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ENHANCING AWAKE FIBEROPTIC NASOTRACHEAL INTUBATION: A COMPARATIVE STUDY OF NEBULIZATION WITH ORAL CLONIDINE VERSUS PREGABALIN PREMEDICATION IN ORAL CANCER SURGERIES

Anaesthesiology

Dr. Smriti Lakra — Third year Postgraduate resident, Department of Anaesthesiology and Pain Medicine, Pt. J.N.M Medical College and Dr. B.R.A.M Hospital, Raipur, C.G, India.

Dr. Sonali Sahu — MD, Assistant Professor, Department of Anaesthesiology and Pain Medicine, Pt. J.N.M Medical College and Dr. B.R.A.M Hospital, Raipur, C.G, India.

Dr. Pratibha Jain Shah* — MD, FICA, FIPM, Professor and Head of the Department, Department of Anaesthesiology and Pain Medicine, Pt. J.N.M Medical College and Dr. B.R.A.M Hospital, Raipur, C.G, India. *Corresponding Author

ABSTRACT

Background: Awake fibreoptic intubation (AFOI) is recommended for managing an anticipated difficult airway. The study aims to compare the effectiveness of clonidine versus pregabalin as oral premedication for awake fiberoptic nasotracheal intubation in oral cancer surgeries. **Materials And Methods:** The study involved forty patients undergoing oral cancer surgeries under general anesthesia who were randomly divided into Group 1 (n=20) and Group 2 (n=20). Group 1 patients received oral clonidine 200 µg and Group 2 patients received oral pregabalin 150 mg 90 minutes before fiberoptic intubation. The hemodynamic parameters, levels of anxiety, and sedation were assessed and recorded at baseline and then sequentially at 30 minutes, 60 minutes, 90 minutes after premedication, and post-intubation. Cooperation for nebulization was observed 15 minutes before intubation. The intubation condition was assessed during intubation and the tolerance to intubation was assessed after the placement of the tube in the trachea. The patient satisfaction was assessed and recorded at the end of the surgery. **Result:** Group 2 showed significantly higher tolerance to intubation (p=0.04), better intubation conditions (p=0.02), and higher satisfaction scores compared to Group 1 (p=0.018). Group 2 patients also had lower levels of anxiety, and higher levels of sedation compared to Group 1 but these differences were statistically non-significant. Group 1 exhibited better control of hemodynamic stress response to intubation with better control of post-intubation heart rate (p=0.007), systolic blood pressure (p=0.01), diastolic blood pressure (p=0.02), and mean blood pressure (p=0.04). **Conclusion:** Clonidine 200 µg and pregabalin 150 mg both are equally effective and safe as an oral premedication for awake fiberoptic nasotracheal intubation. Oral pregabalin improved intubating conditions and tolerance to intubation while oral clonidine offered better control of the pressor response to laryngoscopy and intubation, with comparable effects on anxiety and sedation levels.

KEYWORDS

Oral clonidine, pregabalin, premedication, and awake fiberoptic intubation

INTRODUCTION

Oral cancer ranks as the sixth most prevalent cancer worldwide and the third most common in India. Patients with oral cancers have a potentially difficult airway. An awake fibreoptic intubation (AFOI) is a technique recommended by the American Society of Anaesthesiologists Difficult Airway Algorithm (DAA) for managing anticipated difficult airways[1]. Awake fiberoptic nasotracheal intubation can be an unpleasant experience for patients. When the procedure is performed without sedation, it can make the patients anxious, cause discomfort, and result in hemodynamic changes[2]. Therefore, premedication is necessary to blunt the airway reflexes, maintain spontaneous ventilation, make the procedure more tolerable for patients, and ensure optimal intubating conditions. Nasotracheal intubation is preferred to oral intubation in intraoral, dental, and maxillofacial surgeries.

Various sedatives, including benzodiazepines, opioids, α_2-adrenergic agonists, ketamine, and propofol, either alone or in combination, have all been used for conscious sedation during awake fiberoptic intubation.

Clonidine, α_2-adrenergic agonist with a half-life of 5–7 hours, when administered in the pre-anesthetic period provides hemodynamic stability, and reduces the stress response to laryngoscopy and intubation by lowering catecholamine levels. Common side effects are sedation and xerostomia. Pregabalin is a gabapentin analog with a half-life of 4.5–7 hours, offering analgesic, anticonvulsant, and anxiolytic effects. It helps blunt the stress response to laryngoscopy and intubation. Common side effects of pregabalin are dizziness and blurred vision[3,4,5,6].

