



### Original Research Article

## A Comparative Study of Efficacy of Esmolol and Lignocaine for Attenuation of Stress Response during Laryngoscopy and Endotracheal Intubation in Normotensive Patients Undergoing General Anaesthesia

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### Abstract

**Background:** *The stress response to laryngoscopy and intubation can cause tachycardia and hypertension resulting in myocardial ischemia and stroke in vulnerable patients. The objective of our study was to compare the efficacy of bolus dose of Esmolol and Lignocaine (preservative free) in attenuation of haemodynamic stress responses to laryngoscopy and intubation in normotensive patients undergoing general anaesthesia for elective surgical procedure.*

**Material and Methods:** *sixty patients of ASA grade I and II undergoing elective surgeries under general anaesthesia were randomly divided into 2 groups. Group I (n = 30): received Inj. Esmolol (2 mg/kg of body weight) i.v. 3min before laryngoscopy and intubation, over 30seconds. Group II (n = 30): received Inj. lignocaine (2 mg/kg of body weight) i.v. 3min before laryngoscopy and intubation, over 30seconds. Anaesthesia was standardized in both the groups and vital parameters were recorded for upto 15 minutes after intubation.*

**Results:** *There was no statistical significant difference in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure in Esmolol and Lignocaine group in the study period except fall in heart rate and systolic blood pressure after administration of intravenous Esmolol (p<0.05).*

**Conclusion:** *Esmolol and Lignocaine are equally effective in attenuation of stress response to laryngoscopy and intubation.*

**Keywords:** *Esmolol, Lignocaine, Stress response, Intubation, Laryngoscopy.*

## Introduction

Stress response under anesthesia has been universally recognized phenomenon which may be in the form of endocrine or autonomic disturbance. The pressure response to laryngoscopy and endotracheal intubation in the form of tachycardia, hypertension and arrhythmias may be potentially dangerous in vulnerable individuals. These changes are the maximum at 1 minute after intubation and last for 5-10 min<sup>(1)</sup>. There is substantial evidence that, laryngoscopy and intubation is accompanied by a considerable increase in heart rate and arterial blood pressure. These changes are usually of short duration and well-tolerated by the patients in the absence of cardiovascular disease or disturbed intracranial pressure homeostasis. In these conditions, an increase in blood pressure may lead to complications, including arrhythmias, myocardial ischemia, increase in intracranial pressure and rupture of cerebral aneurysms<sup>(2,7)</sup>. Various methods with use of drugs for attenuation of response to laryngoscopy and intubation are still in search from the date of its recognition. Several studies have been made in order to attenuate these haemodynamic response to laryngoscopy and intubation. Many drugs also have been used for blunting of haemodynamic response, the search for ideal drug with minimal adverse effects continues.

Esmolol is an ultra-short acting  $\beta$ -1 adrenergic blocker. It has predominant effect on  $\beta$ -receptors and possesses no significant membrane stabilizing activity. It has rapid onset and a short duration of action<sup>(11)</sup>.

Lignocaine is an antiarrhythmic medication of the class 1b type. Lignocaine works by blocking sodium channels and thus decreasing the rate of contractions of the heart<sup>(12)</sup>. Control of hemodynamic response to endotracheal intubation is important to reduce adverse cardiovascular effects is stressed by various studies. The objective of this study was to compare the efficacy of esmolol and lignocaine in attenuating the pressure response accompanying laryngoscopy

and endotracheal intubation and to look for any adverse effects of these drugs.

## Study Design

A prospective, double blind randomized control study was undertaken in tertiary care hospital on 60 ASA I and II patients of age group 18-60 years of either sex, scheduled for elective surgical procedure under general anaesthesia after getting approval from institutional ethical committee. All the patients in the study were clearly explained about the purpose and nature of the study in the language they could understand. They were included in the study only after obtaining a written informed consent.

