ORIGINAL ARTICLE

Effect of Oral Clonidine and Oral Gabapentine as Premedication on Hemodynamic Stress Responses during Laryngoscopy and Tracheal Intubation and Duration of Post Operative Analgesia

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ABSTRACT

Introduction: Direct laryngoscopy and passage of endotracheal tube are noxious stimuli that can provoke stress response in cardiovascular, respiratory and other physiological systems. This study was planned to evaluate the effect of oral Gabapentin and oral clonidine on laryngoscopic stress response and postoperative pain relief.

Methods: 90 patients between the age group 18 to 60 years belonging to ASA class I and II scheduled for lower abdominal surgeries were devided into three groups. Each patient was given 0.2mg inj. Glycopyrolate i.m and oral tab. Clonidine 0.2mg (group C) or oral tab. Gabapentine 900mg (group G) or oral tab. vitamine C (group P) 30 min before surgery.

Results: Oral Clonidine (0.2 mg) when given in premedication provided better attenuation of hemodynamic stress response to laryngoscopy and tracheal intubation compared to oral Gabapentine (900 mg), where hypertensive response was fairly obtunded, but not the tachycardiac response.

Conclusion: Oral Clonidine has better response over tachycardia than Gabapentine, whereas Gabapentine is superior to clonidine for post-operative analgesia.

Key words: Clonidine, Gabapentine, Laryngoscopy, VAS (visual analogue score)

INTRODUCTION

Anesthesiologists have been trying a variety of drugs from their armamentarium to suppress notorious "pressor response." Drugs which can be used to control this hemodynamic response include α2-agonists, vasodilators, beta blockers, calcium channel blockers, lignocaine, and opioids.

Pain is defined as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[3]

Clonidine is a α2 -adrenergic agonist which decreases central sympathetic outflow and reduces blood pressure by an effect on both cardiac output and peripheral resistance. It tends to attenuate stress response to direct laryngoscopy.

Gabapentin is an antiepileptic drug that has demonstrated analgesic effects in diabetic neuropathy, post herpetic neuralgia and neuropathic pain, affects the nociceptive process by binding to the subunit of voltage dependant calcium channels and reduces excitatory neurotransmitter release in pain pathways, suggests it may have a role in prevention of post-operative allodynia[1].

MATERIAL AND METHODS

The present study was conducted in 90 patients between the age group 18 to 60 years belonging to ASA physical status class I and II scheduled for lower abdominal surgeries at our institute, after approval from the institutional ethical committee of our institute.

Pre-anesthetic evaluation was done by meticulous history taking regarding any present or past major medical illness, past history of any surgical procedure or drug reaction. A detailed general as well as systemic examination was done. The patients were explained about the nature and purpose of the study during preoperative period and informed written consent taken.

Inclusion Criteria

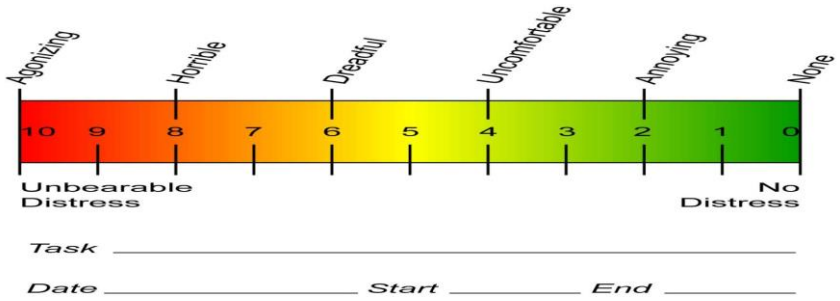
Patients with physical status ASA grade I & II; either sex; aged between 18 to 60 years of age underwent General anaesthesia for any for elective orthopedic or general surgical or gynecological procedures under general anesthesia were included in the study.
All patients were thoroughly examined in pre-anaesthetic clinic and routine investigations were done.

Exclusion criteria: Patients refuse to participate; having history of allergic reaction to any drug used in the study; patient with communication difficulties or not NBM for 6 to 8 Hours before surgery were excluded from the study.

