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Research Article

Comparative Efficacy of Oral Clonidine versus Intravenous Esmolol for Attenuating the Pressor Response to Laryngoscopy and Tracheal Intubation: A Randomised Controlled Trial

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ABSTRACT

Background: Direct laryngoscopy and endotracheal intubation elicit a brisk sympathetic surge that may precipitate myocardial ischaemia or cerebrovascular events in high-risk patients. Although several pharmacologic strategies exist, the relative effectiveness of an α₂-agonist versus an ultra-short-acting ß-blocker in routine elective surgery remains uncertain.

Objective: To compare the haemodynamic-stabilising efficacy and safety of oral clonidine (2 μg kg^{-1}) and intravenous esmolol (0.5 mg kg^{-1}) administered before anaesthetic induction.

Methods: In this single-centre, parallel-group trial, 116 ASA I–II adults (18–60 y) scheduled for elective surgery under general anaesthesia were randomised to receive clonidine 90 min pre-induction (Group C, n = 58) or esmolol 90 s pre-intubation (Group E, n = 58). Standardised anaesthesia (fentanyl–propofol–atracurium, sevoflurane MAC 1·0) was used. Heart rate (HR), systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP) were recorded at baseline, post-induction, immediately after intubation, and 1, 3, 5, 7 and 10 min thereafter. Primary end-points were peak HR and SBP within 3 min of intubation.

Results: Baseline variables were comparable. Peak HR (mean ± SD) rose to 92 ± 6 bpm in Group E but fell to 66 ± 5 bpm in Group C ($p < 0.001$). Corresponding SBP values were 143 ± 8 vs 116 ± 8 mmHg ($p < 0.001$). MAP, DBP and rate-pressure product followed similar patterns. Haemodynamics in Group C returned to baseline by 10 min; Group E remained significantly elevated. No clinically important bradycardia, bronchospasm or hypotension occurred.

Conclusions: A single pre-operative oral dose of clonidine 2 μg kg^{-1} provides superior attenuation of intubation-induced tachycardia and hypertension compared with esmolol 0.5 mg kg^{-1}. Clonidine is a simple, inexpensive, and well-tolerated option for routine adult elective surgery.

Keywords: Clonidine, Esmolol, Laryngoscopy, Intubation Stress Response, Haemodynamics, Randomised Trial.

INTRODUCTION

The sympathoadrenal response to laryngoscopy and tracheal intubation—first delineated (1)—induces abrupt tachycardia and hypertension via glossopharyngeal- and vagus-mediated afferents that trigger a diffuse catecholaminergic discharge. While short-lived in healthy subjects, this surge can provoke myocardial ischaemia, aneurysmal rupture, or raised intracranial pressure in vulnerable populations (2). Pharmacologic blunting with opioids, lignocaine, vasodilators, calcium-channel blockers, β-blockers, or α₂-agonists has been explored, yet each agent carries limitations such as respiratory depression, rebound hypertension, or bronchospasm. Clonidine, a centrally acting α₂-agonist, decreases sympathetic outflow, enhances baroreflex sensitivity, yields anxiolysis and mild sedation, and lowers anaesthetic and opioid requirements (3). Esmolol, an ultra-short-acting cardio-selective β-blocker, rapidly reduces heart rate and contractility without prolonged post-operative bradycardia (4).

Prior head-to-head comparisons are scarce and report conflicting outcomes, often confounded by heterogeneous dosing or concomitant drugs (5). Recognising this gap, we conducted a rigorously standardised randomised trial to determine whether oral clonidine or intravenous esmolol more effectively mitigates peri-intubation haemodynamic perturbations in ASA I–II adults undergoing elective surgery. We hypothesised that clonidine would offer equivalent or superior attenuation of peak HR and SBP compared with esmolol, without increasing adverse events.

METHODS

Study design and ethics

Prospective, randomised, open-label, parallel-group study conducted at Breach Candy Hospital Trust, Mumbai (January 2022 – April 2023). Ethics Committee approval (BCHT/IEC/21-523) and written informed consent were obtained. Trial registration: CTRI/2022/12/045678.

Participants

Inclusion: adults 18–60 y, ASA I–II, elective surgery requiring endotracheal intubation. Exclusion: BMI > 30 kg m^{-2}, anticipated difficult airway, pregnancy, β-blocker/α₂-agonist therapy, cardiovascular instability, OSA, or allergy to study drugs.

Randomisation and masking

Computer-generated blocks (1:1) assigned 116 participants to Clonidine (Group C) or Esmolol (Group E). Allocation was concealed in sealed opaque envelopes; investigators recording data were blinded to group. Anaesthetists could not be blinded due to dosing schedules.

Interventions

- **Group C:** Tablet clonidine 2 μg kg^{-1} (rounded to nearest 25 μg) with 30 mL water, administered in the ward 90 min pre-induction.
- **Group E:** Esmolol 0.5 mg kg^{-1} (10 mg mL^{-1}) given as an intravenous bolus over 30 s, 90 s pre-intubation.

Anaesthesia protocol

Premedication: glycopyrrolate 0.004 mg kg^{-1} IM and ondansetron 0.08 mg kg^{-1} IV 30 min pre-OR. Standard monitoring (ECG, SpO_2, NIBP). Induction: fentanyl 2 μg kg^{-1}, propofol 2 mg kg^{-1}. Neuromuscular block: atracurium 0.5 mg kg^{-1}. Laryngoscopy with McCoy blade; intubation within 20 s by an anaesthetist with >3 y experience. Anaesthesia maintenance: sevoflurane MAC 1.0 in 66 % N_2O/O_2; controlled ventilation. No additional β-blockers, α₂-agonists or lignocaine were allowed intra-operatively.

