

Comparison of Oral Ivabradine, Oral Metoprolol and Placebo to Attenuate the Stress Response in Nasal and Laryngeal Surgeries: A Prospective, Randomized, Double Blind Study

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ABSTRACT

Introduction: Nasal surgeries like septoplasty, polypectomy and laryngeal surgeries for removal of vocal nodule, cysts etc are commonly performed. Changes in haemodynamics due to laryngoscopy and endotracheal intubation are likely to persist during these procedures. These surgeries also require blood less field. The present study was conducted to evaluate and compare the efficacy of oral metoprolol tartrate versus oral ivabradine versus placebo in attenuation of haemodynamic responses during laryngoscopy, tracheal intubation and throughout nasal and laryngeal surgeries.

Methods: This was a prospective, randomized, comparative, double blind study. Patients were randomly allocated by simple randomization into 3 groups having 30 patients in each. Neither the patient nor the investigator was aware, which patient is allocated into which group and were unaware of the drug being administered as it was given to the patient by a person not involved in the study. Data collections were carried out by investigator in a double blind manner. All the patients were explained about the anesthesia technique and written informed consent was taken. Group 1: Oral Ivabradine 5mg tablet was given orally 2 hours before induction of anaesthesia. Group 2: Oral Metoprolol tartrate 50mg tablet was given orally 2 hours before induction of anaesthesia. Group 3: Oral placebo was given 2 hours before induction of anaesthesia.

Results and Conclusion: We concluded that both the drugs can be used as an effective premedication, to attenuate the sympathetic response to laryngoscopy, endotracheal intubation, extubation and throughout nasal and laryngeal surgeries. However Metoprolol was found to have better control than Ivabradine in maintaining the vitals at all points and providing a good hypotensive effect than ivabradine.


Keywords: Ivabradine, Metoprolol, Stress Response, Nasal and Laryngeal Surgeries.

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Article History:

Received: 25-01-2019, Revised: 22-02-2019, Accepted: 17-03-2019

Access this article online	
Website: www.ijmrp.com	Quick Response code 
DOI: 10.21276/ijmrp.2019.5.2.025	

INTRODUCTION

The principal cardiovascular changes seen during laryngoscopy and tracheal intubation are increase in heart rate and blood pressure. Stimulation of tracheal and laryngeal tissue causes increase in both sympathetic and sympathoadrenal reflex activity resulting in haemodynamic stress.¹

Nasal surgeries like septoplasty, polypectomy and laryngeal surgeries for removal of vocal nodule, cysts etc are commonly performed. Changes in haemodynamics due to laryngoscopy and endotracheal intubation are likely to persist during these procedures. These surgeries also require blood less field. Haemodynamic stress response consists of an increased heart rate, increased arterial blood pressure, increased myocardial

oxygen demand, onset of dysrhythmias and increased blood glucose levels were observed during nasal and laryngeal surgery.² Choice of premedication and anesthetic techniques may influence the neurohormonal stress response by modulating pathophysiological pathways.³ Anaesthesiologists have used various measures to obtund these untoward reflexes by means of deepening of general anaesthesia⁴, topical airway anaesthesia⁵, intravenous or trans tracheal lidocaine⁶, Calcium channel blockers⁷ etc.

Ivabradine is the first member of a new group of drugs, the specific heart rate-lowering agents, to be introduced into clinical use. Ivabradine acts by selectively inhibiting the ionic current I_f ,

which modulates pacemaker activity in the sino-atrial node, providing pure heart rate reduction.⁸

“Ivabradine is a very unique drug as it is selective inhibitor of I(f) channels (funny current channels). It reduces heart rate without jeopardizing haemodynamics. Drug can be used not only in hypertensives but also in normotensives, diabetics, patients with bronchial asthma where beta blockers are contra indicated.⁹

It is an extremely selective inhibitor of funny current channel [If]. “This channel inhibition results in diminution in the slope of spontaneous depolarization, leading to prolongation of the time interval between consecutive action potentials in the SA node, thus decreasing the heart rate. This drug combine with the intracellular place of the, “If” channel and hinders it in a dose and voltage dependent manner. As the binding site is situated intracellular, ivabradine needs an open, “If” channel to reach to its required site. Ivabradine reduces the heart rate without altering hemodynamics in unhealthy patients. This drug can be used in both hypertensive & normotensives.¹⁰

Metoprolol, a beta blocker is well known to control the heart rate and it acts preferentially on beta 1 adreno receptors which are located on cardiac muscle. However this preferential effect is not absolute, as metoprolol at higher doses also inhibits beta 2 adrenoreceptors located in vascular and bronchial smooth muscles.¹¹ In recent years, the role of anesthesia and its level of safety in patients have gained prime importance. Stable hemodynamics has become the key to safe and successful induction and intubation. There are many strategies used to blunt the intubation response.¹² Various studies have been performed to study efficacy of drugs on attenuating haemodynamic responses to laryngoscopy and endotracheal intubation.

By far no study has been done to compare the efficacy of oral ivabradine and oral metoprolol tartrate “the immediate release form” in nasal and laryngeal surgeries. Therefore present study was conducted to evaluate and compare the efficacy of oral metoprolol tartrate versus oral ivabradine versus placebo in attenuation of haemodynamic responses during laryngoscopy, tracheal intubation and throughout nasal and laryngeal surgeries.

AIMS AND OBJECTIVES

Aim: Aim of study was to compare oral Ivabradine, Metoprolol and Placebo to attenuate stress response during nasal and laryngeal surgeries.