**Inclusion criteria:** American Society of Anesthesiologist (ASA) Grade I & II, Age between 18-50 years, Weight between 40-80 kg with airway of modified Mallampati Grade I and II were included in the study.

**Exclusion criteria:** Patients refusal, American Society of Anesthesiologist (ASA) Grade III & IV, History of seizure disorders, History of cardiovascular diseases like arrhythmias, hypertension, ischaemic heart disease, valvular heart disease, pregnancy, bronchial asthma, HR < 60 /min, SBP < 100 mm Hg suspected difficult airway and Modified Mallampatti Grade III and IV were excluded from the study. Patients who had Cormark Lehane Score III and above and also those in whom duration of laryngoscopy lasted for more than 15 seconds and more were excluded from the study.

## Method

Detailed pre-anaesthetic evaluation of the patients was performed by an anaesthesiologist a day before the surgery. 60 patients satisfying the inclusion and exclusion criteria were included in the study.

Preliminary Investigations were done in the form of; Complete blood count, Random blood sugar, Bleeding time, Clotting time, Coagulation profile, Liver function tests, Kidney function tests, Electrocardiography (ECG), Chest x ray postero-

anterior (PA) view were noted, Specialized investigation according to the patients for further evaluation if required.

All patients were kept nil by mouth for 8 hrs.

All patients were given overnight sedation in the form of Tab. Alprazolam 0.5 mg orally on the night before and 2 hours before surgery.

In operation theatre, multipara monitoring device with ECG, pulse rate, non invasive blood pressure, SPO<sub>2</sub> was attached to the patient and baseline parameters were noted. Patients were prehydrated with intravenous Ringer lactate after establishing intravenous line with 18 G cannula. Thereafter, intravenous fluids were calculated and given as per body weight and operative loss. Patients also received Inj. Ranitidine 50 mg and Inj.Ondansetron 4 mg IV slowly as a premedication along with IV midazolam 0.05mg/kg. Now the patients were randomly divided by computer generated numbers into two groups.

**Group I (n = 30):** received Inj. Esmolol (2 mg/kg of bodyweight) i.v. 3 min before laryngoscopy and intubation, over 30 seconds.

**Group II (n = 30):** received Inj. Lignocaine (preservative free 2 mg/kg of body weight) ) i.v. 3min before laryngoscopy and intubation, over 30 seconds.

After preoxygenation for 3-5 minutes with 100% oxygen, patients were induced with Inj. Propofol 2mg/kg and Inj. Vecuronium 0.1 mg/kg after confirming a lack of response to voice and a loss of the eyelid reflex. Patients were ventilated with oxygen: nitrous oxide (50:50) and sevoflurane 1% for 3 minutes. Endotracheal intubation was performed by the experienced anaesthesiologist with appropriate size endotracheal tube. Anaesthesia was maintained with controlled ventilation with nitrous oxide and oxygen (60:40) with sevoflurane 2% with intermittent bolus doses of inj. Vecuronium as muscle relaxant. No surgical stimulation was allowed for 10 minutes after intubation.

Cardiorespiratory parameters (pulse rate, respiratory rate, noninvasive blood pressure,

SPO<sub>2</sub>, ETCO<sub>2</sub>) were monitored continuously. Recordings were made till the completion of surgery. At the end of surgery, the residual neuromuscular block was antagonized with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) I.V. and extubation was performed when respiration was adequate and patient was able to obey verbal commands with complete return of muscle power.

Intraoperatively and postoperatively, bradycardia (heart rate <60 beats per minute) was to be treated with 0.3mg of injection atropine and hypotension (systolic blood pressure falling more than 20% basal value or less than 80mm Hg ) with 3-6mg injection mephenteramine as a bolus.

### Statistical Analysis

The heart rate, systolic blood pressure, diastolic blood pressure and mean rterial pressure were monitored before induction, after study drug, during induction, after laryngoscopy and intubation and thereafter till succeeding 15 minutes. Data were collected, tabulated, coded then analyzed using SPSS ® computer software version 20.0.