In each group 30 patients were allocated. Baseline monitoring like temperature, heart rate, blood pressure, respiratory rate, spo2 were recorded in recovery room.

All patients were explained about the Visual Analogue Scale (VAS; 0 = no pain and 10=worst pain) for assessing the intensity of pain during postoperative pain interview.

Visual Analogue Scale



Patients were divided into three groups and Premedication was given accordingly-

Group C: Tablet Clonidine 0.2mg orally half hour before surgery & injection Glycopyrrolate 0.2 mg intramuscularly 30 minutes before surgery.

Group G: Tablet Gabapentine 900mg orally half hour before surgery & injection Glycopyrrolate 0.2 mg intramuscularly 30 minutes before surgery.

Group P: Tablet Vitamin C orally one half hour before surgery & injection Glycopyrrolate 0.2 mg intramuscularly 30 minutes before surgery

General anaesthesia was given with Injection Thiopental sodium 4-6 mg/kg iv, injection Succinylcholine 2 mg/kg iv and Maintain on 0_2 +N_20+Isoflurane +Injection Atracurium. Stress response was observed by measurement of systolic and diastolic and mean blood pressure and heart rate before induction and after induction at 1, 2, 3, 4, 5 min interval**.** Postoperative monitoring for heart rate, systolic blood pressure, Diastolic blood pressure, Mean arterial pressure.

Rescue analgesia was given with inj. Diclofenac Sodium 75 mg intravenously when VAS score > 3.Time for rescue analgesia and total dose of analgesic requirement were observed. Patients were monitored and assessed for any postoperative side effects like nausea, vomiting, vertigo, headache, visual disturbances(diplopia, nystagmus), sedation RSS>5.

The results were expressed as mean ± SD. Statistical analysis consisted of ANOVA test with p value less than 0.05 was considered as significant and p value less than 0.01 was considered as highly significant. P value greater than 0.05 was considered as non-significant.

Ramsey Sedation Score

SCORE	DISCRIPTION
0	awake, oriented
1	agitated, anxious
2	awake, co-operative
3	sleeping but co-operative
4	deep sedation, quick reaction to painful stimuli
5	deep sedation, slow reaction to painful stimuli
6	deep sedation, no reaction to painful stimuli

RESULT

There was no statistically significant difference between the three groups in terms of age, weight, gender and duration of surgery.

Heart Rate (Table 1)

In control group baseline heart rate remained high compared to clonidine and gabapentine group ($p<0.05$). Heart rate increased from baseline value during laryngoscopy and tracheal intubation, ($p<0.001$).Similar finding were observed at 1, 2, 3, 4 minutes after intubation ($p<0.001$). At 5 minutes after intubation heart rate remained high compared to baseline value. (table 1)

Systolic, Diastolic And Mean Arterial Pressure (Tables 2,3 and 4)

At pre oxygenation, all groups were comparable for systolic blood pressure ($p>0.05$). Significant decrease in diastolic and mean arterial pressure was observed in clonidine and gabapentine group ($p<0.05$) compared to control group, in which it remained comparable to baseline ($p>0.05$).

Immediately after laryngoscopy and intubation, increase in systolic, diastolic and mean arterial pressure from baseline value in all groups was observed(p<0.001) At 1 minute after intubation, maximum increase in systolic, diastolic and mean arterial pressure from baseline value were seen in all groups(p<0.001). At 2 minute after intubation, increase in systolic, diastolic and mean arterial pressure from baseline value were seen in all group (p<0.001).

