40	126.04±8.55	0.180
1 minute	136.02±10.01	134.64±8.12	0.451
3 minutes	127.08±8.78	134.76±7.07	0.000
5 minutes	120.16±8.16	130.88±9.01	0.000
10 minutes	118.76±8.06	127.48±9.15	0.000

The preoperative systolic blood pressure in the Pregabalin group has mean and SD of 128.76±11.40 at baseline. The preoperative SBP in the clonidine group has a baseline mean and SD of126.04±8.55, and then a rise in SBP with a mean of 134.64±8.12 at 1 min after intubation. It remained the same at 3 min to134.64±7.07 and then just a marginal decrease to 130.88±9.01 at 5 minutes and 127.48±9.15 at 10 minutes. The mean systolic blood pressure at 3 minutes, 5 minutes and 10 minutes time interval is clinically and statistically lesser in Pregabalin group than in the clonidine group and the p value was <0.05 and is statistically significant indicating pregabalin group attenuates the systolic blood pressure response to laryngoscopy and intubation better when compared to clonidine group (Table 3).

The preoperative diastolic blood pressure in the Pregabalin group has at baseline mean and SD of 80.160±7.01. At 1 minute after intubation there is an increase in the DBP, with a mean of 87.84±7.68.At 3 minutes the DBP slightly decreased to a mean of 81.58±8.22. Then at 5 minutes further decrease in DBP with mean of 74.68±6.54.At 10 minutes there is slight decrease in DBP than the 5th minute with a mean of 71.20±6.56. The mean diastolic blood pressure at 1 minute, 3 minute, 5 minute and 10 minute time interval is clinically and statistically decreased in pregabalin group than in the clonidine group. p value was <0.001 at 1 minute,3 minute 5 minute and 10 minute intervals and is statistically significant indicating pregabalin group attenuates the diastolic blood pressure response to laryngoscopy and intubation better compared to the clonidine group (Table 4).

Table 4: Diastolic blood pressure at different intervals.

DBP (mmHg)	Group P	Group C	P value
Baseline	80.160±7.01	81.6±6.31	0.283
1 minute	81.38±5.88	87.84±7.68	<0.001
3 minutes	74.32±6.31	81.58±8.22	<0.001
5 minutes	68.36±6.69	74.68±6.54	<0.001
10 minutes	64.62±6.90	71.20±6.56	<0.001

Table 5: Mean arterial pressure at different recording intervals.

MAP (mmHg)	Group P	Group C	P value
Baseline	96.34±6.39	96.4±4.66	0.90
1 minute	99.60±5.37	103.36±5.68	<0.001
3 minutes	91.94±5.53	99.36±5.80	<0.001
5 minutes	85.60±5.7	93.46±4.80	<0.001
10 minutes	82.68±5.85	89.92±4.28	<0.001

The preoperative mean arterial pressure in the pregabalin group has at baseline mean and SD of 96.34±6.39. After 1 minute after intubation the MAP increased to a mean of 103.36±5.56. Then after 3 minutes after intubation the MAP remained higher than the baseline with a mean of 99.36±5.80. At 5 minutes the MAP decreased slightly than the baseline with a mean of 93.46±4.80. There was a further decrease in the MAP at 10 minutes with a mean of 89.92±4.28. The mean blood pressure at 1 minute, 3 minute, 5 minute and 10 minute time interval is clinically

lesser in pregabalin group than in the clonidine group. At all time intervals P<0.05 hence it is significant. The fall to baseline value in the pregabalin group was at 3rd minute and in clonidine group at 10th minute and statistically it was significant (P<0.05) indicating pregabalin group showed earlier recovery to baseline values compared to clonidine group (Table 5).

The preoperative rate pressure product in the pregabalin group has at baseline mean and SD of 1026.44±1276. After 1 minute after intubation the RPP increased to a mean of11817±1061. Then after 3 minutes after intubation the RPP remained higher than the baseline with a mean of11673±978. At 5 minutes the RPP remained higher than the baseline with a mean of 10385±994. There was a slight decrease in the RPP at 10 minutes with a mean of 9737.16±992. The difference rate pressure product at 3 minute intervals are insignificant. At 1, 5, 10th minute rate pressure product of pregabalin is significantly less compared to clonidine (p<0.05). The fall to baseline value in the pregabalin group was at 5th minute and in clonidine group at 10th minute and statistically it was significant (P<0.05) indicating Pregabalin group showed earlier recovery to baseline values compared to clonidine group (Table 6).