While numerous studies have explored each drug individually, and comparison with other medications, research specifically comparing oral clonidine and pregabalin as premedication for awake fiberoptic intubation remains scarce. To address this gap, this study was therefore carried out to compare the effectiveness of oral clonidine and pregabalin as premedication for awake fiberoptic nasotracheal intubation in oral cancer surgeries in terms of tolerance to intubation as the primary outcome. The secondary outcomes were hemodynamic changes, intubation conditions, levels of sedation and anxiety, cooperation for nebulization, and patient satisfaction at the end of the surgery.

MATERIALS AND METHODS

After obtaining Institutional Scientific and Ethics Committee approval and written informed consent from all patients, this double-blinded randomized, prospective, and time-bound study was conducted among 41 patients of either gender, aged 20-60 years, belonging to the American Society of Anesthesiologists physical status (ASA-PS) II and III, BMI <30 kg/m^2 posted for elective oral cancer surgery under general anesthesia from July 2022 to April 2024. Patients who refused to participate, patients with systemic disorders of liver, kidney, cardiac, respiratory diseases, patients on sedatives, hypnotics, and sympatholytics, and those who required a second attempt at intubation were excluded from the study. Preoperative assessment was done a day before the surgery including the complete history, clinical examination, and recording of vital parameters along with routine investigations. After considering the inclusion and exclusion criteria, patients were randomly divided into two groups by the sealed envelope method. Group 1 (n=21) patients received oral clonidine 200 µg and group 2 (n=20) patients received oral pregabalin 150 mg 90 minutes before fiberoptic intubation. Both the anesthesiologist performing the intubation and the one recording the data were blinded to the group allocations.

All the patients were advised nil per oral for 6 hours before surgery, and briefed on the procedure to be performed on them. In the preoperative room, a multi-channel monitor was attached and an intravenous (IV) access was secured with an 18 G cannula. The hemodynamic parameters (systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and SpO_2), levels of anxiety, and sedation were observed and recorded at baseline. An independent anesthesiologist prepared and gave the assigned premedications to patients 90 minutes before intubation with a sip of water. The hemodynamic parameters, levels of anxiety, and sedation were then observed and recorded sequentially at 30 minutes, 60 minutes, and 90 minutes after the premedication. The anxiety was evaluated using a 4-point score as 0 - Patient quiet and comfortable, 1 – uneasy, 2 - worried or anxious, 3 - very worried or upset. The level of sedation was evaluated by the Observer's assessment of alertness scale (OAA/S) as sum scores: 20-

18 = alert, 17-15 = light sedation, 14-11 Heavy sedation, under 10 = unable to cooperate (Table 1). The patency of both the nostrils was tested and the nostril with better patency was chosen for awake fiberoptic nasotracheal intubation. Topicalization of both upper and lower airway was achieved by nebulization with 3 ml of 4 % xylocaine 15 minutes before the intubation and patients were evaluated for their cooperation for nebulization with their response recorded as yes or no.

Table 1 Observer's Assessment Of Alertness Scale

Responsiveness	Speech	Facial Expression	Eyes	Score level
Responds readily to name spoken in a normal tone	Normal	Normal	Clear, no ptosis	5 Alert
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	4
Respond only after the name is called loudly and/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed and marked ptosis (half the eye or more)	3
Responds only after mild protruding or shaking	Few recognizable Words	-	-	2
Does not respond to mild protruding or shaking	-	-	-	1Deep sleep

In the operating room, a multi-channel monitor was applied to record hemodynamic parameter changes, and an injection of glycopyrrolate 0.2 mg IV was given to dry oral cavity secretions. Xylometazoline nasal drops were administered to both nostrils for decongestion. The tongue and hypopharynx were sprayed with two puffs of 10 % lignocaine (20 mg) to add topicalization. After lubrication, the fiberscope was loaded with an appropriate size cuffed polyvinyl chloride endotracheal tube. Awake fiberoptic intubation was performed by the same anesthesiologist in all patients. The fiberoptic bronchoscope was inserted with the tip of the scope advancing beyond the epiglottis. When the glottis was identified, the scope was inserted between the vocal cords into the trachea, and by holding the fiberscope steady, the endotracheal tube was advanced into the trachea.