Objectives: Objectives were to compare and assess these two drugs i.e ivabradine and metoprolol v/s placebo in regards to following parameters:-

- Heart rate
- Systolic blood pressure
- Diastolic blood pressure
- Mean arterial pressure
- Blood sugar level

MATERIALS AND METHODS

Type of Study

This was a prospective, randomized, comparative, double blind study.

Place of Study

It was performed in Anaesthesiology department, MGMCH, Jaipur between January 2017 and august 2018.

Inclusion Criteria

Ninety patients of age 20-50 years planned for nasal and laryngeal surgeries were included in this study.

Exclusion Criteria

- Patients not giving consent
- Patients > ASA II
- Patients on beta blockers, sedative, hypnotics, antihypertensive drugs
- Patients having diabetes mellitus
- Inability to communicate with the patient due to any reason
- Patients with history of respiratory diseases like asthma, chronic obstructive pulmonary disease
- Patients with history of chest pain, palpitations, syncope or with baseline heart rate less than 60 beats per minute
- ECG abnormalities

Methods

Routine pre-operative investigations were done for all patients. Patients were randomly allocated by simple randomization into 3 groups having 30 patients in each. Neither the patient nor the investigator was aware, which patient is allocated into which group and were unaware of the drug being administered as it was given to the patient by a person not involved in the study. Data collections were carried out by investigator in a double blind manner. All the patients were explained about the anesthesia technique and written informed consent was taken.

Group 1: Oral Ivabradine 5mg tablet was given orally 2 hours before induction of anaesthesia.

Group 2: Oral Metoprolol tartrate 50mg tablet was given orally 2 hours before induction of anaesthesia.

Group 3: Oral placebo was given 2 hours before induction of anaesthesia.

- No hypnotic or sedative drug was given to patient before surgery
- Upon arrival in operation theatre monitoring of heart rate, NIBP, SpO₂, ECG were done.
- 18 (G) intracatheter was taken on the non dominant hand and ringer lactate was started.
- Patients were given glycopyrrolate 0.2 mg, fentanyl 2mcg per kg and ondansetron 4 mg i.v as premedication.
- Patients were oxygenated with 100% oxygen for 3 mins. Induction was done with propofol 2mg per kg and tracheal intubation with succinyl choline 2mg per kg.
- Maintenance of anaesthesia was done by oxygen, nitrous oxide, isoflurane and vecuronium.
- Anesthesiologists was ready to manage hypotension with a fluid bolus of normal saline 250–300 ml and ephedrine 6-12mg i.v if needed. At end of surgery residual neuro muscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg and extubated. Parameters were recorded as per proforma.

Statistical Analysis

Data were entered in Microsoft excel worksheet. Mean and standard deviation was calculated. Appropriate statistical test (chi square, anova etc.) was done to find significant association. P value <0.05 was considered statistically significant.

Table 1: Distribution of Cases according to age group (years) all three groups

Age Group (years)	Ivabradine		Metoprolol		Placebo		Total	
	No.	%	No.	%	No.	%	No.	%
20-30	19	63.3	10	33.3	16	53.3	45	50.0
31-40	5	16.7	12	40.0	14	46.7	31	34.4
>40	6	20.0	8	26.7	0	-	14	15.6
Total	30		30		30		90	
Mean	30.10		34.93		30.70			
SD	9.97		8.97		5.96			
f			2.901					
p			0.060					

