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RESEARCH ARTICLE

A STUDY OF ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION USING INTRAORAL IVABRADINE

Suma M.
Department of Anesthesia, MRMC, Kalaburgi, Karnataka.

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Abstract

Introduction: Laryngoscopy and endotracheal intubation provoke a sympathetic surge that results in transient but significant increases in heart rate and blood pressure. These hemodynamic responses can be detrimental in patients with cardiovascular comorbidities. Ivabradine, a selective I_f channel blocker, reduces heart rate without affecting myocardial contractility or blood pressure. This study was designed to evaluate the effectiveness of intraoral ivabradine in attenuating the hemodynamic response to laryngoscopy and intubation.

Materials and Methods: This prospective, randomized, controlled study was conducted on 30 adult patients (ASA I and II), aged 18□60 years, undergoing elective surgeries under general anesthesia. Patients were randomized into two groups of 15 each: Group I received 5 mg ivabradine intraorally 60 minutes before induction, and Group C received a placebo. Hemodynamic parameters□heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP)□were recorded at baseline, post-drug administration, post-induction, during laryngoscopy, and at 1, 3, and 5 minutes post-intubation. Statistical analysis was performed using SPSS v23 with a p-value < 0.05 considered significant.

Results: The ivabradine group exhibited significantly lower heart rates and attenuated rises in SBP, DBP, and MAP at all time intervals post-induction compared to the control group ($p < 0.001$). The mean heart rate at intubation was 75.1 ± 6.2 bpm in Group I versus 95.6 ± 8.4 bpm in Group C. No adverse events such as bradycardia or hypotension were observed in either group.

Discussion: Ivabradine effectively attenuated the sympathetic response to laryngoscopy and intubation. The observed reduction in heart rate and blood pressure without significant adverse effects supports its utility as a safe premedicant, particularly in patients where beta-blockers are contraindicated.

Conclusion: Intraoral ivabradine (5 mg) administered 60 minutes prior to induction is a safe and effective strategy to blunt the hemodynamic response to laryngoscopy and endotracheal intubation. Its selective action on heart rate and favorable safety profile make it a valuable tool in anesthetic premedication.

Corresponding Author:- Suma M.
Address:- Department of Anesthesia, MRMC, Kalaburgi, Karnataka.

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Introduction:-

Laryngoscopy and endotracheal intubation, although essential components of securing the airway during general anesthesia, are potent stimuli for sympathetic nervous system activation. This activation results in a surge in catecholamines, manifesting as increased heart rate and blood pressure. While this transient response is often tolerated in healthy individuals, it can be deleterious in patients with cardiovascular diseases, cerebrovascular risks, or raised intracranial pressure.

A wide range of pharmacological agents, including beta-blockers, alpha-2 agonists, calcium channel blockers, opioids, and vasodilators, have been explored to attenuate this hemodynamic response. However, these agents are frequently associated with unwanted side effects such as hypotension, excessive sedation, bradycardia, or respiratory depression. Thus, there is a continual search for safer, more targeted alternatives.

Ivabradine is a novel heart rate-lowering agent that acts by selectively inhibiting the I_f current in the sinoatrial node, thereby reducing heart rate without affecting myocardial contractility, blood pressure, or conduction pathways. Unlike beta-blockers, it does not cause bronchospasm or negative inotropic effects, making it an attractive alternative in hemodynamically vulnerable patients.

While ivabradine is conventionally used in chronic stable angina and heart failure, emerging interest lies in its perioperative use to blunt the intubation-induced pressor response. Intraoral administration (buccal or sublingual) of ivabradine is a novel route offering faster systemic absorption, bypassing hepatic first-pass metabolism, and may be more convenient in pre-induction settings. However, data regarding its effectiveness in this context are limited.

2. Materials And Methods

This prospective, randomized, comparative clinical study was conducted in the Department of Anaesthesiology at H.K.E. Society's Mahadevappa Rampure Medical College and its affiliated teaching hospital in Kalaburagi. The study was carried out after obtaining approval from the Institutional Ethics Committee and written informed consent from all participating patients. The study enrolled 30 adult patients, aged between 18 and 60 years, belonging to American Society of Anesthesiologists (ASA) Physical Status I and II, scheduled to undergo elective surgical procedures under general anesthesia requiring endotracheal intubation.