Table 1: Heart Rate (Rate/Minute)

	Group C Mean ± SD	Group G Mean ± SD	Group P Mean ± SD	P Value
pre-operative(Baseline)	77.53 ± 6.98	79.80 ± 5.21	82.07 ± 6.02	<0.05
pre-oxygenation	83.87 ± 3.23	81.93 ± 4.35	85.07 ± 4.86	<0.001
immediate after intubation	90.33 ± 5.09	103.93 ± 6.09	111.07 ± 6.72	<0.001
1 min after intubation	97.73 ± 4.92	113.33 ± 7.07	141.80 ± 8.11	<0.001
2 min after intubation	89.67 ± 3.07	105.53 ± 5.93	130.40 ± 6.88	<0.001
3 min after intubation	88.00 ± 3.82	101.33 ± 4.21	121.87 ±7.12	<0.001
4 min after intubation	86.53 ± 4.30	99.07 ±2.91	114.67 ± 7.73	<0.001
5 min after intubation	85.00 ± 3.85	96.53 ± 3.01	108.60 ± 7.11	<0.001

Table 2: Systolic Blood Pressure (Mm Of Hg)

	Group C Mean ± SD	Group G Mean ± SD	Group P Mean ± SD	P Value
pre-operative(Baseline)	122.33 ± 8.64	124.60 ± 9.64	126.27 ± 7.48	>0.05
pre-oxygenation	122.07 ± 10.76	123.53 ± 10.39	127.20 ± 7.35	>0.05
immediate after intubation	134.87 ± 8.85	138.40 ± 8.01	144.33 ± 6.97	<0.001
1 min after intubation	151.53 ± 9.11	155.47 ± 7.01	164.73 ± 6.67	<0.001
2 min after intubation	144.67 ± 7.90	147.13 ± 9.54	157.47 ± 6.26	<0.001
3 min after intubation	140.87 ± 7.62	142.53 ± 8.93	151.87 ± 7.14	<0.001
4 min after intubation	137.53 ± 7.02	137.47 ± 7.70	145.33 ± 7.53	<0.001
5 min after intubation	133.73 ± 6.43	132.73 ± 8.49	140.13 ± 8.53	<0.001

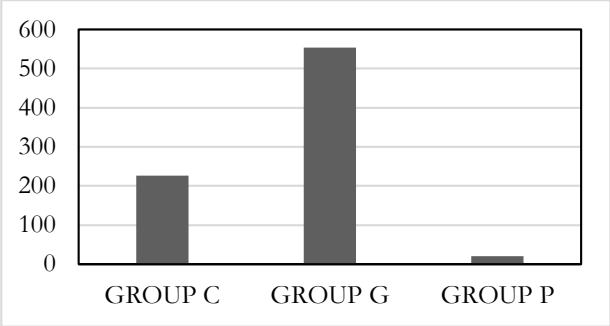
Table 3: Diastolic Blood Pressure (Mm Of Hg)

	Group C Mean ± SD	Group G Mean ± SD	Group P Mean ± SD	P Value
pre-operative	82.47 ± 3.81	82.53 ± 5.04	82.47 ± 2.27	>0.05
pre-oxygenation	74.53 ± 3.86	76.00 ± 4.00	82.87 ± 3.85	<0.001
Immediate after intubation	79.60 ± 4.05	79.73 ± 3.85	85.73 ± 3.67	<0.001
1 min after intubation	86.07 ± 3.73	87.27 ± 3.91	92.80 ± 4.16	<0.001
2 min after intubation	83.80 ± 3.61	84.73 ± 3.26	90.87 ± 4.06	<0.001
3 min after intubation	81.93 ± 3.34	82.87 ± 2.86	88.40 ± 3.94	<0.001
4 min after intubation	78.20 ± 3.80	80.67 ± 3.17	86.20 ± 3.98	<0.001
5 min after intubation	75.67 ± 3.72	77.27 ± 3.38	83.20 ± 3.59	<0.001

Table 4: Mean Arterial Pressure (Mm Of Hg)

	Group C Mean ± SD	Group G Mean ± SD	Group P Mean ± SD	P Value
pre-operative	95.76 ± 4.01	96.56 ± 6.09	97.07 ± 2.83	>0.05
pre-oxygenation	90.38 ± 3.99	91.84 ± 4.19	97.64 ± 3.43	<0.001
Immediate after intubation	98.02 ± 3.76	99.29 ± 3.65	105.27 ± 3.53	<0.001
1 min after intubation	107.89 ± 4.00	110.00 ± 3.22	116.78 ± 4.06	<0.001
2 min after intubation	104.09 ± 3.34	105.53 ± 3.86	113.07 ± 3.61	<0.001
3 min after intubation	101.58 ± 3.63	102.76 ± 3.49	109.56 ± 3.91	<0.001
4 min after intubation	97.98 ± 3.33	99.60 ± 3.09	105.91 ± 4.03	<0.001
5 min after intubation	95.02 ±3.28	95.76 ± 3.69	102.18 ± 4.09	<0.001