Table 6: Rate pressure product at different recording intervals.

RPP (bpm *mmHg)	Group P	Group C	P value
Baseline	10626.44±1276	10024.98±1041	0.011
1 minute	12520.84±1265	11817.62±1061	0.003
3minutes	11292±1151	11673.52±978	0.077
5minutes	9862.78±969	10355.72±994	0.014
10minutes	9214.82±881	9737.16±922	0.005

Table 7: preoperative sedation scores.

Sedation score	Group C		Group P	
	No.	%	No.	%
Score 0	-	-	-	-
Score 1	25	50.0	3	6
Score 2	22	44	15	30
Score 3	3	6	32	64
Total	50	100.0	50	100.0
Mean±SD	1.56±0.611		2.58±0.609	

In pregabalin group 64% of the patients had a sedation score of 3 followed by 30.0% with sedation score of 2 and rest 6% had a score of 1. In clonidine group 50%of the patients had a sedation score of 1 followed by 44% with sedation score of 2 and rest 6% had a score of 3.

The mean sedation scores were found to be clinically and statistically more in pregabalin group than clonidine group with p value<0.001. There were no perioperative side effects like dizziness, bradycardia or hypotension in both the groups (Table 7).

DISCUSSION

In our study heart rate response was better controlled in the clonidine group than pregabalin group and was statistically significant (p=0.001 at 1 minute and P<0.01 at 5 minutes). Our study correlates with the study done by Raichurkar et al who showed that clonidine better reduced the heart rate than pregabalin.[7] Similar study was done by Chakraborthy R et al, and Chaudhary A et al, where both the groups did a study between pregabalin and clonidine and inferred that pregabalin reduced the blood pressure but did not reduce the heart rate and clonidine reduced the heart rate effectively.[8,9]

In our study Pregabalin group had a decrease in the SBP and DBP and the p value was significant <0.001. In our study, pregabalin better attenuated the SBP and DBP at serial intervals soon after intubation when compared to the clonidine group. These findings correlates well with the study done by Raichurkar A et al, where they compared pregabalin with clonidine and came to an inference that pregabalin was better in attenuating the systolic blood pressure and diastolic blood pressure.[7] Our findings were similar to the studies done by Sunder et al, where they conducted a study between pregabalin and clonidine on OPCAB surgeries and conferred that pregabalin attenuated the stress response to instrumentation.[10]

In our study there was a significant difference in the mean arterial pressure with pregabalin group than for clonidine group. At 10th min and (p=<0.001) MAP increased at intubation and then, decreased significantly in the pregabalin group. Thus, pregabalin better attenuated the MAP than clonidine. These findings were correlating well with the study done by Raichurkar et al and Gupta K et al where they inferred that mean arterial pressure was better attenuated with pregabalin.[7,11]

Rate pressure product (RPP) is an indirect measure of myocardial oxygen consumption (MVO2). Myocardial oxygen consumption is correlated with the rate-pressure product (heart rate x systolic blood pressure) and this hemodynamic parameter has been shown to follow a circadian pattern similar to that observed with cardiovascular events.

In our study attenuation of maximum rise in the rate pressure product by pregabalin is evident and statistically highly significant when compared with clonidine group (p<0.001). This correlates with the study done by Raichurkar et al and Gupta K et al where they concluded in their study that rate pressure product was significantly reduced in the pregabalin group than the clonidine group.[7,10]

Sedation scores which was measured using four point scale described by Chernik DA et al showed the mean sedation scores to be clinically and statistically significant more in Pregabalin group than clonidine group

with p value <0.001.[12] This correlates with the studies done by Gupta K et al.[13]

CONCLUSION

The patients in clonidine group documented the mean diastolic blood pressure as more compared to the patients in the pregabalin group at various time intervals. We conclude that use of pregabalin is more effective in comparison to use of clonidine in terms of controlling the hemodynamic parameters. But it has been found that bradycardia may not be properly attenuated with the use of pregabalin.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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