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ORIGINAL RESEARCH

Comparison of two different doses of tablet clonidine (100mcg and 150mcg) given 90 minutes prior to surgery to attenuate haemodynamic changes during endotracheal intubation

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ABSTRACT

Background: Endotracheal intubation can elicit significant haemodynamic responses, posing risks for patients with cardiovascular conditions. Clonidine, an alpha-2 adrenergic agonist, is used to mitigate these responses, but the optimal dosing is uncertain. This study compares the efficacy and safety of two doses of oral clonidine, 100 µg and 150 µg, administered 90 minutes before surgery. **Methods:** Sixty patients aged 18–55 years, classified as ASA physical status I or II and scheduled for elective lower abdominal surgeries, were randomly assigned to two groups. Group A received 100 µg of oral clonidine, and Group B received 150 µg. Haemodynamic parameters—heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP)—were recorded at baseline, during induction, immediately after intubation, and at intervals up to 15 minutes post-intubation. Side effects and the need for rescue analgesia were also assessed. **Results:** Group A demonstrated significantly lower SBP and HR at induction and during the immediate post-intubation period compared to Group B ($p < 0.05$). No significant differences were observed in DBP and MAP at most time points. The incidence of hypotension was higher in Group B but not statistically significant. Group B required significantly less rescue analgesia postoperatively ($p < 0.001$). **Conclusion:** A 100 µg dose of oral clonidine is more effective in attenuating haemodynamic responses during endotracheal intubation compared to a 150 µg dose. While the higher dose offers improved postoperative analgesia, it does not enhance haemodynamic stability and may increase the risk of hypotension.

Keywords: Clonidine, Haemodynamic Response, Endotracheal Intubation, Premedication, Alpha-2 Agonist, Analgesia

INTRODUCTION

Endotracheal intubation is a critical component of general anesthesia, enabling secure airway management and ventilation during surgical procedures. However, the process of laryngoscopy and intubation is known to provoke significant sympathetic stimulation, leading to acute haemodynamic responses such as hypertension and tachycardia[1]. While these transient cardiovascular changes are often tolerated by healthy individuals, they can pose substantial risks to patients with preexisting cardiovascular conditions, potentially precipitating myocardial ischemia, arrhythmias, or cerebrovascular events[2].

Attenuation of these haemodynamic responses is therefore a vital consideration in anesthetic practice. Various pharmacological agents have been employed to mitigate these effects, including opioids, beta-blockers, calcium channel blockers, and vasodilators[3]. Clonidine, a selective alpha-2 adrenergic agonist, has emerged as a particularly effective agent due to its ability to decrease central sympathetic outflow, resulting in reduced heart rate and blood pressure[4]. Additionally, clonidine possesses sedative and

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analgesic properties, which can enhance patient comfort and reduce anesthetic requirements[5].

Oral clonidine premedication has been demonstrated to effectively blunt the haemodynamic responses associated with laryngoscopy and intubation[6]. However, the optimal dosing regimen remains a subject of clinical interest. Higher doses may offer greater haemodynamic stability but are associated with an increased risk of adverse effects such as excessive sedation, hypotension, and bradycardia[7]. Conversely, lower doses may be insufficient to adequately attenuate sympathetic responses. Despite its widespread use, there is limited comparative data on the efficacy and safety of different oral clonidine doses administered prior to surgery[8].

This study aims to compare the effects of two different doses of oral clonidine—100 µg and 150 µg—administered 90 minutes before surgery, on haemodynamic changes during endotracheal intubation. By evaluating these dosing strategies, we seek to determine the dose that optimally balances efficacy in haemodynamic attenuation with safety and minimal side effects. The findings from this research could have significant implications for perioperative management, potentially guiding dosage recommendations and improving patient outcomes, particularly in individuals at elevated cardiovascular risk.

Understanding the dose-response relationship of clonidine in this context is crucial for anesthesiologists aiming to optimize perioperative care. This study not only addresses a gap in the existing literature but also strives to enhance clinical protocols for managing the haemodynamic challenges associated with endotracheal intubation.

MATERIALS AND METHODS

Study Design and Setting

This observational, comparative study was conducted in the Department of Anesthesiology at Jaipur National University Institute of Medical Sciences and Research Centre, Jaipur, Rajasthan, from September 2022 to May 2024.