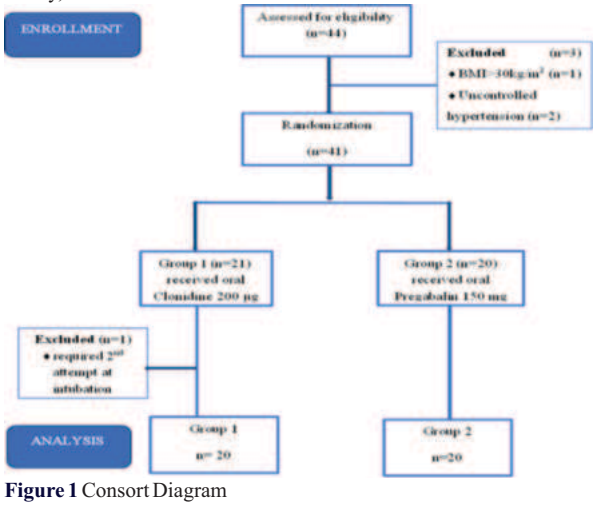


Figure 1 Consort Diagram

Intubation condition was observed and recorded during intubation as cough scores: 1 = no cough, 2 = slight cough (no more than two coughs in sequence), 3 = moderate cough (3-5 coughs in sequence), 4 = severe cough (>5 coughs in sequence). A cough score of ≤ 2 was considered optimal intubation condition. Tolerance to intubation which was our primary outcome was evaluated and recorded as a post-intubation score after placement of the tube in the trachea as: 1=cooperative, 2 = minimal resistance, 3 = severe resistance. The patient satisfaction score was evaluated and recorded at the end of the surgery as scores: 1 = very unsatisfied, 2 = unsatisfied, 3 = adequate, 4 = satisfied, and 5 = very satisfied. The patients were monitored throughout the procedure and noted for any adverse events.

Statistical Analysis

The data was collected in a master chart in Excel which was exported to SPSS (Statistical Package for Social Sciences) 20.0 for statistical analysis. Forty-one patients undergoing elective oral cancer surgery were randomly divided into two groups (Group 1 = 21 patients and Group 2 = 20 patients). Finally, data from 40 patients were included for analysis in the study after considering the inclusion and exclusion criteria (Figure 1). Numerical data i.e. demographic profile, and hemodynamic parameters (heart rate, blood pressure, oxygen saturation, and respiratory rate) were presented as mean ± standard deviation, and their inter-group comparisons were performed using the independent t-test, and intra-group comparisons were conducted using the paired t-test. Categorical data i.e. cooperation for nebulization, anxiety score, sedation score, cough score, post-intubation score, and patient satisfaction score were expressed as percentages and compared using the chi-square test. The p-value < 0.05 was considered statistically significant.

RESULTS

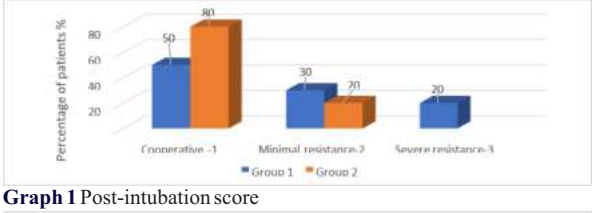
The demographic profiles of the patients in both groups were statistically comparable (Table 2).

Table 2 Demographic Profile

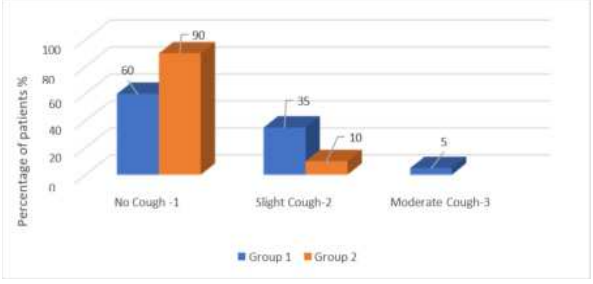
Variables	Group 1 (n=20)	Group 2 (n=20)	p-value
Mean age + SD	41±10.97 years	39.9±14.43 years	0.78
BMI (Kg/m2) + SD	23.09±2.82	22.27±2.2	0.3
Gender (M: F)	(75:25)	(75:25)	1.00
ASA grade II	80 %	85 %	0.68

SD=Standard deviation, BMI= Body Mass Index, M: F= Male: Female

Tolerance to intubation was significantly better in the pregabalin group, with no cases of severe resistance to intubation, compared to 20% in the clonidine group (p = 0.03) (Graph 1). Pregabalin provided a better intubation condition (90 % versus 60 %; p=0.02 having a cough score of 1) (Graph 2). The pregabalin group had consistently lower levels of anxiety and higher levels of sedation compared to the clonidine group, although the difference was statistically not significant (p>0.05).