Fig 1: Distribution of Cases according to age group (years) all three groups

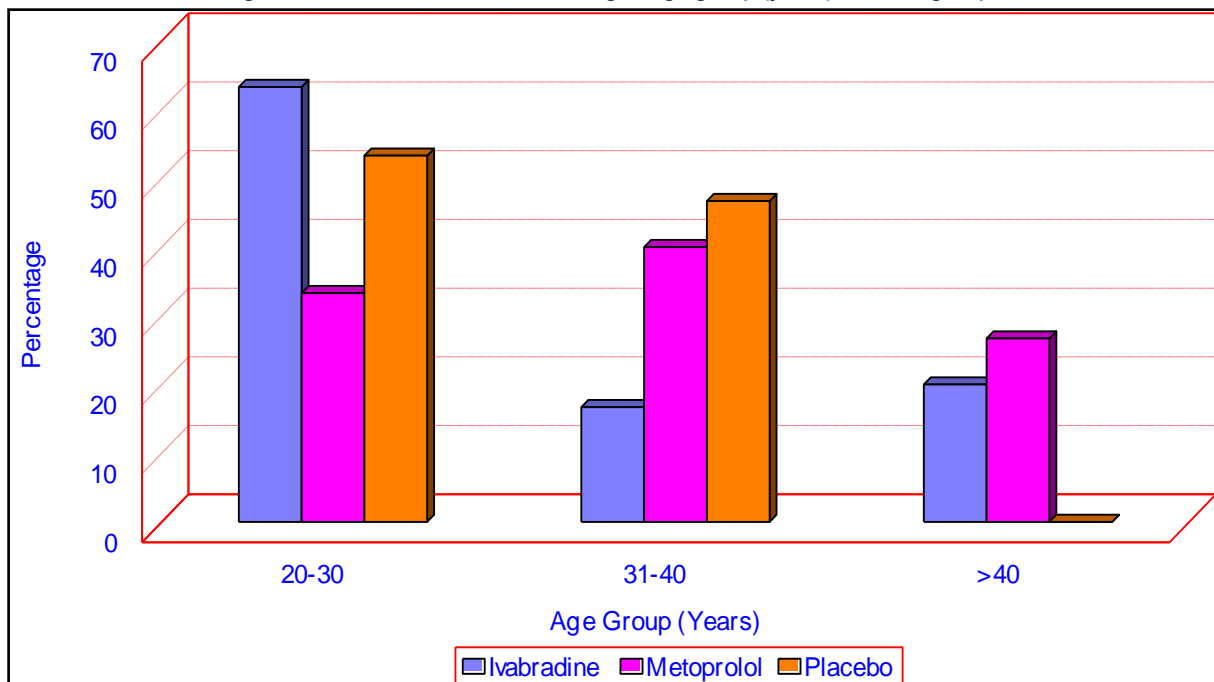


Table 2: Distribution of Cases according to surgery planned in all three groups

Surgery Planned	Group I		Group II		Group III		Total	
	No.	%	No.	%	No.	%	No.	%
External DCR	1	3.3	1	3.3	0	-	2	2.2
OPEN Septoplasty	3	10.0	0	-	0	-	3	3.3
Turbinectomy	1	3.3	0	-	0	-	1	1.1
Septoplasty with polypectomy	0	-	1	3.3	0	-	1	1.1
Endonasal DCR	2	6.7	2	6.7	0	-	4	4.4
Endonasal Polypectomy	1	3.3	0	-	0	-	1	1.1
Rhinoplasty	2	6.7	0	-	0	-	2	2.2
FESS	7	23.3	6	20.0	10	33.3	23	25.6
FESS with Septoplasty	6	20.0	2	6.7	3	10.0	11	12.2
MLS	2	6.7	3	10.0	3	10.0	8	8.9
EndoscopicSeptoplasty	5	16.7	14	46.7	13	43.3	32	35.6
χ^2			31.307					
P			0.145					

Table 3: Statistical analysis of Heart rate in all three groups

Time Interval	Group I		Group II		Group III		f	P
	Mean	SD	Mean	SD	Mean	SD		
Base Line	69.93	5.76	71.33	8.48	72.57	5.99	1.109	0.335
Just After Intubation	104.23	6.83	101.17	7.39	121.47	8.01	65.153	<0.001
1 Min	92.70	6.33	92.07	7.82	114.53	10.14	34.430	<0.001
3 Min	88.50	5.89	84.43	7.06	98.07	9.21	23.449	<0.001
5 Min	82.80	9.91	79.53	7.54	93.40	6.83	23.449	<0.001
10 Min	77.57	8.64	73.67	10.08	85.30	8.64	12.558	<0.001
15 Min	71.87	8.88	67.47	9.21	80.50	9.55	15.517	<0.001
30 Min	70.17	8.97	62.00	6.95	75.70	7.86	22.441	<0.001
45 Min	68.33	8.60	61.70	7.34	73.30	6.49	17.949	<0.001
60 Min	66.43	7.08	61.80	7.08	73.40	4.24	25.963	<0.001
90 Min	67.30	7.19	62.33	7.01	81.00	18.71	18.638	<0.001
Just After Extubation	105.20	18.43	103.40	6.89	125.87	6.50	32.658	<0.001