Sample Size and Groups

A total of 60 patients scheduled for elective lower abdominal surgeries under general anesthesia were enrolled. They were randomly divided into two groups (n=30 each):

- **Group A**: Received oral clonidine 100 µg 90 minutes prior to surgery.
- **Group B**: Received oral clonidine 150 µg 90 minutes prior to surgery.

Inclusion Criteria

- Patients aged between 18 and 55 years.
- Both male and female patients.
- Classified as American Society of Anesthesiologists (ASA) physical status I or II.
- Provided written informed consent.

Exclusion Criteria

- Patients not meeting inclusion criteria.
- History of bronchial asthma or allergy to clonidine.
- Severe coronary insufficiency or recent myocardial infarction.
- Concomitant use of monoamine oxidase inhibitors.
- Refusal to provide informed consent.

Preoperative Assessment

All patients underwent a thorough preanesthetic evaluation, including:

- **Medical History and Physical Examination**: Assessment of vital signs (temperature, blood pressure, pulse rate, respiratory rate) and evaluation for pallor, icterus, cyanosis, and lymphadenopathy.
- **Airway Assessment**: Conducted using standard protocols.
- **Laboratory Investigations**:
  - Complete blood count
  - Blood grouping and Rh typing
  - Fasting blood sugar
  - Blood urea and serum electrolytes
  - Liver and renal function tests
  - Coagulation profile (bleeding time, clotting time, prothrombin time, INR)
  - Chest X-ray (posteroanterior view)
  - Electrocardiogram (ECG)

Anesthetic Protocol

- **Preoperative Medication**: All patients fasted overnight and received tablet alprazolam 0.5 mg and tablet ranitidine 150 mg the night before surgery.
- **Oral Clonidine Administration**: On the day of surgery, Group A and Group B received 100 µg and 150 µg of oral clonidine, respectively, 90 minutes before induction.
- **Monitoring**: Standard monitors were used, including non-invasive blood pressure (NIBP), pulse oximetry, ECG, and end-tidal CO_2 ($EtCO_2$).

Data Collection

Hemodynamic parameters were recorded at specific intervals:

- After premedication (baseline)
- During induction
- Immediately after intubation
- At 1, 3, 5, 10, and 15 minutes post-intubation

Parameters measured included:

- Heart rate (HR)
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Mean arterial pressure (MAP)
- Oxygen saturation (SpO_2)

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Intraoperative Management

- **Anesthesia Induction and Maintenance**: Standard anesthetic agents and techniques were employed for all patients.
- **Adverse Events Management**:
  - **Hypotension**: Defined as SBP decrease >20% from baseline or <100 mm Hg; managed with increased fluid infusion and intravenous ephedrine 6 mg as needed.
  - **Bradycardia**: Treated with intravenous atropine 0.6 mg.
  - **Nausea**: Managed with intravenous ondansetron 4 mg.
  - **Pruritus**: Treated with intravenous pheniramine.
  - **Respiratory Depression**: Defined as respiratory rate <8 breaths/min or SpO_2 <94% on room air; managed with oxygen supplementation or ventilatory support.

Equipment Used

- Multiparameter monitor (NIBP, pulse oximeter, ECG, $EtCO_2$)
- Anesthetic drugs for premedication, induction, and maintenance
- Airway equipment: Hudson's mask, Bain circuit, face masks, laryngoscopes with Macintosh blades, cuffed/un-cuffed endotracheal tubes, stylets, bougies
- Suction apparatus
- Syringes and gloves
- Resuscitation equipment was readily available.

Postoperative Care

Patients were monitored in the recovery room for hemodynamic stability and any adverse events before being transferred to the ward.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25. Quantitative variables were expressed as mean ± standard deviation (SD) or median ± interquartile range (IQR). Qualitative variables were presented as frequencies and percentages. Statistical comparisons between groups were made using appropriate tests (e.g., Student's t-test, Chi-square test). A p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethical Committee of Jaipur National University Institute of Medical Sciences and Research Centre. Written informed consent was obtained from all participants. Patient confidentiality was maintained, and data were used exclusively for research purposes

RESULTS

A total of 60 patients were enrolled in the study, evenly divided into two groups of 30 each. Group A received 100 µg of oral clonidine, while Group B received 150 µg. The demographic and baseline characteristics are summarized in Table 1. The mean age was significantly lower in Group B (33.73 ± 11.09 years) compared to Group A (39.67 ± 10.49 years, $p = 0.03$). However, there were no significant differences between the groups regarding gender distribution, body mass index (BMI), or American Society of Anesthesiologists (ASA) physical status classification.