Graph 1 Post-intubation score



Graph 2 Cough score

In the clonidine group, the mean heart rate (HR) remained consistently below baseline at all time intervals till 90 minutes, with a significant decrease from the baseline value at 60 minutes (p=0.01), and 90 minutes post-premedication (p<0.001). In the pregabalin group, the mean HR decreased significantly from the baseline value at 90 minutes post-premedication (p=0.02). The post-intubation mean HR increased in both groups, with a significant increase from the baseline in the pregabalin group (p=0.007) (Table 3). No patients in either group experienced bradycardia (HR < 50 bpm).

Table 3 Mean Heart Rate (HR)

Point of observation	Mean Heart Rate (beats per minute)				
	Group 1 (n=20)	p-value	Group 2 (n=20)	p-value	p-value (Group 1 vs Group 2)
Baseline	87.3±11.51	-	88.2±11.83	-	0.809

After Drug Administration	85.65±9.84	0.06	88.25±10.52	0.93	0.424
At 30 Minutes	85.95±9.96	0.22	89±11.01	0.44	0.364
At 60 Minutes	83.8±10	0.01	87.95±11.04	0.81	0.22
At 90 Minutes	80.6±9.22	<0.001	85.55±11.48	0.02	0.141
Post Intubation	92.7±10.77	0.01	102.1±9.9	<0.001	0.007

In the clonidine group, mean blood pressure (MBP) was consistently below baseline at all time intervals, with a significant decrease from the baseline observed at 90 minutes (p=0.01). In contrast, the pregabalin group exhibited MBP values consistently above baseline at all time intervals, with a significant increase from the baseline at post-intubation in the pregabalin group (p<0.001) (Table 4).

Table 4 Mean Blood Pressure (MBP)

Point of observation	Mean Blood Pressure (mmHg)				
	Group 1 (n=20)	p-value	Group 2 (n=20)	p-value	P-value (Group 1 vs Group 2)
Baseline	87.15±8.18	-	84.2±9.07	-	0.29
After Drug Administration	87.15±8.18	1.00	84.2±9.07	1.00	0.29
At 30 Minutes	85.9±6.06	0.22	84.6±5.61	0.81	0.49
At 60 Minutes	84.35±6.13	0.08	84.6±5.16	0.82	0.89
At 90 Minutes	82.3±5.49	0.01	84.3±5.79	0.95	0.27
Post Intubation	86.9±6.32	0.87	91.1±6.68	<0.001	0.04

An increase in mean HR and MBP due to pressor response was observed in both groups following intubation; however, post-intubation MBP in the clonidine group remained below baseline (p=0.04), suggesting better control of pressor response compared to pregabalin. Patients in the pregabalin group exhibited higher satisfaction levels (p=0.018). At the end of the surgery, three patients were unsatisfied in the clonidine group, but none in the pregabalin group. No significant difference was observed between both groups in terms of cooperation during nebulization.

DISCUSSION

In our study, pregabalin provided significantly more tolerance to intubation (p=0.04), better intubating conditions (p=0.02), and patient satisfaction (p=0.018) with consistently lower levels of anxiety and higher levels of sedation compared to the clonidine group, although the difference was statistically not significant (p>0.05). None of the patients in either group experienced heavy sedation or deep sleep (sedation scores 10-14). While patients in the clonidine group had better hemodynamic control at all time intervals. No significant difference was observed between groups for cooperation for nebulization.

Awake fiberoptic nasotracheal intubation (AFOI) is the preferred method for securing a difficult airway in patients with oral cancers. AFOI can be an unpleasant experience for patients. Hence, it requires a safe premedication that can blunt the airway reflexes, maintain spontaneous ventilation, and make the procedure more tolerable for patients, to ensure smooth intubating conditions and hemodynamic stability without respiratory depression. The studies reviewed have shown that both clonidine and pregabalin have improved the intubation conditions. Clonidine, an α_2 agonist reduces the stress response to laryngoscopy and intubation and provides hemodynamic stability while pregabalin blunted the stress response to intubation due to its anxiolytic and sedative properties.

