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COMPARISON OF ORAL GABAPENTIN AND ORAL CLONIDINE FOR ATTENUATION OF HAEMODYNAMIC, SEDATIVE, AND ANXIOLYTIC RESPONSES TO DIRECT LARYNGOSCOPY AND TRACHEAL INTUBATION: A RANDOMISED DOUBLE-BLIND STUDY

Anaesthesiology

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ABSTRACT

Background: Laryngoscopy and tracheal intubation (LETI) evoke significant haemodynamic responses, potentially hazardous in vulnerable patients. Clonidine, an alpha-2 agonist, and Gabapentin, an antiepileptic with analgesic properties, are used as premedication to mitigate this pressor response. **Methods:** A prospective, randomised, double-blind study involving 100 ASA I–II normotensive patients undergoing elective surgery under general anaesthesia was conducted. Patients received either oral Clonidine 200 mcg or Gabapentin 900 mg 90 minutes pre-induction. Primary outcomes included changes in heart rate (HR), mean arterial pressure (MAP), sedation, and anxiety scores. **Results:** Both drugs reduced HR and MAP during and after intubation compared to baseline. Clonidine resulted in significantly lower HR at intubation (87.2 vs. 92.3 bpm, p=0.042) and at 1, 3, and 5 minutes post-intubation. MAP was also significantly lower in the Clonidine group at all time points post-intubation. Sedation and anxiolysis were slightly better with Clonidine, though differences were not statistically significant. **Conclusion:** Oral Clonidine (200 mcg) is more effective than oral Gabapentin (900 mg) in attenuating the haemodynamic responses to LETI, with comparable sedative and anxiolytic effects.

KEYWORDS

Clonidine, Gabapentin, laryngoscopy, intubation, haemodynamic response, sedation, anxiety, general anaesthesia

INTRODUCTION

Airway manipulation during anaesthetic induction is known to provoke intense sympathetic stimulation, manifesting as tachycardia and hypertension, particularly during laryngoscopy and endotracheal intubation (LETI) [1–4]. Although typically tolerated by healthy individuals, these pressor responses can be catastrophic in patients with cardiovascular or neurological comorbidities [5–7]. Additionally, preoperative anxiety is a prevalent factor that exacerbates haemodynamic instability and increases anaesthetic and analgesic requirements [8–10].

Multiple pharmacologic agents—including beta-blockers, calcium channel blockers, opioids, and alpha-2 agonists—have been evaluated to mitigate these responses[11,12]. Clonidine, a selective partial alpha-2 agonist, exerts sympatholytic, sedative, and analgesic effects[13,14]. Gabapentin, a structural analogue of GABA, attenuates nociceptive transmission and has been shown to blunt sympathetic responses to stress[15,16].

This study aimed to compare the effectiveness of oral Clonidine and Gabapentin in attenuating haemodynamic, sedative, and anxiolytic responses to LETI.

MATERIALS AND METHODS

Study Design and Participants

A prospective, double-blind, randomised, controlled trial was conducted at a tertiary care centre over 18 months. After ethics approval and informed consent, 100 normotensive ASA I–II patients aged 18–65 years undergoing elective surgeries were recruited.

Exclusion Criteria included emergency surgery, systemic disorders (cardiovascular, renal, hepatic, neurological), drug hypersensitivity, pregnancy, difficult airway, and use of interfering medications.

Randomisation and Blinding

Participants were randomly assigned (1:1) to either:

- Group C: Oral Clonidine 200 mcg
- Group G: Oral Gabapentin 900 mg administered 90 minutes pre-induction. Blinding was maintained for patients, anaesthetists, and assessors.

Anaesthetic Protocol

Standard premedication included midazolam, glycopyrrolate, and tramadol. Induction was with propofol (2 mg/kg) and vecuronium (0.1 mg/kg). Intubation was performed with a Macintosh laryngoscope by an experienced anaesthesiologist. Anaesthesia was maintained with isoflurane (MAC 1.15%), N2O/O2 (60:40), and additional vecuronium.

Data Collection and Outcomes

Haemodynamic parameters (HR, MAP) were recorded at baseline, post-induction, at intubation, and 1, 3, 5, and 10 minutes post-intubation.

Sedation was assessed using a 4-point scale: 1 = Awake
2 = Sleeping but responsive
3 = Deep sleep, arousable
4 = Unarousable

Anxiety was assessed using a 4-point scale: 0 = Relaxed
1 = Uneasy
2 = Anxious
3 = Very anxious

Statistical Analysis

Data were analysed using Stata 17.1. Means, SDs, medians, and proportions were calculated. Intergroup comparisons used Student's t-test and chi-square test. A p-value <0.05 was considered significant.

RESULTS

All 100 patients completed the study (n=50 per group). Demographics were comparable (p>0.05 for age, gender, ASA grade, and intubation time).