Fig 2: Statistical analysis of Heart rate in all three groups

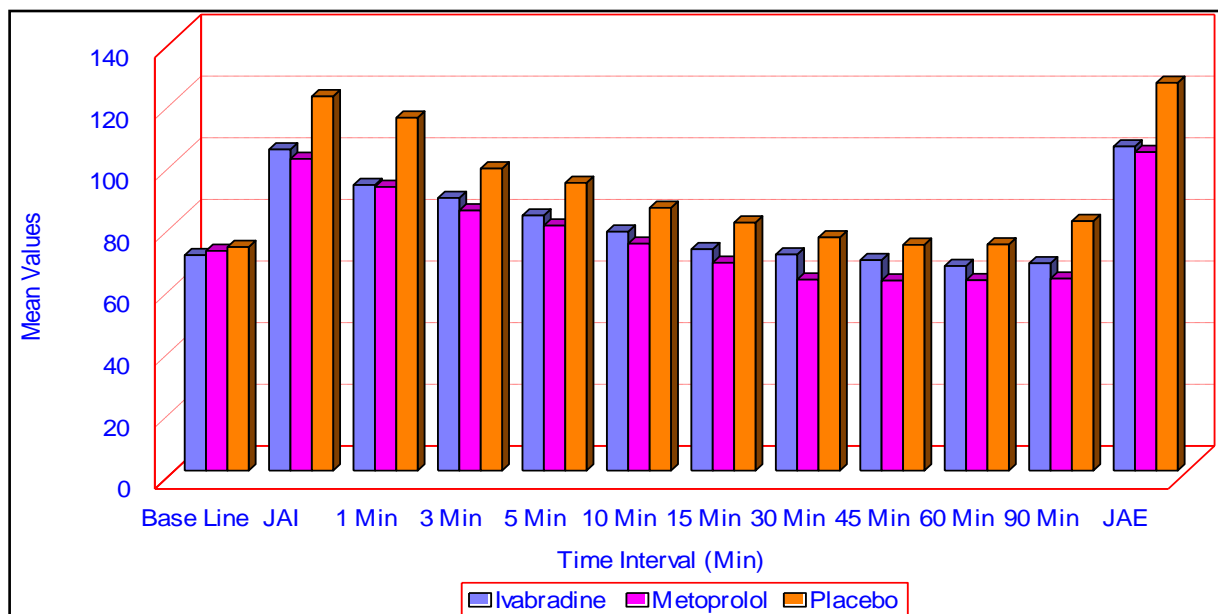


Table 4: Statistical analysis of Systolic Blood Pressure in all three groups

Time Interval	Group I		Group II		Group III		f	P
	Mean	SD	Mean	SD	Mean	SD		
Base Line	118.40	8.09	117.13	8.44	120.90	8.34	1.601	0.208
Just After Intubation	143.07	6.25	137.20	6.33	145.20	11.77	7.095	0.001
1 Min	135.40	6.35	128.13	7.24	133.00	5.94	9.637	<0.001
3 Min	130.07	6.72	121.27	8.72	127.57	6.77	11.091	<0.001
5 Min	125.80	5.88	113.80	8.98	122.60	10.93	14.806	<0.001
10 Min	119.93	8.73	103.70	9.85	116.73	6.92	30.096	<0.001
15 Min	104.90	17.84	94.87	8.04	107.80	5.07	10.135	<0.001
30 Min	98.47	8.72	88.27	6.90	104.70	6.98	35.929	<0.001
45 Min	91.13	5.19	85.40	5.71	101.33	5.07	68.785	<0.001
60 Min	90.80	5.42	84.97	5.46	102.20	5.05	81.628	<0.001
90 Min	89.27	5.16	85.53	5.06	103.90	6.27	92.811	<0.001
Just After Extubation	141.73	4.47	138.87	4.89	149.53	11.94	14.704	<0.001

Fig 3: Statistical analysis of Systolic Blood Pressure in all three groups

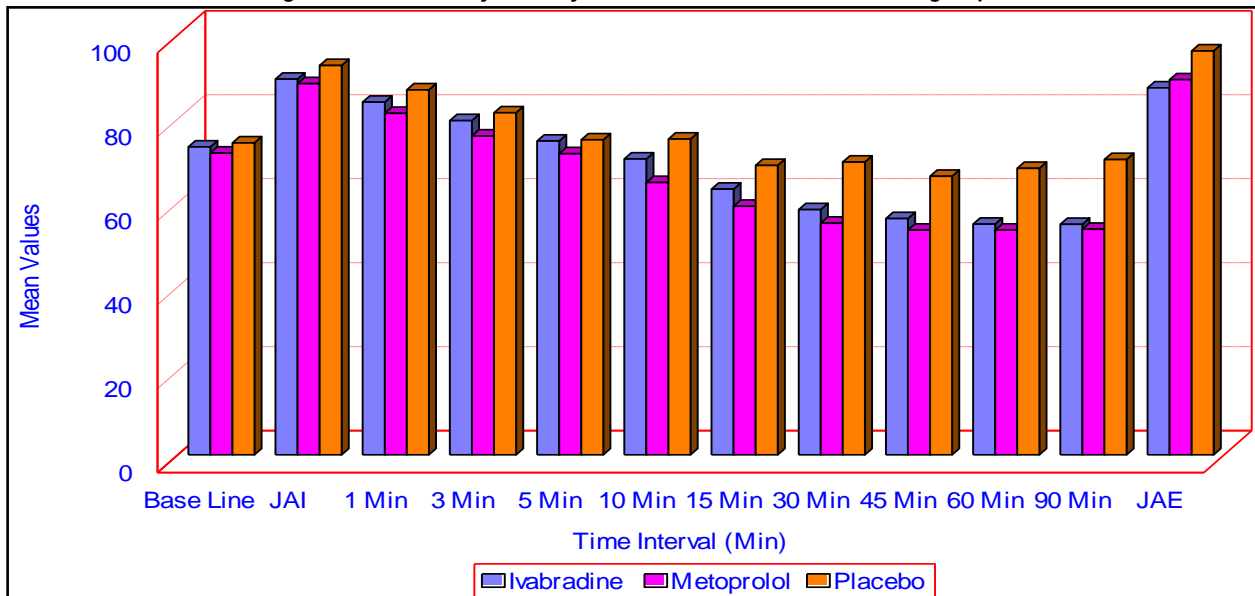


Table 5: Statistical analysis of Diastolic Blood Pressure in all three groups

Time Interval	Group I		Group II		Group III		f	P
	Mean	SD	Mean	SD	Mean	SD		
Base Line	73.33	6.81	71.87	7.61	74.30	8.44	0.769	0.466
Just After Intubation	89.47	3.71	88.40	4.44	92.73	5.44	7.268	0.001
1 Min	84.00	4.64	81.33	5.88	86.93	4.13	9.657	<0.001
3 Min	79.60	4.41	75.93	6.09	81.47	4.78	8.990	<0.001
5 Min	74.73	5.16	71.73	6.41	75.03	5.61	3.023	0.054
10 Min	70.47	6.25	64.87	4.72	75.20	6.34	23.724	<0.001
15 Min	63.27	4.94	59.20	4.77	68.93	4.60	31.461	<0.001
30 Min	58.40	4.65	55.17	4.02	69.73	4.23	94.669	<0.001
45 Min	56.27	3.66	53.53	3.39	66.33	6.45	61.516	<0.001
60 Min	54.93	3.74	53.53	4.42	68.23	3.36	132.08	<0.001
90 Min	54.90	3.60	53.73	3.98	70.33	4.14	168.07	<0.001
Just After Extubation	87.40	3.97	89.33	2.70	96.20	5.46	36.422	<0.001