In our study, pregabalin provided better tolerance to intubation and intubation conditions which could be attributed to its anxiolytic and sedative properties. Tsai CJ et al[13] used similar post-intubation scores for awake fiberoptic intubation and observed better tolerance in the dexmedetomidine group compared to the propofol group (Post intubation score of 1 in Dexmedetomidine versus 2 in the propofol group) (p=0.014). Mondal S et al[15] compared intubation conditions between dexmedetomidine and fentanyl during awake fiberoptic bronchoscopy using a similar cough score. They also considered a cough score of <2 as a favorable intubation condition. They observed better intubation conditions in the dexmedetomidine group compared to the fentanyl group (p<0.0001). Comparative conclusions in terms of tolerance to intubation and intubation conditions cannot be drawn from these studies due to different study drugs.

Similar to our study, Kaur H et al[6] also observed lower anxiety scores and, greater anxiolysis in the pregabalin group compared to the clonidine group till 30 minutes post-premedication. However, they observed pronounced anxiolysis and sedation in the pregabalin group at 1 hour and, 1.5 hours post-premedication (p<0.05). Parveen S et al[10] assessed the level of sedation levels using the Ramsay Sedation Scale in their study. They observed significantly higher levels of sedation in the pregabalin group both pre- and post-operatively (p<0.001). The anxiolytic and sedative effects of pregabalin can be due to its action on presynaptic voltage-gated calcium channels in the CNS. The differences in the levels of anxiety and sedation observed in our study can be due to different demographic profiles.

In our study, baseline HR and MBP were comparable between the study groups. An increase in mean HR and MBP due to pressor response was observed in both groups following intubation; however, post-intubation MBP remained below the baseline value in the clonidine group but was significantly higher from the baseline value in the pregabalin group (p<0.001), suggesting better hemodynamic control in the clonidine group. The hemodynamic control in the clonidine group may be attributed to its α_2 – adrenergic agonist action. The studies done by Kaur et al[6], Arief et al[2], Murari et al[9], and Thomas et al[12] also noted attenuation of HR and a lower mean HR in the clonidine group compared to the pregabalin group similar to our study. Kaur H et al[6] noted a significantly lower mean arterial blood pressure (MAP) in the clonidine group compared to pregabalin before induction, immediately after intubation, and after intubation. Murari T et al[9] and Parveen et al[10] observed a significantly lower mean MAP in the clonidine group compared to the pregabalin group at all time intervals (p<0.05), except at 10 minutes post-intubation and 15 minutes post-intubation. Avanthi I et al[3] compared the mean rate pressure product and observed a 21 % rise in the mean rate pressure from the baseline in the pregabalin group at 1-minute post-intubation while a 2.8 % fall from the baseline in the clonidine group. The findings of our study also align with those of Kaur H et al[6], Parveen et al[10], and Murari T et al[9].

In our study, patients in the pregabalin group showed higher satisfaction at the end of the surgery. Bull[16] defined patient experience as "what" happened during an episode of care and "how" it happened from the patient's perspective. In contrast, patient satisfaction rather captures the personal expectations and subjective opinions of the received care. The satisfaction scores observed in our study were higher in the pregabalin group compared to the clonidine group, with the difference being statistically highly significant (p=0.018), which can be attributed to lower anxiety levels, higher sedation, better intubating conditions, and more tolerance to intubation. This suggests pregabalin's potential advantages in improving the overall patient experience during procedures requiring awake fiberoptic intubation. No studies reviewed have included the patient satisfaction score in their studies.

We documented no incidences of symptomatic bradycardia, hypotension, heavy sedation or deep sleep, blurred vision, somnolence, or abnormal thinking. Dry mouth was the most common complaint after premedication. The second most common complication was nausea. These complaints were transient and subsided with reassurance and an anti-emetic Injection of Ondansetron 0.1 mg/kg IV.

LIMITATIONS AND FUTURE SCOPE

Our study had some limitations as we did not assess the level of recall, the need for analgesics, varying drug dosages, and postoperative VAS scores. In the future, this study can be extended to patients other than oral cancers, and include measurements of plasma catecholamines, post-operative VAS scores, and evaluation of the need for analgesics. Further research could explore optimizing dosages and combinations with other sedatives to enhance patient outcomes.

CONCLUSION

Clonidine 200 µg and pregabalin 150 mg both are equally effective and safe as an oral premedication for awake fiberoptic nasotracheal intubation. Oral pregabalin improved intubating conditions and tolerance to intubation while oral clonidine offered better control of the pressor response to laryngoscopy and intubation, with comparable effects on anxiety and sedation levels.

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Conflict Of Interest
None.

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