Hemodynamic Parameters

Systolic blood pressure (SBP) readings at various time intervals are presented in Table 2. Baseline SBP and SBP after premedication showed no significant differences between the groups. However, at the time of induction, Group B exhibited a significantly higher SBP compared to Group A (107.57 ± 6.04 mm Hg vs. 102.40 ± 11.66 mm Hg, $p = 0.03$). This trend continued immediately after intubation and at 1, 3, and 5 minutes post-intubation, with Group B consistently showing higher SBP readings ($p < 0.001$). No significant differences were observed at 10 and 15 minutes post-intubation.

Heart rate (HR) measurements are detailed in Table 3. There were no significant differences in baseline HR between the groups. Similar to SBP, Group B had significantly higher HR at induction (81.77 ± 10.88 beats/min) compared to Group A (76.17 ± 9.30 beats/min, $p = 0.045$). This significant difference persisted immediately after intubation and at 1, 3, and 5 minutes post-intubation ($p < 0.01$). By 10 and 15 minutes post-intubation, HR differences were no longer significant.

Side Effects

The incidence of side effects is summarized in Table 4. Hypotension occurred in 4 patients (13.3%) in Group A and 8 patients (26.7%) in Group B, but this difference was not statistically significant ($p = 0.19$). Pruritus was observed in 1 patient (3.3%) in Group B and none in Group A ($p > 0.05$). Shivering was reported in 2 patients (6.7%) in Group A and 1 patient (3.3%) in Group B, with no significant difference between the groups.

Analgesic Requirements

As shown in Table 5, a significantly lower number of patients in Group B required rescue analgesia at 6 hours postoperatively compared to Group A (3 patients [10%] vs. 25 patients [83.3%], $p < 0.001$). This suggests a potential analgesic benefit with the higher dose of clonidine.

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Table 1: Demographic and Baseline Characteristics of Patients

Parameter	Group A (Clonidine 100 µg) n=30	Group B (Clonidine 150 µg) n=30	*p*-value
Age (years, mean ± SD)	39.67 ± 10.49	33.73 ± 11.09	0.03*
Age Groups, n (%)			
- <30 years	6 (20%)	12 (40%)	0.21
- 31–45 years	14 (46.7%)	12 (40%)	
- 46–55 years	10 (33.3%)	6 (20%)	
Gender, n (%)			
- Male	18 (60%)	20 (66.7%)	0.59
- Female	12 (40%)	10 (33.3%)	
Body Mass Index (BMI), n (%)			0.17
- Normal (18.5–22.9 kg/m²)	11 (36.7%)	5 (16.7%)	
- Overweight (23–24.9 kg/m²)	14 (46.7%)	16 (53.3%)	
- Obese (>25 kg/m²)	5 (16.7%)	9 (30%)	
ASA Physical Status, n (%)			0.28
- I	21 (70%)	17 (56.7%)	
- II	9 (30%)	13 (43.3%)	

Table 2: Systolic Blood Pressure (SBP) at Different Time Intervals

Time Interval	Group A (Mean ± SD)	Group B (Mean ± SD)	*p*-value
Baseline (Pre-op)	120.23 ± 5.89	121.00 ± 5.08	0.72
After Premedication	119.40 ± 13.00	116.80 ± 11.79	0.40
At Induction	102.40 ± 11.66	107.57 ± 6.04	0.03*
Immediately After Intubation	101.70 ± 7.34	112.23 ± 5.03	<0.001*
1 Minute Post-Intubation	96.70 ± 6.83	104.87 ± 4.21	<0.001*
3 Minutes Post-Intubation	92.57 ± 6.53	98.77 ± 3.29	<0.001*
5 Minutes Post-Intubation	89.70 ± 6.53	95.97 ± 3.24	<0.001*
10 Minutes Post-Intubation	111.97 ± 13.91	115.20 ± 11.78	0.33
15 Minutes Post-Intubation	112.60 ± 13.17	116.67 ± 11.05	0.20