Fig 4: Statistical analysis of Diastolic Blood Pressure in all three groups

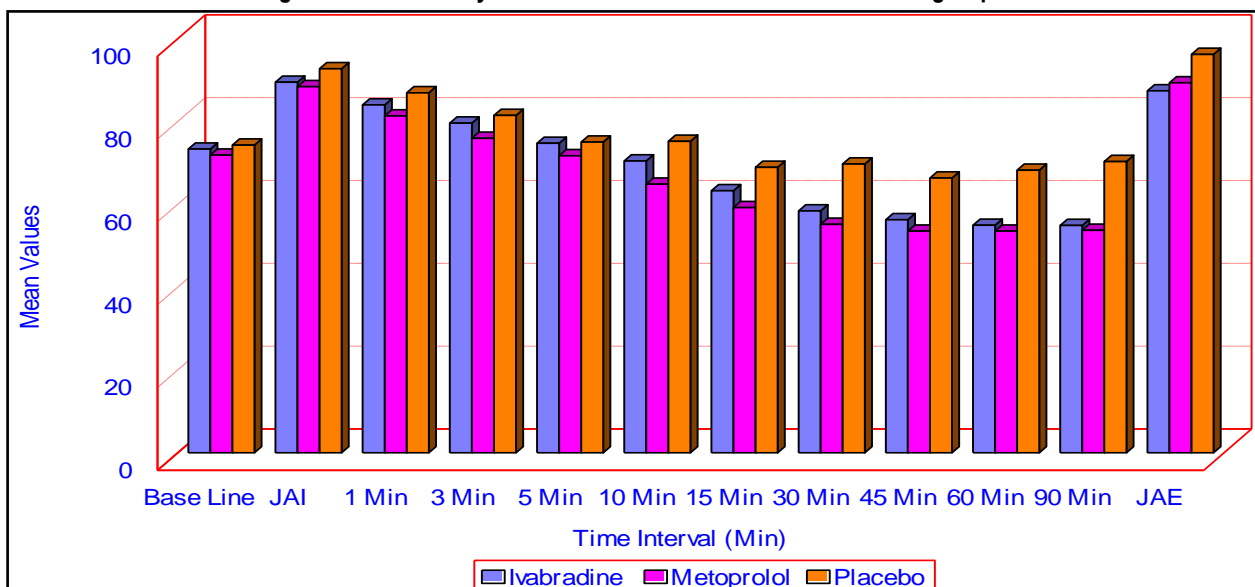


Table 6: Statistical analysis of Mean Arterial Blood Pressure in all three groups

Time Interval	Group I		Group II		Group III		f	p
	Mean	SD	Mean	SD	Mean	SD		
Base Line	88.30	6.68	87.03	7.28	89.83	7.00	1.206	0.304
Just After Intubation	107.33	3.91	104.67	4.59	110.20	6.26	9.109	<0.001
1 Min	101.20	4.62	97.03	5.51	102.33	4.23	9.934	<0.001
3 Min	96.47	4.73	91.00	6.48	96.87	4.57	11.348	<0.001
5 Min	91.73	4.66	85.70	6.74	90.83	5.15	10.172	0.054
10 Min	87.00	6.46	77.73	5.73	89.13	5.61	31.173	<0.001
15 Min	77.20	7.21	71.10	5.43	81.93	4.05	27.132	<0.001
30 Min	71.90	5.42	66.27	4.77	81.50	4.15	76.995	<0.001
45 Min	67.87	3.54	64.10	3.73	77.97	5.36	83.914	<0.001
60 Min	66.90	3.81	63.93	4.52	79.60	3.18	138.219	<0.001
90 Min	66.27	3.92	64.47	3.92	81.60	4.12	167.358	<0.001
Just After Extubation	105.43	3.38	105.73	2.82	114.40	3.95	60.764	<0.001

Fig 5: Statistical analysis of Mean Arterial Pressure in all three groups

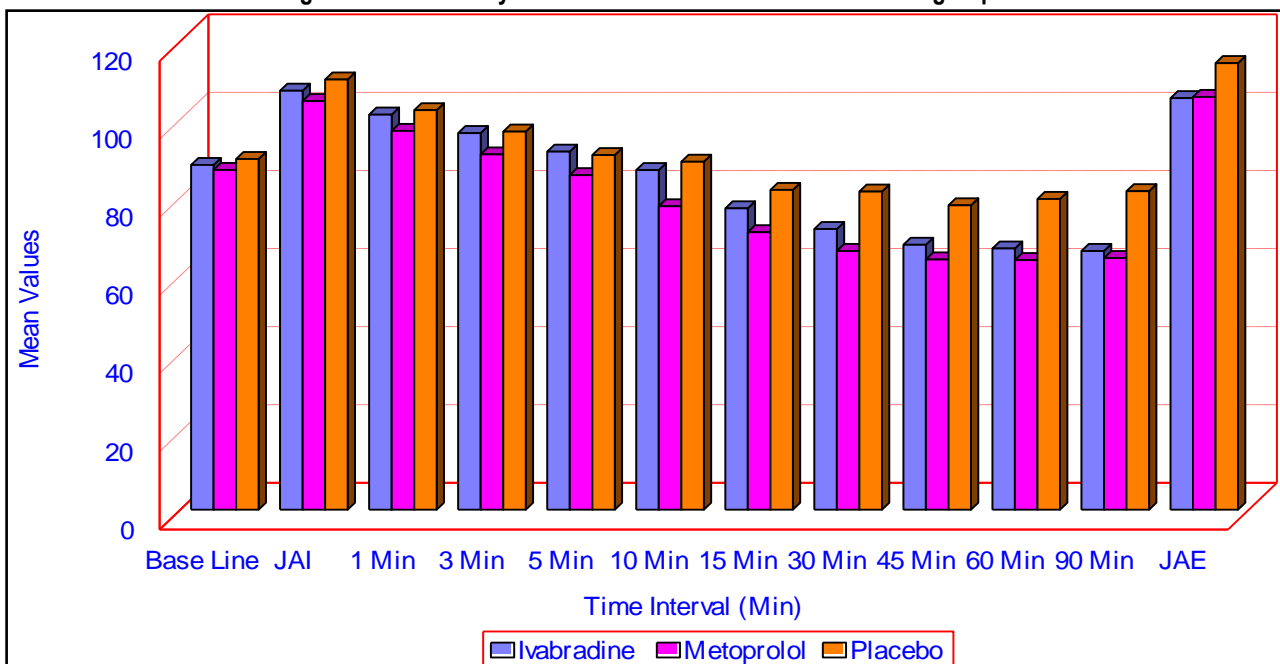


Fig 6: Distribution of case according to blood glucose after extubation in all three groups