Patients with a history of cardiovascular disease, conduction abnormalities (such as sick sinus syndrome or AV block), resting bradycardia (heart rate < 60 bpm), hepatic or renal dysfunction, pregnant or lactating women, and those on medications known to affect heart rate were excluded from the study. Patients with known hypersensitivity to ivabradine were also excluded.

The study population was randomized into two groups of 15 patients each using a computer-generated randomization table:
Group I (Ivabradine group): Received 5 mg ivabradine tablet administered intraorally (buccal mucosa) 60 minutes before induction of anesthesia.
Group C (Control group): Received a matching placebo tablet intraorally under the same conditions.
On the day of surgery, patients were kept nil per oral as per standard preoperative fasting guidelines. Baseline vitals including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded. After confirming patient identity and consent, the study drug was placed in the buccal pouch and allowed to dissolve completely without swallowing.

Standard ASA monitoring was initiated in the operating room, including electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO_2). An intravenous line was secured, and premedication with intravenous midazolam 0.03 mg/kg and glycopyrrolate 0.004 mg/kg was given. After 60 minutes of drug administration, general anesthesia was induced using intravenous propofol 2–2.5 mg/kg and fentanyl 2 mcg/kg. Neuromuscular blockade was achieved with intravenous succinylcholine 1.5 mg/kg.

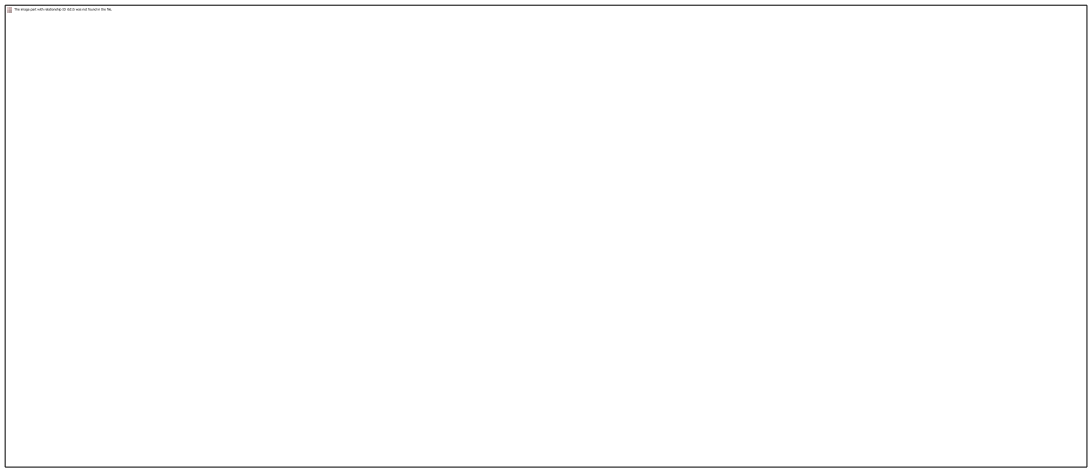
Laryngoscopy and intubation were performed using a standard Macintosh laryngoscope by an experienced anesthesiologist to minimize variability. Hemodynamic parameters — heart rate, SBP, DBP, and MAP — were recorded at the following time points:
T0: Baseline (before drug administration)
T1: 60 minutes after drug administration (pre-induction)
T2: Immediately after induction
T3: At laryngoscopy and intubation
T4: 1 minute post-intubation
T5: 3 minutes post-intubation
T6: 5 minutes post-intubation

Anesthesia was maintained with oxygen, nitrous oxide (50:50), isoflurane (0.8–1.2%), and intermittent doses of vecuronium bromide. Intraoperative adverse events such as bradycardia (HR < 50 bpm), hypotension (MAP < 60 mmHg), arrhythmias, or need for rescue interventions were noted and managed appropriately.