- Numerical variables were presented as mean & standard deviation (SD).
- As regard numerical variables; unpaired student – t test was done.
- p value

>0.05	Non Significant
<0.05	Significant
<0.001	Highly Significant

### Observations and Results

The demographic data were comparable in both the groups and are given in table 1 and 2.

**Table No. 1.** Demographic Characteristics

Demographic character		group E (n=30)	group L(n=30)	P value
Age (years)	Mean ± S.D.	30.57 ± 8.23	30.77± 8.09	0.919(NS)
	Range	18 - 45	18- 45	
Weight (kg)	Mean ± S.D.	55.63 ± 7.63	55.23 ± 6.40	0.813(NS)
	Range	45- 75	45-68	
ASA classification	Class I	30	30	
	Class II	0	0	

Test applied- student unpaired t-test

**Table No. 2:** Gender Incidence

Gender	group E(n=30)	group L(n=30)
Male (%)	26(86.66%)	27(90.0%)
Female (%)	4(13.33%)	3(10.0%)
Total (%)	30(100%)	30(100%)

**Table No.3:** Mean (±SD) Pulse Rate Alterations In Group I (Esmolol)

PULSE RATE	PR BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	79.00±7.241	72.13±5.866	77.67±10.65	81.60±7.241	81.07±8.803	82.33±5.627	81.27±6.80	81.07±9.091	81.93±6.724	82.07±6.053	82.33±6.945
P-VALUE		<b>0.016 (S)</b>	0.710 (NS)	0.421 (NS)	0.503 (NS)	0.222 (NS)	0.484 (NS)	0.485 (NS)	0.340 (NS)	0.299(N S)	0.312 (NS)

There is significant fall in heart rate after administration of i.v. Esmolol. Thereafter, there is no significant change in heart rate in the study

period. Fall in the heart rate was never <60 beats/min requiring Inj. Atropine for the treatment.

**Table No.4 :** Mean (±SD) Pulse Rate Alterations in Group II (Lignocaine)

PULSE RATE	PR BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
LIGNOCAINE	77.80±8.026	79.07±7.015	76.80±6.527	80.13±8.305	78.67±5.381	80.60±5.110	78.67±5.273	79.33±5.024	79.80±4.617	79.47±4.627	80.60±6.127
P-VALUE		0.577 (NS)	0.705 (NS)	0.442 (NS)	0.739 (NS)	0.232 (NS)	0.709 (NS)	0.491 (NS)	0.295 (NS)	0.423 (NS)	0.304 (NS)

There is no significant change in heart rate in i.v. Lignocaine group in the study period.

**Table No.5:** Comparison of Mean Pulse Rate Changes between the Groups

PULSE RATE	PR BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	79.00±7.241	72.13±5.866	77.67±10.65	81.60±7.241	81.07±8.803	82.33±5.627	81.27±6.80	81.07±9.091	81.93±6.724	82.07±6.053	82.33±6.945
LIGNOCAINE	77.80±8.026	79.07±7.015	76.80±6.527	80.13±8.305	78.67±5.381	80.60±5.110	78.67±5.273	79.33±5.024	79.80±4.617	79.47±4.627	80.60±6.127
P VALUE	0.626 (NS)	<b>0.007 (S)</b>	0.790 (NS)	0.645 (NS)	0.375 (NS)	0.385 (NS)	0.252 (NS)	0.523 (NS)	0.320 (NS)	0.197 (NS)	0.475 (NS)

On intergroup comparison, there was no statistically significant difference in pulse rate till 15 minutes except the pulse rate in Esmolol group

was significantly lower than Lignocaine after drug administration.