Chart 1: Time of 1st Rescue Analgesia



At 3 and 4minutes after intubation, Increase in systolic and mean arterial pressure from baseline in all three group ($p<0.001$). In group C and G diastolic blood pressure returns toward baseline values Whereas in group P diastolic blood pressure increased from baseline($p<0.001$).

At 5 minutes after intubation, increase in systolic blood pressure from baseline value were seen in all group ($p<0.001$). In group C and G diastolic blood pressure returns toward baseline values Whereas in group P diastolic blood pressure increased from baseline($p<0.001$).In clonidine and gabapentine group, mean arterial pressure returned back to baseline value ($p>0.05$) compared to control group, in which it still remained higher than baseline ($p<0.001$).

Time of 1st Rescue Analgesia (Chart 1)

Rescue analgesia was required at 225.6 ± 8.63min in group C, 554.06 ± 26.84min in group G and 20.66 ± 5.76min in group P($P <0.001$). Number of analgesic supplements required in group C was 2.13 ± 0.35 times, 1.07 ± 0.25 times in group G and 3.07 ± 0.25 times in group P, thus requirement of total analgesic was more in control group P (225 mg) compared to group C (150 mg) and group G (75 mg) and the difference among three groups was statistically highly significant ($P <0.001$).

Table 5: Adverse Effects

Adverse effect	No. of Patients		
	Gr C	Gr G	Gr P
Nausea/vomiting	3	2	0
vertigo/headache	0	0	0
visual disturbance*	0	0	0
sedation RSS >5	0	0	0

*diplopia, nystagmus

Total doses of analgesic supplements was significantly less in both Clonidine (2.13 ± 0.35) and Gabapentine (1.07 ± 0.25) groups compared to control group (3.07 ± 0.25) ($P <0.001$). Thus total doses of analgesic supplements was less with Gabapentine group compared to Clonidine group ($P<0.05$).

DISCUSSION

Gabapentin, a structural analogue of gamma-amino butyric acid, has been shown to have multi-modal effects which make it a potentially useful drug for premedication in adults, providing postoperative analgesia and preoperative anxiolysis while preventing chronic postsurgical pain, Clonidine has known sedative, analgesic, and anxiolytic properties. Its central sympatholytic action, it tends to attenuate the hemodynamic response to any surgical nociceptive stimulus and to improve overall perianesthetic cardiovascular stability.

In our study, it was observed that, in control group baseline heart rate remained high compared to clonidine and gabapentine group ($p<0.05$) during laryngoscopy and tracheal intubation and at 1, 2, 3, 4 and 5 minutes after intubation (Table 1).

In Gabapentine group, baseline heart rate remained on lower side compared to control group, ($p<0.05$). But during laryngoscopy and tracheal intubation heart rate increased from baseline value, which was statistically highly significant ($p<0.001$). Similar findings were observed at 1, 2, 3, 4 minutes after intubation. At 5 minutes after intubation heart rate remained increased compared to baseline. But increase in heart rate remains lower in comparison to control group and higher in comparison to clonidine group ($p<0.001$) (Table 1).

In Clonidine group, baseline heart rate remained low compared to control group, which was statistically significant ($p<0.001$). But during laryngoscopy and tracheal intubation heart rate increased from baseline value, which was statistically highly significant ($p<0.001$). Similar findings were observed at 1, 2, 3, 4 minutes after intubation. At 5 minutes after intubation, heart rate remained increased compared to baseline (Table 1).