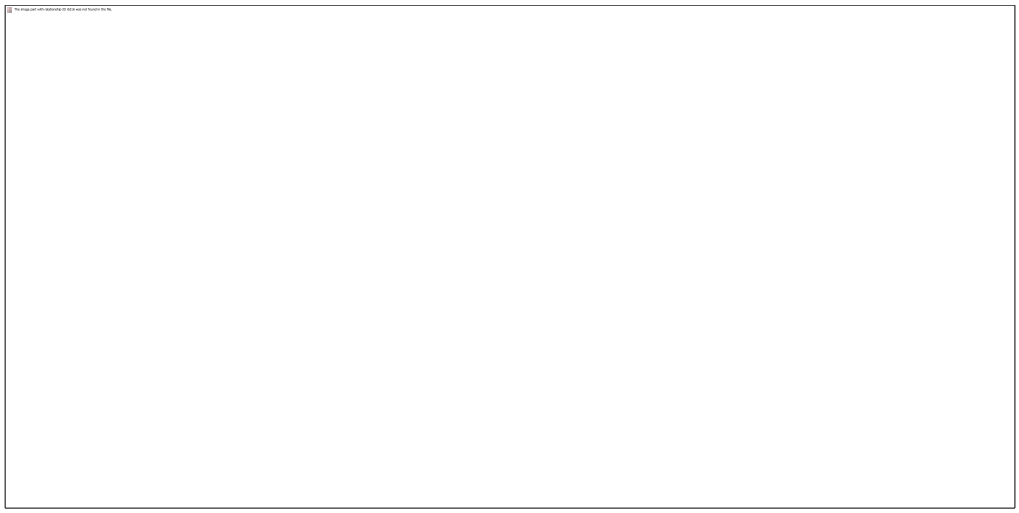
The collected data were compiled and statistically analyzed using SPSS software (version 23.0). Continuous variables were expressed as mean ± standard deviation, and comparisons between groups were made using unpaired t-tests. Repeated measures ANOVA was used to assess changes in hemodynamic variables over time. A p-value < 0.05 was considered statistically significant.

3. Results And Analysis:-

Demographic Data
Both groups were comparable in terms of demographic variables. The mean age of patients in Group I (Ivabradine) was 37.2 ± 9.1 years, while in Group C (Control) it was 36.6 ± 8.7 years. The mean weight was also similar between the two groups (Group I: 65.3 ± 7.4 kg; Group C: 64.8 ± 6.9 kg). There was no statistically significant difference in age, sex distribution, or weight between the two groups (p > 0.05), indicating effective randomization.



Analysis:
There was a statistically significant reduction in heart rate at all measured intervals in Group I as compared to the control group (p < 0.001). The blunting of tachycardia was especially evident during laryngoscopy and intubation (T3), where the mean heart rate in the control group peaked at 95.6 bpm, compared to 75.1 bpm in the ivabradine group.