**Table No.6:** Mean (±SD) Systolic Blood Pressure Alterations In Group I (Esmolol)

SYSTOLIC BP	SBP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	123.27 ±6.81	<b>106.0±2.903</b>	121.27±23.57	127±9.071	126.40±16.51	121.87±16.59	120.27 ±9.26	126.60 ±7.99	121.33 ±8.52	121.60 ±9.82	121.07 ±9.22
P-VALUE		<b>0.000 (HS)</b>	0.772 (NS)	0.210 (NS)	0.484 (NS)	0.754 (NS)	0.280 (NS)	0.160 (NS)	0.485 (NS)	0.529 (NS)	0.535 (NS)

In our study, there was significant fall in systolic blood pressure after administration of i.v. Esmolol. Thereafter systolic blood pressure

remained near the basal values till 15 minutes. Fall in the SBP did not required any treatment.

**Table No.7:** Mean (±SD) Systolic Blood Pressure Alterations In Group II (Lignocaine)

SYSTOLIC BP	SBP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
LIGNOCAINE	121.13 ±5.89	116.07 ±8.31	120.13 ±9.22	126.00±8.00	125.73±14.97	120.20 ±9.00	121.60 ±5.69	123.87 ±7.87	120.13 ±8.06	119.47 ±8.33	119.67 ±7.87
P-VALUE		0.067 (NS)	0.754 (NS)	0.065 (NS)	0.313 (NS)	0.743 (NS)	0.816 (NS)	0.296 (NS)	0.602 (NS)	0.464 (NS)	0.614 (NS)

In our study, there was statistically insignificant change in systolic blood pressure in i.v. Lignocaine group.

**Table No.8:** Comparison of Mean Systolic Blood Pressure Changes between the Groups

SYSTOLIC BP	SBP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	123.27 ±6.81	<b>106.0±2.903</b>	121.27±23.57	127±9.071	126.40±16.51	121.87±16.59	120.27 ±9.26	126.60 ±7.99	121.33 ±8.52	121.60 ±9.82	121.07 ±9.22
LIGNOCAINE	121.13 ±5.89	<b>116.07±8.311</b>	120.13±9.22	126.00±8.00	125.73±14.97	120.20±9.00	121.60 ±5.69	123.87 ±7.87	120.13 ±8.06	119.47 ±8.33	119.67 ±7.87
P-VALUE	0.366' (NS)	<b>0.000 (HS)</b>	0.864 (NS)	0.751 (NS)	0.909 (NS)	0.735 (NS)	0.638 (NS)	0.353 (NS)	0.695 (NS)	0.526 (NS)	0.658 (NS)

On intergroup comparison, there was no statistically significant difference in systolic blood pressure till 15 minutes except the systolic blood

pressure in Esmolol group was significantly lower than Lignocaine after drug administration.

**Table No.9:** Mean (±SD) Diastolic Blood Pressure Alterations In Group I (Esmolol)

DIASTOLIC BP	DBP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	75.13±7.43	79.60±7.80	69.40±8.71	70.14±8.81	69.25±6.88	76.20±16.32	76.93±9.92	75.40±6.29	72.33±10.06	70.07±9.66	74.13±7.05
P-VALUE		0.082 (NS)	0.056 (NS)	0.265 (NS)	0.105 (NS)	0.819 (NS)	0.617 (NS)	0.916 (NS)	0.475 (NS)	0.190 (NS)	0.522 (NS)

There was statistically insignificant change in diastolic blood pressure in i.v. Esmolol group.

**Table No.10:** Mean (±SD) Diastolic Blood Pressure Alterations in Group II (Lignocaine)

DIASTOLIC BP	DBP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
LIGNOCAINE	74.33±7.43	77.00±7.17	71.33±6.09	73.36±6.11	72.92±4.01	75.80±9.53	77.00±6.40	74.93±4.73	71.53±7.53	71.60±8.39	72.60±5.36
P-VALUE		0.270 (NS)	0.145 (NS)	0.793 (NS)	0.312 (NS)	0.610 (NS)	0.234 (NS)	0.718 (NS)	0.286 (NS)	0.285 (NS)	0.288 (NS)

There was statistically insignificant change in diastolic blood pressure in i.v. Lignocaine group.