Table 1. Baseline Characteristics

Variable	Clonidine (n=50)	Gabapentin (n=50)	p-value
Age (years)	44.0 ± 14.7	42.9 ± 13.8	0.087
Gender (M/F)	28/22	24/26	0.423
ASA I/II	28/22	23/27	0.317
Intubation time (sec)	20.5 ± 2.9	20.0 ± 2.7	0.478

Haemodynamic Response

At all measured time points post-intubation, Clonidine significantly blunted HR and MAP compared to Gabapentin

Table 2. Haemodynamic Trends

Time Point	HR (bpm) Clonidine	HR Gabapentin	MAP (mmHg) Clonidine	MAP Gabapentin
Baseline	82.3 ± 6.6	82.9 ± 6.9	90.0 ± 0.1	89.9 ± 3.6
Intubation	87.2 ± 7.1	92.4 ± 7.5	93.6 ± 0.8	97.1 ± 4.8
1 min post	89.2 ± 6.4	94.7 ± 6.5	94.1 ± 0.3	98.1 ± 4.6
3 min post	84.8 ± 5.8	89.7 ± 5.7	93.0 ± 0.9	95.1 ± 6.2
5 min post	82.6 ± 8.3	85.4 ± 7.4	91.0 ± 0.6	93.3 ± 5.5
10 min post	79.2 ± 5.6	81.9 ± 5.6	90.0 ± 0.3	92.6 ± 5.7

Sedation and Anxiety

At 60 minutes post-drug:

- 54% in Clonidine and 48% in Gabapentin group were sedated (Score 2).
- 46% and 52%, respectively, remained awake.
- Anxiety score decreased in both groups; 46% (Clonidine) and 36% (Gabapentin) were relaxed (Score 0) post-drug.

Table 3. Sedation and Anxiety Scores

Score	Clonidine n (%)	Gabapentin n (%)
Sedation Score 2 (responsive sleep)	27 (54%)	24 (48%)
Anxiety Score 0 (relaxed)	23 (46%)	18 (36%)

Differences were not statistically significant ($p>0.05$)

DISCUSSION

The results of this study suggest that oral Clonidine (200 mcg) offers superior attenuation of haemodynamic responses to laryngoscopy and tracheal intubation compared to oral Gabapentin (900 mg). While both agents were effective in blunting the sympathetic response, Clonidine demonstrated a more pronounced reduction in heart rate and mean arterial pressure, particularly in the critical post-intubation period. This reinforces its clinical utility in situations where cardiovascular stability is paramount.

The sympathetic surge associated with direct laryngoscopy and intubation is well documented to provoke tachycardia, hypertension, and arrhythmias[1,2]. These effects are typically transient but can precipitate myocardial ischaemia, especially in patients with underlying coronary artery disease or cerebrovascular risk[3,4]. Therefore, pharmacological strategies to blunt these responses remain a focus of perioperative anaesthetic care.

Clonidine's mechanism of action as a centrally acting partial alpha-2 adrenergic agonist leads to inhibition of sympathetic outflow, resulting in decreased circulating catecholamines, reduced heart rate, and lower blood pressure[5,6]. These effects were clearly demonstrated in our study, where Clonidine consistently outperformed Gabapentin across all haemodynamic parameters following intubation. The observed attenuation in heart rate and MAP aligns with previous studies by Waikar et al.[17] and Gupta et al.[8], who also reported significantly improved haemodynamic profiles in patients premedicated with Clonidine.

Gabapentin, although originally developed as an anticonvulsant, has emerged as a multimodal agent with analgesic, anxiolytic, and sympatholytic properties. Its efficacy in attenuating pressor responses is attributed to binding with the α2δ subunit of voltage-gated calcium channels in the central nervous system, thereby modulating neurotransmitter release[15,19]. Several studies, such as those by Memis et al.[6] and Fassoulaki et al.[15], support the use of Gabapentin in reducing blood pressure and stress responses during intubation. However, consistent with our findings, the drug's effect on heart rate appears less predictable compared to Clonidine.

In the present study, the heart rate in the Clonidine group remained significantly lower than in the Gabapentin group at all critical points post-intubation. While both drugs prevented excessive hypertension and tachycardia, Clonidine's more stable haemodynamic profile is clinically advantageous, particularly in patients with compromised myocardial function. Interestingly, while previous literature (e.g., Marashi et al.[5]) suggested Gabapentin to be superior, such discrepancies could stem from variations in dosage, timing, patient demographics, and concurrent medications.

Sedation and anxiolysis are desirable secondary effects of premedication in elective surgery. Both study drugs produced mild-to-moderate sedation, with Clonidine exhibiting slightly greater sedative efficacy. Although the difference was statistically insignificant, the trend supports the findings of Singhal et al.[9] and Bafna et al.[21], who documented enhanced preoperative sedation with Clonidine. Clonidine's anxiolytic effect, mediated through suppression of central noradrenergic activity, may contribute to a smoother induction and better patient experience[6,13].

It is noteworthy that both drugs were well-tolerated. No adverse effects such as bradycardia, hypotension, excessive sedation, or respiratory depression were recorded in either group, reaffirming the safety of the selected doses in normotensive patients. The absence of significant intergroup differences in sedation and anxiety scores suggests that Gabapentin remains a viable option when bradycardia or hypotension is a concern, although caution is warranted in patients with renal impairment due to its primary renal excretion.

The findings of this study have important clinical implications. In patients undergoing elective surgery, especially those with potential cardiovascular vulnerability, preoperative oral Clonidine provides a safer and more effective strategy to mitigate the stress response to intubation. Gabapentin, though less effective in attenuating HR, remains useful for its additional postoperative analgesic and antiemetic benefits, making it a useful component of multimodal anaesthesia.

Limitations

This study was limited to normotensive ASA I–II patients. Thus, the results may not be generalisable to hypertensive, elderly, or high-risk cardiac patients. Additionally, plasma catecholamine levels were not measured, which could have provided objective biochemical confirmation of sympathetic attenuation. Future studies should include these subgroups and investigate postoperative pain and recovery profiles, especially as Gabapentin's utility may be more evident in the longer-term perioperative period.

CONCLUSION

Oral Clonidine (200 mcg) is more effective than oral Gabapentin (900 mg) in attenuating haemodynamic responses during laryngoscopy and intubation. Both agents offer comparable sedation and anxiolysis. Clonidine should be preferred in patients where haemodynamic stability is paramount.

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