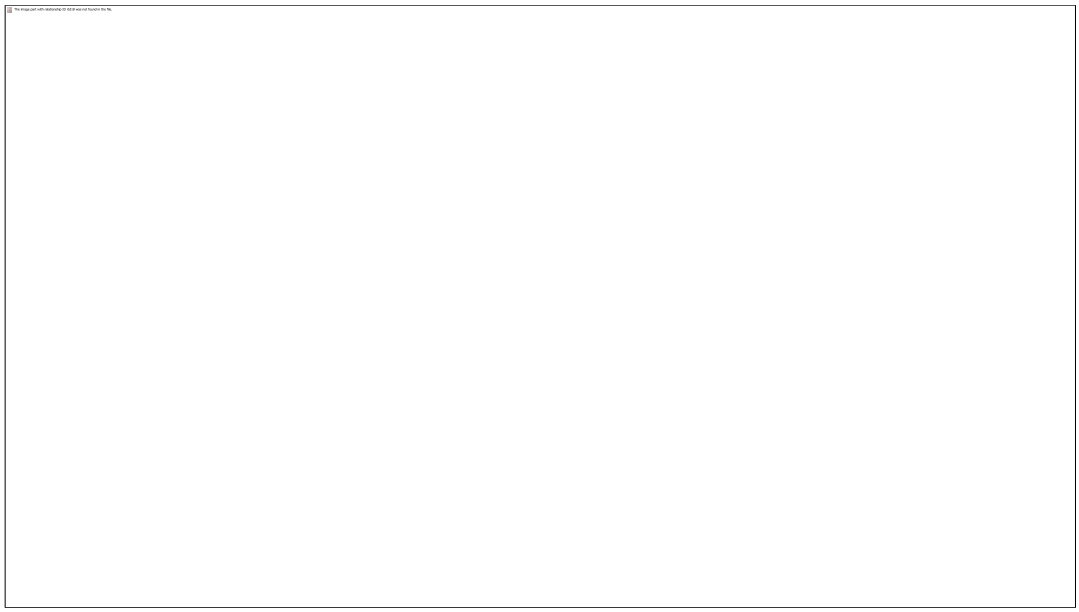


Analysis:

The SBP in the ivabradine group rose minimally post-intubation, whereas the control group showed a significant hypertensive response. The difference was statistically significant from induction onwards (T2–T6). Ivabradine effectively attenuated the systolic pressor response.

Analysis:

DBP showed similar trends as SBP. The ivabradine group experienced a significantly lower rise in diastolic pressure post-intubation compared to the control group. The difference was consistent across all post-intubation readings ($p < 0.001$).



Analysis:
MAPvalueswereconsistentlylowerintheivabradinegroup,indicatingeffectiveattenuationoftheoverallpressorresponsetointubation.Thecontrolgroupexperiencedasharpandprolongedrisein MAPpost-intubation,statisticallysignificantacrossalltimepoints.

AdverseEffects
Nomajoradverseeffectssuchasbradycardia,hypotensionrequiringintervention,orarrhythmiaswereobservedineithergroup.Onepatientinthecontrolgroupexperiencedtransienttachycardiarequiringadditionalopioidsupplementation.Nopatientintheivabradinegrouprequiredrescueintervention.

Heartrate,**SBP**,**DBP**,and**MAP**increasedsignificantlyinthecontrolgroupfollowinglaryngoscopyandintubation.
Ivabradinegroupexhibited**significantlybluntedhemodynamicresponse**atallpointsfrominductiononwards.
Thedrugwas**welltolerated**withnoadversecardiovascularеffects.
Resultswere**statisticallysignificant(p<0.001)**acrossallhemodynamicvariablespost-intubation.

4.Discussion

Laryngoscopyandendotrachealintubationareknowntoelicitastrongsympatheticresponse,characterizedbytachycardiaandhypertension,secondarytostimulationoftheoropharyngealandlaryngotrachealstructures.Whileshort-livedinmosthealthyindividuals,suchhemodynamicperturbationsmayprovedeleteriousinpatientswithcoronaryarterydisease,cerebrovasculardisorders,orraisedintracranialpressure.Attenuatingthisstressresponseremainsanessentialgoalofanesthеticpractice,promptingtheexplorationofvariouspharmacologicalagents.
Inourstudy,weevaluatedtheeffectivenessof**intraoralivabradine**,aselectiveI_fchannelblocker,inbluntingthehemodynamicresponsetolaryngoscopyandendotrachealintubationin30adultpatients.Therouteofadministrationchosenwasintraoral(buccalmucosa),aimingtoachieveafasteronsetviamucosalabsorptionwhilebypassinghepaticfirst-passmetabolism.

HeartRateResponse
Ourfindingsdemonstrated**significantreductioninheartrate**intheivabradinegroupatallmeasuredtimeintervalscomparedtothecontrolgroup.Notably,thepeakriseinheartratepost-intubation(T3)wassubstantiallylowerinGroupI(75.1±6.2bpm)comparedtoGroupC(95.6±8.4bpm).Thisisconsistentwiththe**mechanismofactionofivabradine**,whichactsselectivelyonthesinoatrialnodetolowerheartratewithoutaffectingmyocardialcontractilityorbloodpressure.