**Table No.11:** Comparison of Mean Diastolic Blood Pressure Changes between the Groups

DIASTOLIC BP	DBP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	75.13±7.43	79.60±7.80	69.40±8.71	70.14±8.81	69.25±6.88	76.20±6.32	76.93±9.92	75.40±6.29	72.33±1.06	70.07±9.66	74.13±7.05
LIGNOCAINE	74.33±7.43	77.00±7.17	71.33±6.09	73.36±6.11	72.92±4.01	75.80±9.53	77.00±6.40	74.93±4.73	71.53±7.53	71.60±8.39	72.60±5.36
P-VALUE	0.711 (NS)	0.350 (NS)	0.487 (NS)	0.272 (NS)	0.125 (NS)	0.935 (NS)	0.983 (NS)	0.820 (NS)	0.807 (NS)	0.646 (NS)	0.508 (NS)

On intergroup comparison, there was statistically insignificant change in diastolic blood pressure in both the groups.

**Table No.12:** Mean (±SD) Arterial Pressure Alterations in Group I (Esmolol)

MEAN ARTERIAL BP	MAP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	91.18±6.85	88.40±5.17	96.33±17.97	86.711±4.77	81.15±2.317	91.42±15.28	91.38±8.34	92.47±5.49	86.20±6.99	87.24±6.44	89.78±5.36
P-VALUE		0.176 (NS)	0.354 (NS)	0.053 (NS)	0.206 (NS)	0.955 (NS)	0.946 (NS)	0.515 (NS)	0.088 (NS)	0.173 (NS)	0.451 (NS)

There was statistically insignificant change in mean arterial pressure in i.v. Esmolol group.

**Table No.13:** Mean (±SD) Arterial Pressure Alterations in Group II (Lignocaine)

MEAN ARTERIAL BP	MAP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
LIGNOCAINE	89.93±3.75	90.02±5.79	94.98±8.61	87.60±3.87	83.35±23.53	90.60±7.11	91.87±4.52	91.24±4.22	86.20±5.69	87.55±6.06	88.29±4.27
P-VALUE		0.964 (NS)	0.065 (NS)	0.076 (NS)	0.339 (NS)	0.771 (NS)	0.279 (NS)	0.359 (NS)	0.104 (NS)	0.219 (NS)	0.323 (NS)

There was statistically insignificant change in mean arterial pressure in i.v. Lignocaine group.

**Table No.14:** Comparison of Mean Arterial Pressure Changes between the Groups

MEAN ARTERIAL BP	MAP BASAL	AFTER DRUG	AF INDUCTION	AFT INTUBATION	1 MIN	2 MIN	3 MIN	4 MIN	5 MIN	10 MIN	15 MIN
ESMOLOL	91.18±6.85	88.40±5.17	96.33±17.97	86.711±4.77	81.15±2.317	91.42±15.28	91.38±8.34	92.47±5.49	86.20±6.99	87.24±6.44	89.78±5.36
LIGNOCAINE	89.93±3.75	90.02±5.79	94.98±8.61	87.60±3.87	83.35±23.53	90.60±7.11	91.87±4.52	91.24±4.22	86.20±5.69	87.55±6.06	88.29±4.27
P-VALUE	0.542 (NS)	0.425 (NS)	0.794 (NS)	0.579 (NS)	0.798 (NS)	0.851 (NS)	0.843 (NS)	0.500 (NS)	1.000 (NS)	0.893 (NS)	0.408 (NS)

On intergroup comparison, there was statistically insignificant change in mean arterial pressure in both the groups.

**Perioperative Complication**

None of the patient developed any complications like hypotension, bradycardia, arrhythmias and allergic reaction in perioperative period.