Table 3: Heart Rate (HR) at Different Time Intervals

Time Interval	Group A (Mean ± SD)	Group B (Mean ± SD)	*p*-value
Baseline (Pre-op)	79.23 ± 3.89	80.03 ± 4.08	0.74
After Premedication	85.97 ± 9.66	83.90 ± 10.86	0.44
At Induction	76.17 ± 9.30	81.77 ± 10.88	0.045*
Immediately After Intubation	72.23 ± 9.37	85.57 ± 11.22	0.006*
1 Minute Post-Intubation	66.97 ± 8.42	81.67 ± 9.45	0.001*
3 Minutes Post-Intubation	62.83 ± 7.52	80.30 ± 8.53	0.01*
5 Minutes Post-Intubation	57.77 ± 7.29	78.73 ± 7.69	0.01*
10 Minutes Post-Intubation	71.83 ± 10.49	73.37 ± 15.49	0.65
15 Minutes Post-Intubation	71.23 ± 9.47	74.10 ± 13.51	0.34

Table 4: Side Effects Observed in Both Groups

Side Effect	Group A (n=30)	Group B (n=30)	*p*-value
Hypotension	4 (13.3%)	8 (26.7%)	0.19
Pruritus	0 (0%)	1 (3.3%)	>0.05
Shivering	2 (6.7%)	1 (3.3%)	>0.05

Table 5: Need for Rescue Analgesia at 6 Hours Postoperatively

Need for Rescue Analgesia	Group A (n=30)	Group B (n=30)	*p*-value
Yes	25 (83.3%)	3 (10%)	<0.001*
No	5 (16.7%)	27 (90%)	

DISCUSSION

The present study aimed to compare the efficacy of two doses of oral clonidine—100 µg and 150 µg—administered 90 minutes before surgery in attenuating haemodynamic responses during endotracheal intubation. Our findings indicate that the lower dose of clonidine (100 µg) was more effective in stabilizing systolic blood pressure (SBP) and heart rate (HR)

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during induction and intubation compared to the higher dose (150 µg).[9]

Contrary to the expectation that a higher dose would provide better haemodynamic stability, Group B (150 µg clonidine) exhibited higher SBP and HR readings immediately after intubation and in the subsequent minutes. This suggests that increasing the dose beyond 100 µg may not confer additional benefits and could potentially lead to diminished efficacy. Similar observations were reported by Parikh et al. (2015), who found that escalating doses of clonidine did not proportionally enhance haemodynamic control during laryngoscopy and intubation[9,10]

One possible explanation for the diminished efficacy at higher doses is the saturation of central alpha-2 adrenergic receptors, beyond which additional clonidine may not produce further sympatholytic effects. Moreover, higher doses could stimulate peripheral alpha-1 receptors, leading to vasoconstriction and counteracting the desired haemodynamic effects[11,12].

The higher incidence of hypotension in Group B, although not statistically significant, raises concerns about the safety profile of the 150 µg dose. Hypotension can compromise organ perfusion, particularly in patients with limited cardiovascular reserve. Khan et al. (2016) also reported an increased risk of hypotension with higher doses of clonidine, emphasizing the need for careful dose selection[13].

Interestingly, Group B required significantly less rescue analgesia postoperatively, indicating enhanced analgesic benefits with the higher dose. Clonidine's analgesic properties are well-documented and are attributed to its action on alpha-2 adrenergic receptors in the spinal cord, which inhibit nociceptive neurotransmission[12]. This aligns with the findings of Bajwa et al. (2012), who demonstrated improved postoperative analgesia with higher doses of clonidine.[13]

These findings highlight the complex pharmacodynamics of clonidine, where a balance must be struck between haemodynamic stability and analgesic efficacy. While a higher dose may enhance analgesia, it does not necessarily improve haemodynamic control and may increase the risk of adverse effects.

Limitations

This study has limitations that should be considered. The sample size was relatively small and conducted at a single center, which may affect the generalizability of the results. Additionally, we did not assess sedation levels or measure plasma catecholamine levels, which could provide deeper insights into the pharmacological effects of clonidine at different doses.

Future Directions

Further research with larger, multicenter trials is necessary to confirm these findings and establish optimal dosing guidelines. Studies exploring intermediate doses between 100 µg and 150 µg could help identify a dose that offers both haemodynamic stability and analgesic benefits with minimal adverse effects. Monitoring additional parameters such as sedation scores and catecholamine levels could enhance our understanding of clonidine's dose-response relationship.

CONCLUSION

In conclusion, administering 100 µg of oral clonidine 90 minutes prior to surgery is more effective in attenuating haemodynamic responses during endotracheal intubation compared to a 150 µg dose. While the higher dose provides better postoperative analgesia, it does not enhance haemodynamic stability and may increase the risk of hypotension. Therefore, a lower dose of clonidine may be preferable for patients where haemodynamic control during intubation is the primary concern.

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