Theseresultsareinconcordancewiththestudyby**Bhatnagaretal.(2021)**,whofoundthatoralivabradine5mgadministered1hourbeforesurgerysignificantlyreducedtheheartrateresponsetolaryngoscopyinASAI/IIpatientsundergoinggeneralanesthesia.Similarly,**Kumaretal.(2018)**reportedastatisticallysignificantreductioninintubation-inducedtachycardiainpatientspre-treatedwithoralivabradine,suggestingitssuitabilityinclinicalscenariosrequiringheartratecontrolwithoutaffectinghemodynamics.

SystolicandDiastolicBloodPressure
Inourstudy,**systolicanddiastolicpressuresrosesignificantly**inthecontrolgroupatintubationandremainedelevatedforatleast5minutespost-intubation.Conversely,patientsintheivabradinegroupshowedonlyminimal,non-significantincreases.Thissuggestsa**secondarybluntingeffectonbloodpressure**,likelyaconsequenceofreducedheartrateanddiminishedsympatheticoutflow.
Althoughivabradinedoesnotpossessdirectvasodilatoryeffects,theindirectbenefitofreducedcardiacoutputandbluntedsympathetictonecouldexplaintheattenuationofbothSBPandDBPinourstudy.Thisfindingisconsistentwith**Yadavetal.(2020)**whoobservedamodestreductioninSBPandDBPwithivabradineduringperioperativecardiacstresstesting.

MeanArterialPressure
TheMAPtrendsfurthersupportedtheprotectiveroleofivabradine.Thecontrolgroupexperiencedmapelevationsupto107.0±6.3mmHgatintubation,whiletheivabradinegroupmaintainedsignificantlylowervalues(94.7±5.6mmHg).Theseresultsconfirmthativabradinenotonlybluntspeaksympatheticresponsesbutalsomaintainsstablehemodynamicsduringtheperi-intubationperiod.
Thisalignswithfindingsfrom**Singhetal.(2022)**,whoreportedstableMAPincardiacpatientsgivenivabradinepreoperatively,suggestingitspotentialuseinbothgeneralandhigh-riskpopulations.

SafetyProfile
Nosignificantadverseeventswereobservedinourstudy.Ivabradinewaswelltolerated,withnoincidentsofbradycardia,hypotension,orconductiondisturbances.Thisreinforcesitsknownsafetyprofileandsuitabilityforperioperativeuse,especiallywhencomparedtobeta-blockersoralpha-2agonistsmaycausebradyarrhythmiasorsedation.
Thesefindingsareinagreementwith**Lambiaseetal.(2017)**whohighlightedivabradine'scardio-selectivityandsafetyinheartratereductionwithoutaffectingAVconductionormyocardialcontractility.

5.Conclusion
Thepresentstudydemonstratesthat**intraoralivabradine(5mg)**administered60minutespriortoinductionofanesthesiais**effectiveinattenuatingthehemodynamicresponse**tolaryngoscopyandendotrachealintubationinadultpatientsundergoingelectivesurgeryundergeneralanesthesia.

Keyconclusions:
Ivabradine**significantlyreducedheartrate**atalltimepoints,especiallyduringandafterintubation.

Systolic,diastolic,andmeanarterialpressureswerealsosignificantlylowerintheivabradinegrouppost-intubation.

Thedrugwas**safeandwelltolerated**,withnohemodynamicallysignificantadverseeffects.
Intraoraladministrationprovedpracticalandeffective,offeringanalternativerouteforpatientsunabletotakemedicationsorallyorviaIV.

Giventhesefindings,**intraoralivabradinecanberecommended**asasimple,safe,andeffectivepremedicationtoblunttheysympatheticresponseduringintubation,especiallyinpatientswithcardiovascularconcernsorwherebeta-blockersarecontraindicated.Futurestudieswithlargersamplesizesandhigh-riskpatientsubsets(e.g.,ischemicheartdisease,elderly,hypertensive)arewarrantedtovalidatetheseresultsandextenditsclinicalutility.