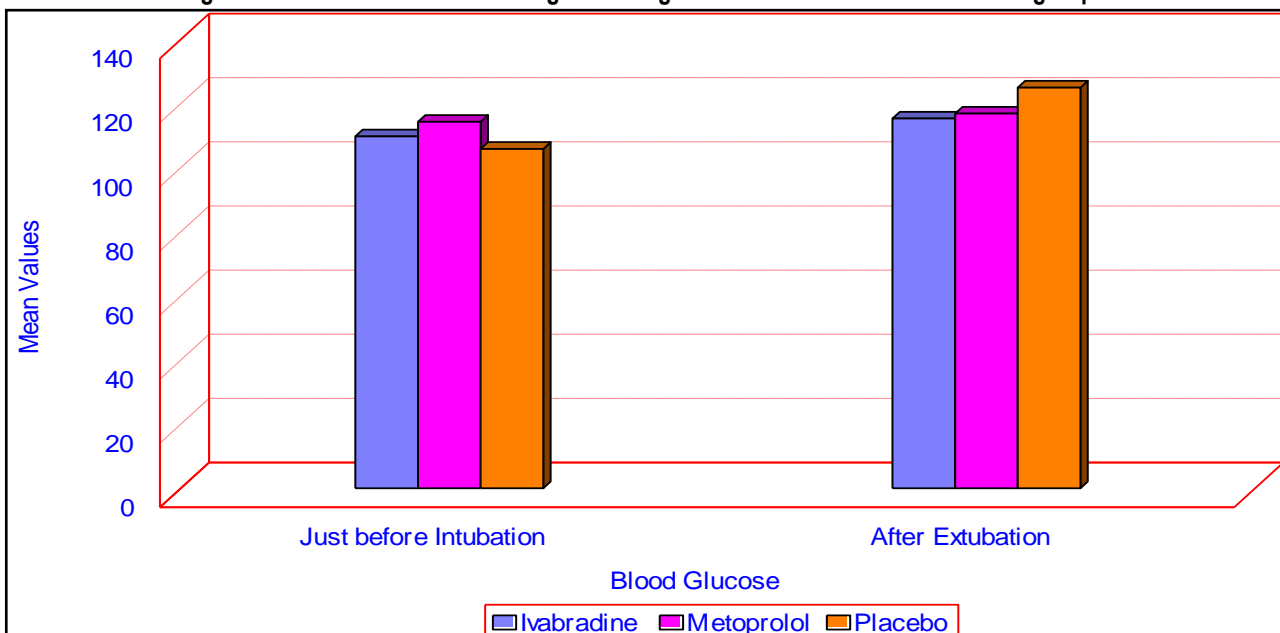


Table 7: Distribution of case according to blood glucose just before intubation in all three groups

Blood Glucose	Ivabradine		Metoprolol		Placebo		f	p
	Mean	SD	Mean	SD	Mean	SD		
Just Before Intubation	109.77	7.82	114.30	9.10	105.87	5.58	9.154	<0.001
After Extubation	115.33	7.53	116.87	9.82	124.97	5.81	12.895	<0.001

OBSERVATIONS

Mean age in Ivabradine group was 30.10±9.97 years, in Metoprolol group it was 34.93±8.97 and in Placebo it was 30.70±5.96 years and this difference was found statistically insignificant (p>0.05).

Majority of cases of planned surgery belonged to Endoscopic Septoplasty where total 32 cases were operated and out of them 5, 14 and 13 cases belonged to group I, II and III respectively, followed by FESS type where total 23 cases were found and out of them 23.3%, 20% and 33.3% belonged to group I, II and III respectively, 8 patients had MLS surgery and out of them 2, 3 and 3 belonged to Group I, II and III respectively. Four cases had endonasal DCR, 3 cases had open septoplasty, 2 cases each had External DCR and Rhinoplasty while 1 case each had turbinectomy, septoplasty with polypectomy and endonasal polypectomy.

According to heart rate at different time intervals, all the time heart rate had a highly significant difference in all three groups (p<0.001) except baseline.

Table 4 shows statistical analysis of systolic blood pressure at different time intervals. Systolic blood pressure had all the time highly significant difference in all three groups (p<0.001) except baseline where the difference was found statistically insignificant.

Table 5 shows statistical analysis of diastolic blood pressure at different time intervals. Diastolic blood pressure had all the time highly significant difference in all three groups (p<0.001) except baseline where the difference was found statistically insignificant (p>0.05)

Table 6 shows statistical analysis of mean arterial blood pressure at different time intervals. Mean arterial pressure had all the time highly significant difference in all three groups (p<0.001) except baseline where the difference was found statistically insignificant (p>0.05).

Mean blood glucose before induction in Ivabradine was 109.77±7.82mg/dl, in Metoprolol it was 114.30±9.10mg/dl and in Placebo it was 105.87±5.58mg/dl. On applying ANOVA test, the difference was found statistically highly significant (p<0.001).

Mean blood glucose after extubation in Ivabradine was 115.33±7.53mg/dl, in Metoprolol it was 116.87±9.82mg/dl and in Placebo it was 124.97±5.81mg/dl. On applying ANOVA test, the difference was found statistically highly significant (p<0.001).