A. Fassoulaki et al[5] (2006) ,Saikat Majumdar et al[6] (2008) ,Seyed Mojtaba, Marashi et al[7] (2009) ,Kumkum and Colleagues et al[9] in 2011, Tahira Iftikhar and Colleagues et al[21] (2011) ,Usha Bafna and Colleagues et al[2] (2011) ,Seyed Mojtaba Marashi and Colleagues et al[15] (2014), Suresh K. Singhal et al[4] (2014) ,Abhishek Chatterjee and Colleagues et al[16] (2015) ,Satyen Parida and Colleagues et al[17] (2015) and Upendra Kumar Kapsey et al[1] (2016) conducted studies and results of present study are consistent with all these studies.

In present study, pre-operative baseline systolic, diastolic and mean arterial pressure were comparable in all three groups ($p>0.05$). At pre oxygenation, all groups were comparable for systolic blood pressure

(p>0.05). Significant decrease in diastolic and mean arterial pressure was observed in clonidine and gabapentine group (p<0.05) compared to control group, in which it remained comparable to baseline (p>0.05).

Immediately after laryngoscopy and intubation, increase in systolic, diastolic and mean arterial pressure from baseline value in all groups more in control than clonidine and gabapentine group was observed, which was statistically highly significant (p<0.001). At 1 and 2 minute after intubation, maximum increase in systolic, diastolic and mean arterial pressure from baseline value were seen in all groups (p<0.001). At 3 and 4 minutes after intubation, Increase in systolic and mean arterial pressure from baseline in all three groups (p<0.001). (Table 2,3,4). At 5 minutes after intubation, increase in systolic blood pressure from baseline value were seen in all group (p<0.001).

The finding of this study correlates with findings of studies conducted by A. Fassoulaki et al[5] (2006) ,Saikat Majumdar et al[6](2008) ,Seyed Mojtaba. Marashi et al[7](2009) ,Kumkum and Colleagues et al[9] (2011) ,Tahira Iftikhar and Colleagues et al[10] (2011) ,Usha Bafna and Colleagues et al[2] (2011) ,Seyed Mojtaba Marashi and Colleagues et al[15] (2014) ,Suresh K. Singhal et al[4] (2014) ,Abhishek Chatterjee and Colleagues et al[16] (2015) ,Satyen Parida and Colleagues et al[17] (2015) and Upendra Kumar Kapsey et al[1] (2016) .

In our study**,** rescue analgesia was given at VAS > 3. The mean time for rescue analgesia was 225.6 ± 8.63 minutes in Clonidine group, 554.06 ± 26.84 minutes in Gabapentine group and 20.66± 5.76 minutes in Placebo group. So, requirement of rescue analgesic was earlier in control group as compared to Clonidine and Gabapentine group. The difference between three groups was statistically highly significant (P < 0.001). Thus, effective postoperative analgesia was significantly prolonged in both Clonidine (225.6 ± 8.63 minutes) and Gabapentine (554.06 ± 26.84 minutes) group as compared to control group (20.66 ± 5.76 minutes).

Total duration of effective post-operative analgesia was more in Gabapentine group as compared to Clonidine group and the difference was statistically highly significant (P<0.001).The finding of this study correlates with findings of studies conducted by Sussan Soltani Mohammadi et al[8] in (2009) ,Shivinder Singh et al[11] , Marashi SM et al[12] in(2012) , F Frouzanfard et al[13] and Smita Musti et al[14] in (2013).

Nausea/Vomiting was seen in 3 patients of clonidine group and 2 patients of gabapentine group but none of the patient in control groups developed nausea/vomiting in our study. None of the patients were developed Vertigo/headache, visual disturbances like diplopia and nystagmus, sedation RSS>5 in any patient of any group.

CONCLUSION

Oral Clonidine (0.2 mg) when given in premedication provided better attenuation of hemodynamic stress response to laryngoscopy and tracheal intubation compared to oral Gabapentine (900 mg), where hypertensive response was fairly obtunded, but not the tachycardiac response. Oral Clonidine has better response over tachycardia than Gabapentine, whereas Gabapentine is superior to clonidine for postoperative analgesia.

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