Outcomes

Primary: peak HR and SBP observed from intubation to 3 min post-intubation. Secondary: DBP, MAP, rate-pressure product (RPP), return-to-baseline time, and adverse events (HR < 50 bpm, SBP < 90 mmHg, bronchospasm, nausea).

Data collection

Haemodynamic variables recorded: baseline (T_{-10 min}), post-induction, immediately after intubation (T₀), and T₁, T₃, T₅, T₇, T₁₀ min.

Sample-size calculation

Using mean ± SD SBP values (140 ± 22 vs 130 ± 16 mmHg) from Bhavani et al., a difference of 10 mmHg, α 0.05, power 0.8 required 52 patients per arm. Allowing 10 % attrition, 58 per group were recruited.

Statistical analysis

SPSS v21.0. Continuous data: mean ± SD; compared with unpaired t-test or repeated-measures ANOVA with Bonferroni correction. Categorical data: χ^2 test. $p < 0.05$ denoted significance.

RESUL

Table 1. Baseline demographics

Variable	Clonidine (n = 58)	Esmolol (n = 58)	p value
Age, y (mean ± SD)	37.6 ± 12.4	40.3 ± 13.3	0.25
Male, n (%)	34 (59)	30 (52)	0.56
BMI, kg m^{-2}	23.1 ± 3.7	22.8 ± 3.2	0.61
ASA II, n (%)	25 (43)	27 (47)	0.68

Table 2. Haemodynamic variables (mean ± SD)

Time-point	HR (bpm)	SBP (mmHg)	MAP (mmHg)
Baseline	84 ± 6 vs 81 ± 9	131 ± 8 vs 130 ± 7	94 ± 8 vs 93 ± 6
Post-induction	67 ± 5 vs 95 ± 7 *	116 ± 8 vs 140 ± 7 *	89 ± 7 vs 105 ± 4 *
Peak (T_1)	66 ± 5 vs 92 ± 6 *	117 ± 8 vs 143 ± 8 *	84 ± 7 vs 98 ± 5 *
T_{10}	70 ± 6 vs 97 ± 7 *	121 ± 7 vs 148 ± 9 *	90 ± 6 vs 106 ± 5 *

*p < 0.001 between groups

- HR and SBP decreased below baseline in Group C post-induction and remained blunted throughout 10 min.
- Group E exhibited significant HR and BP surges peaking at T_1 and persisting to T_{10} ($p < 0.001$).
- RPP mirrored HR/SBP, remaining <9 000 mmHg·bpm in Group C vs >13 000 in Group E.

Adverse Events

No patient required atropine or vasopressor support. Two patients in Group C reported mild dry mouth in recovery; none experienced excessive sedation (Ramsay > 3). No bronchospasm or PONV differences observed.

DISCUSSION

In this adequately powered randomised study, oral clonidine 2 μg kg^{-1} produced a clinically and statistically superior blunting of tachycardia and hypertension associated with laryngoscopy and intubation compared with an evidence-based esmolol bolus of 0.5 mg kg^{-1}. Haemodynamic stability in the clonidine arm was evident immediately after induction and persisted for at least 10 min, with values returning to baseline by T_{10}, whereas esmolol merely tempered heart-rate rise but failed to prevent appreciable blood-pressure elevations.

Our findings corroborate and extend earlier work. Intravenous clonidine 0.6–1.25 μg kg^{-1} attenuated intubation responses more effectively than placebo (3), while intravenous clonidine 3 μg kg^{-1} was superior to esmolol 2 mg kg^{-1} (5). The present trial differs by using an inexpensive oral dose, facilitating day-case and ward administration. The 90-min lead-time aligns with clonidine's *t*_{max}, ensuring peak central sympatholysis at induction. Conversely, despite esmolol's rapid onset, the single 0.5 mg kg^{-1} bolus chosen to minimise hypotension was insufficient to restrain pressor surges; higher doses (1–2 mg kg^{-1}) described earlier (4) mitigate blood-pressure rises more effectively but are often accompanied by bradycardia and negative inotropy.

Mechanistically, clonidine augments the baroreceptor reflex, reduces central sympathetic drive, and diminishes plasma catecholamines, thereby lowering both HR and systemic vascular resistance. Esmolol's sole β_1-blockade curtails chronotropy and inotropy but leaves α-mediated vasoconstriction unchecked, explaining the divergent SBP/MAP trends. Importantly, neither regimen caused clinically significant hypotension or bradyarrhythmia in our ASA I–II cohort, highlighting safety at these doses.

Limitations include the open-label design (though outcome assessors were blinded); absence of invasive arterial monitoring (non-invasive BP at 1-min intervals may miss transient peaks); exclusion of high-risk hypertensive or cardiac patients limits external validity; and lack of plasma catecholamine assays. Future work should compare combined low-dose esmolol + clonidine, evaluate recovery profiles, and include objective stress biomarkers.

CONCLUSION

Oral clonidine 2 μg kg^{-1} administered 90 min before induction provides superior haemodynamic stability during laryngoscopy and intubation compared with a standard esmolol bolus, without excess adverse effects. Incorporating clonidine into pre-operative protocols may enhance patient safety, especially in settings lacking invasive monitoring or in resource-limited environments.

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