DISCUSSION

The present study entitled "Comparison of Oral Ivabradine, Oral Metoprolol and Placebo to attenuate the stress response in nasal and laryngeal surgeries – A prospective, randomized, double blind study" was undertaken to evaluate the effects of both the drugs in attenuation of haemodynamic responses throughout nasal and laryngeal surgeries.

During laryngoscopy and intubation there is rise in heart rate and blood pressure due to stimulation of sympathetic nervous system. A study conducted by Bruder et al¹² and Shorberg et al¹³ showed

that there is an average increase in 20% in heart rate and 40-50% in blood pressure from baseline values.

It was a prospective randomized double blind comparative study done on 90 patients undergoing nasal and laryngeal surgeries in the Department of Anaesthesiology at Mahatma Gandhi Medical College, Jaipur during January 2017 to August 2018. Patients were randomly divided into three groups of 30 each with the help of a chit box method. All patients were explained about the anesthesia technique and written informed consent was taken. Group 1 – (30 patients) was administered oral ivabradine 5mg tablets 2 hrs before surgery. Group 2 – (30 patients) was administered oral metoprolol tartrate 50 mg tablets 2 hrs before surgery. Group 3 – (30 patients) was administered oral placebo tablets 2 hrs before surgery. HR, SBP, DBP, MAP and Blood sugar levels were recorded at various time intervals.

Demographic Data

According to Table 1 mean age in Ivabradine group was 30.10±9.97 years, in Metoprolol group it was 34.93±8.97 and in Placebo it was 30.70±5.96 years and this difference was found statistically insignificant (p>0.05).

Various studies done by Raghuram¹⁴ et al in 2004, on patients with age group between 20 to 50 years and Ibrahim et al¹⁵ in 2016, on patients with age group 30 to 55 years age range showed similar results as compared to our study.

Heart Rate

In this study comparison between ivabradine, metoprolol and placebo was done to attenuate stress response during laryngoscopy, endotracheal intubation and various other time intervals during surgery. We found that both the drugs are effective in lowering heart rate when compared with placebo. In all three groups baseline heart rate the difference was found statistically insignificant (p>0.05).

After laryngoscopy and endotracheal intubation maximum rise in heart rate was seen in placebo group, than in ivabradine and least in metoprolol group. Heart rate returned to base line earliest in group metoprolol than in group ivabradine and latest in group placebo. During extubation it was observed that there was least rise in heart in metoprolol group as compared to ivabradine and placebo group. It was observed that attenuation of heart rate in group 2 i.e metoprolol was more than in group 1 i.e ivabradine and these results are statistically significant as (p<0.0001) as seen in table 3. Similar studies were done by Menz et al¹⁶ in 2003 and reported that ivabradine decreases heart rate as compared to placebo. Heart rate was reduced by a mean of 17.6 ±4.7% relative to baseline in ivabradine treated patients. Raghuram et al¹⁴ in 2004 stated that there was no significant escalation in haemodynamic changes during laryngoscopy and endotracheal intubation in the ivabradine group as compared to control group. Ptaszynski et al¹⁷ in 2013 concluded that ivabradine and metoprolol exerts a similar effect on H.R where as in our study attenuation of heart rate was more in metoprolol group than ivabradine group.

Systolic Blood Pressure

Ivabradine and Metoprolol both cause lowering of blood pressure. In this study systolic blood pressure was lower than base line at most of the time during surgery except at laryngoscopy, intubation and extubation in metoprolol and ivabradine group than control group i.e placebo.

Systolic blood pressure had all the time highly significant difference in all three groups ($p < 0.001$) except baseline where the difference was found statistically insignificant.

A better control of systolic blood pressure was found with Metoprolol than Ivabradine when compared to control group i.e placebo and significant correlation was seen at laryngoscopy and endotracheal intubation, throughout surgery and at extubation.

Systolic blood pressure returned to base line earliest in Metoprolol group than in Ivabradine group when compared to control group as seen in table 4.

Similar studies were done by Raghuram et al¹⁴ in year 2004 found that Ivabradine is extremely useful drug to prevent abnormal increase in heart rate but blood pressure to a lesser extent when compared with beta blockers.

In a study done by Borer and Tradif et al⁹ in 2009 showed that both Ivabradine and Metoprolol decreases heart rate but Ivabradine does not have significant negative inotropic effect like beta blockers.

Diastolic Blood Pressure

According to Table 5, Ivabradine and Metoprolol both cause lowering of Diastolic blood pressure. In our study diastolic blood pressure was lower than base line at most of the time during surgery except at laryngoscopy, intubation and extubation in metoprolol and ivabradine group than control group i.e placebo.

Diastolic blood pressure had all the time highly significant difference in all three groups ($p < 0.001$) except baseline where the difference was found statistically insignificant ($p > 0.05$) and just after intubation where the difference was found significant ($p < 0.01$).

A better control of diastolic blood pressure was found with Metoprolol than Ivabradine when compared to control group i.e placebo and significant correlation was seen at laryngoscopy and endotracheal intubation, throughout surgery and at extubation.

Diastolic blood pressure returned to base line earliest in Metoprolol group than in Ivabradine group when compared to control group as seen in table 5. Similar studies were done by Raghuram et al¹⁴ in year 2004 found that Ivabradine is extremely useful drug to prevent abnormal increase in heart rate but blood pressure to a lesser extent when compared with beta blockers.

In a study done by Borer and Tradafi et al⁹ in 2009 showed that both Ivabradine and Metoprolol decreases heart rate but Ivabradine does not have significant negative inotropic effect like beta blockers.