**Discussion**

Endotracheal intubation as well as laryngoscopy provides an intense stimulus via vagal and glossopharyngeal afferents that results in a reflex

autonomic stimulation manifested in the form of hypertension and tachycardia in adults and adolescents. This autonomic activation may result in bradycardia in infants and small children. Hypertension and bradycardia are usually of short duration; however, they may have consequences in patients with significant cardiac disease. Central nervous system activation as a result of airway management results in increase in electroencephalographic (EEG) activity, increase

cerebral blood flow and cerebral metabolic rate which may result in an increase in intracranial pressure in patients with decreased intracranial compliance<sup>(3)</sup>. Esmolol is a cardio selective beta adrenergic blocking drug with rapid onset and short elimination half life (9 min) without any significant drug interaction with commonly used anaesthetic drugs. Esmolol decrease the heart rate and force of contraction by blocking of beta adrenergic receptors of the heart, blood vessels, and other organs of the body. Esmolol attenuates the tachycardia and hypertension due to laryngoscopy and intubation by preventing the action of two naturally occurring neurotransmitters epinephrine and nor epinephrine. There have been various studies describing the effects on heart rate and blood pressure during laryngoscopy and intubation of esmolol. Korpinen et al<sup>(5)</sup> concluded that bolus Esmolol 2mg/kg 2 min before laryngoscopy and intubation prevented increase in heart rate rather than increase in arterial blood pressure. Singh S et al<sup>(6)</sup> justified the usage of higher dose of Esmolol 2mg/kg in ghanian population without any hypotension and bradycardia. Suresh kumar singhal et al<sup>(7)</sup> reported that bolus intravenous dose of Esmolol 1.5mg/kg is safe and more effective in attenuating the hemodynamic response to laryngoscopy and intubation when administered three minutes before intubation. M. Andrew levitt et al<sup>(8)</sup> concluded that esmolol 2mg/kg and lignocaine 2mg/kg have similar efficacies to attenuate hemodynamic response to intubation of patients with isolated head trauma. In our study, Esmolol 2mg/kg as a bolus was found to be effective in attenuation of hypertensive stress response as well as tachycardia during laryngoscopy and tracheal intubation till 5 min without any deleterious effect.

Lignocaine attenuates haemodynamic responses during laryngoscopy and intubation due to its direct cardiac depressant effect along with peripheral vasodialatory action. Lignocaine also suppress airway reflexes due to irritation of tracheal mucosa and has analgesic and

antiarrhythmic properties. Singh S et al<sup>(6)</sup> found that lignocaine 1.5 mg/kg and Esmolol 2mg/kg are effective in suppressing the haemodynamic response to laryngoscopy and intubation without any deleterious effect. Lev and Rosen<sup>(9)</sup> concluded that IV lignocaine 1.5mg/kg 3 minutes before intubation was optimal for attenuation of sympathoadrenal response to laryngoscopy and intubation. Jain P, vats A<sup>(10)</sup> reported that intravenous lignocaine 2mg/kg and esmolol 2 mg/kg are effective in attenuating the haemodynamic response to laryngoscopy and intubation for about 5 min without any deleterious effect.

However some studies conducted by Gupta A et al<sup>(11)</sup>, Kindler et al<sup>(12)</sup>, Miller CD et al<sup>(13)</sup> and Van den berg et al<sup>(14)</sup> disagree the lignocaine' s effect on attenuation of stress response to laryngoscopy and intubation as bolus intravenous dose of 1.5mg/kg. Hence we modify the dose of intravenous lignocaine as 2 mg/kg. In our study, lignocaine 2mg/kg was found to be effective in blunting the haemodynamic response to laryngoscopy and intubation.

### Conclusion

From the present study, based on the results and methodology applied, we conclude that intravenous Lignocaine (preservative free) 2 mg/kg and Esmolol 2 mg/kg are effective in attenuating the haemodynamic stress response to laryngoscopy and tracheal intubation for about 15 minutes without any deleterious effect.

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