Mean Arterial Blood Pressure

As shown in table 6 Ivabradine and Metoprolol both cause lowering of mean arterial blood pressure. Mean arterial pressure had all the time highly significant difference in all three groups ($p < 0.001$) except baseline where the difference was found statistically insignificant ($p > 0.05$).

A better control of mean arterial blood pressure was found with Metoprolol than Ivabradine when compared to control group i.e placebo and significant correlation was seen at laryngoscopy and endotracheal intubation, throughout surgery and at extubation.

Raghuram et al¹⁴ in year 2004, Borer and Tradafi et al⁹ in 2009 and Ptaszynski et al¹⁷ in 2013 showed similar results in their studies.

Blood Sugar Level

Mean blood glucose before induction in Ivabradine was 109.77 ± 7.82 mg/dl, in Metoprolol it was 114.30 ± 9.10 mg/dl and in Placebo it was 105.87 ± 5.58 mg/dl. On applying ANOVA test, the difference was found statistically highly significant ($p < 0.001$).

Mean blood glucose after extubation in Ivabradine was 115.33 ± 7.53 mg/dl, in Metoprolol it was 116.87 ± 9.82 mg/dl and in Placebo it was 124.97 ± 5.81 mg/dl. On applying ANOVA test, the difference was found statistically highly significant ($p < 0.001$).

We can see that both the drugs are effective in attenuating the increasing blood glucose levels due to stress response when compared to control group i.e placebo. Whereas similar study conducted by Ibrahim et al¹⁵ concluded that both the drugs didn't show any significant effect on perioperative blood glucose levels.

COMPLICATIONS

During this study complications like bradycardia, hypotension, bronchospasm etc were not present. Ibrahim et al (2016) on 60 patients in similar study also did not found any complications.¹⁵

SUMMARY

- It was a Prospective randomized double blind comparative study done in 90 patients undergoing nasal and laryngeal surgeries.
- Patients were randomly divided into three groups group 1 – (30 patients) who received oral tablet Ivabradine 5 mg 2 hrs before surgery. Group 2 – (30 patients) who received oral tablet metoprolol tartrate 50 mg 2 hrs before surgery. Group 3- (30 patients) who received tablet placebo 2 hrs before surgery. Heart rate, SBP, DBP, MAP, Preoperative and Post operative blood glucose were monitored.
- Mean age in Group I was 30.10 ± 9.97 years, in group II it was 34.93 ± 8.97 and in group III it was 25.63 ± 6.11 years and this difference was found statistically highly significant ($p < 0.001$).
- We found that both the drugs are effective in lowering heart rate when compared with placebo. In all three groups baseline heart rate the difference was found statistically insignificant ($p > 0.05$).
- After laryngoscopy and endotracheal intubation maximum rise in heart rate was seen in placebo group, than in ivabradine and least in metoprolol group. Heart rate returned to base line earliest in group metoprolol than in group ivabradine and lastest in group placebo. During extubation it was observed that there was least rise in heart in metoprolol group as compared to ivabradine and placebo group.
- We observed that attenuation of heart rate in group 2 i.e metoprolol was more than in group 1 i.e ivabradine and these results are statistically significant as ($p < 0.0001$) as seen in table 3.
- A better control of systolic blood pressure was found with Metoprolol than Ivabradine when compared to control group i.e placebo and significant correlation was seen at laryngoscopy and endotracheal intubation, throughout surgery and at extubation.

- Diastolic blood pressure had all the time highly significant difference in all three groups ($p < 0.001$) except baseline where the difference was found statistically insignificant ($p > 0.05$) and just after intubation where the difference was found significant ($p < 0.01$).
- A better control of diastolic blood pressure was found with Metoprolol than Ivabradine when compared to control group i.e placebo and significant correlation was seen at laryngoscopy and endotracheal intubation, throughout surgery and at extubation.
- As shown in table 6 Ivabradine and Metoprolol both cause lowering of mean arterial blood pressure. Mean arterial pressure had all the time highly significant difference in all three groups ($p < 0.001$) except baseline where the difference was found statistically insignificant ($p > 0.05$).
- A better control of mean arterial blood pressure was found with Metoprolol than Ivabradine when compared to control group i.e placebo and statistically significant correlation was seen at laryngoscopy and endotracheal intubation, throughout surgery and at extubation.
- In this study both the drugs were effective in attenuating the increasing blood glucose levels due to stress response when compared to control group i.e placebo.
- There were no complications seen in our study like bradycardia, hypotension, bronchospasm etc.

CONCLUSION

We concluded that both the drugs can be used as an effective premedication, to attenuate the sympathetic response to laryngoscopy, endotracheal intubation, extubation and throughout nasal and laryngeal surgeries. However Metoprolol was found to have better control than Ivabradine in maintaining the vitals at all points and providing a good hypotensive effect than ivabradine. Ivabradine can be recommended in cases where beta blockers are contra indicated like in bronchial asthma.

LIMITATIONS

- We did not compare different doses of Ivabradine and Metoprolol at different time intervals.
- We didn't include other variables in haemodynamic stress response like catecholamines, glucagon and cortisol.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

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Cite this article as: Vijay Mathur, Ankit Godara, Durga Jethawa, S.P Sharma, Kalpana Verma. Comparison of Oral Ivabradine, Oral Metoprolol and Placebo to Attenuate the Stress Response in Nasal and Laryngeal Surgeries: A Prospective, Randomized, Double Blind Study. *Int J Med Res Prof*. 2019 Mar; 5(2):115-23. DOI:10.21276/ijmrp.2019.5.2.025