International Journal of Anesthesia and Clinical Medicine
2021; 9(2): 32-37
http://www.sciencepublishinggroup.com/j/ijacm
doi: 10.11648/j.ijacm.20210902.13

Attenuation of Pressor Response to Laryngoscopy in Severe Preeclampsia: Comparison the Efficacies Between Intravenous Nitroglycerine and Intravenous Hydralazine

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To cite this article:

Nahida Sultana, ABM Rashedul Amir, Hasina Momtaz, Md. Abu Taher. Attenuation of Pressor Response to Laryngoscopy in Severe Preeclampsia: Comparison the Efficacies Between Intravenous Nitroglycerine and Intravenous Hydralazine. *International Journal of Anesthesia and Clinical Medicine*. Vol. 9, No. 2, 2021, pp. 32-37. doi: 10.11648/j.ijacm.20210902.13

Received: February 13, 2021; **Accepted**: June 4, 2021; **Published**: August 11, 2021

Abstract: *Introduction*: Preeclampsia is one of the most commonly disorders of pregnancy. The pressor response to laryngoscopy is known to be exaggerated in patients with severe preeclampsia. The aim of this study was to assess the preoperative blood pressure control in severe preeclamptic mother with intravenous nitroglycerine is more effectively attenuate the haemodynamic response to laryngoscopy in comparison to treatment with intravenous hydralazine. *Methods*: This randomized fixed sealed envelope lottery method study was conducted in the Department of anaesthesiology of Dhaka Medical College Hospital, Dhaka, between October 2014 to March 2015 Total of 60 patients with severe preeclampsia and gestational age more than 36 weeks, who were presented for elective or urgent caesarean delivery under general anaesthesia were randomly divided into two groups, group A, n=30 received 50 mcg intravenous nitroglycerine. Group B received 5mg hydralazine intravenously very slowly. Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) were simultaneously recorded in the mother at pre-induction, pre-laryngoscopy, and at 1min, 3 min, and 5 min after laryngoscopy. *Result*: The patients in group A and group B showed no significant difference in HR, SAP, DAP and MAP at pre induction and pre laryngoscopy. But there is significant difference ($P<0.05$) at 1, 3, 5 min after laryngoscopy. The mean heart rate at 1, 3 and 5 minutes after laryngoscopy were significantly ($p<0.05$) higher in group B than group A. The mean SAP, DAP, MAP were also significantly ($p<0.05$) higher in group B than group A at 1, 3, 5 min after laryngoscopy. *Conclusion*: Women with severe preeclampsia who were preoperatively treated with intravenous nitroglycerine provides a safe and more effective prophylaxis for patients with severe preeclampsia undergoing cesarean delivery under general anesthesia, in attenuating haemodynamic responses to laryngoscopy.

Keywords: Attenuation, Pressor, Laryngoscopy, Preeclampsia, Intravenous Nitroglycerine & Hydralazine

1. Introduction

Preeclampsia is one of the most commonly encountered hypertensive disorders of pregnancy. It is mostly feared because of its serious maternal and fetal mortalities and morbidities.10% of women have high blood pressure during pregnancy, and preeclampsia complicates 5-8% of pregnancies. [1] Overall, 10% to 15% direct maternal deaths are associated with preeclampsia and eclampsia. [2] Worldwide, hypertensive disorder of pregnancy accounts for more than 50000 maternal death per year according to world health organization (WHO). [3] The diagnosis of hypertension in pregnancy is reached when two BP reading show a systolic blood pressure (SBP) of>140mmHg and/or a diastolic blood pressure of>90 mmHg, taken over a period of 4 to 6 hours after 20 weeks of gestation, in previously normotensive women. [4] Direct laryngoscopy causes an increase in blood pressure and heart rate. [5] It involves an

average increase in blood pressure of 40-50% and a 20% increase in heart rate [6]. In 1950 Newman and Hopinto first reported that laryngoscopy and intubation stimulate the sympathetic system. Pressor response to laryngoscopy and intubation increase myocardial oxygen requirement and risk of cerebrovascular accident, decrease uterine blood flow and increase cardiac arrhythmias and pulmonary oedema. [7-10] Consequently, there is an increased risk of morbidity and mortality of both mother and baby. In order to reduce the occurrence and severity of these haemodynamic complications, many drugs such as hydralazine [11], magnesium sulphate [12], labetalol [13], fentanyl [7], nitriglycerine [14, 15], nifedipine [16] have been used with varying degrees of success. For many years' hydralazine has been the recommended antihypertensive of first choice for severe hypertension in pregnancy. [17-19] Its side effects such as headache, nausea, vomiting are common and mimic symptoms of deteriorating preeclampsia. Although a precipitous hypotensive overshoot may occur with any antihypertensive agent used to treat the severe hypertension of preeclampsia, [20-24] a meta-analysis of clinical trials showed that maternal hypotension may be more common with parenteral hydralazine. [25] Nitroglycerin has also been administered for rapid perioperative treatment of maternal hypertension. [14] Longmire and colleagues [14] showed that intravenous nitroglycerine infusion is effective in lowering maternal blood pressure and in blunting haemodynamic response to endotracheal intubation in severe preeclampsia.

The purpose of preoperative blood pressure control of pre-eclamptic mother with nitroglycerine more effectively attenuate the haemodynamic response to laryngoscopy in a comparison with intravenous hydralazine.

2. Objectives

a) General objective:

To assess that, preoperative blood pressure control in severe preeclamptic mother with intravenous nitroglycerine is more effectively attenuate the haemodynamic response to laryngoscopy in compairison to treatment with intravenous hydralazine.

b) Specific Objectives:

1) To see the haemodynamic response to laryngoscopy in severe preeclamptic mothers who had been treated with intravenous nitroglycerine for hypertention.
2) To see the haemodynamic response to laryngoscopy in severe preeclamptic mothers had been treated with intravenous hydralazine.
3) To compare the haemodynamic effects to laryngoscopy in severe preeclamptic mother who had been treated with intravenous nitroglycerine and intravenous hydralazine.

3. Methodology & Materials

This was a randomized control trial method study was conducted in the Department of anaesthesiology and ICU of Dhaka Medical College Hospital, Dhaka, between October 2014 to March 2015. Patients with severe preeclampsia and gestational age of more than 30 weeks, who were presented for elective or urgent cesarean delivery under general anaesthesia in Dhaka Medical College Hospital. Sampling was done by fixed sealed envelope lottery method. Total of 60 patients with severe preeclampsia and gestational age more than 36 weeks, who were presented for elective or urgent caesarean delivery under general anaesthesia were randomly divided into two groups, group A, n=30 received 50 mcg intravenous nitroglycerine. Same dose was administered every 5min interval until systolic arterial pressure (SAP) <140mmHg but not <120 and decrease in diastolic arterial pressure (DAP) <100mmHg but not <80mmHg. Group B received 5mg hydralazine intravenously very slowly, further 5mg dose had been given after 20min interval until therapeutic goal was reached. Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) were simultaneously recorded in the mother at pre-induction, pre-laryngoscopy, and at 1min, 3 min, and 5 min after laryngoscopy.

4. Result

Group A=Received 50 mcg nitroglycerine intravenously, Group B=Received 5 mg hydralazine intravenously, ns=not significant, *P* value reached from chi square test. In the age distribution of the patients observed that majority patients were belonged to age 20-24 years in both groups, which was 12 (40.0%) in group A and 15 (50.0%) in group B. The age difference was not statistically significant ($p>0.05$) between two groups. On the gestational age of patients was observed that majority patients had gestational age 37-38 weeks in both groups, which was 15 (50.0%) in group A and 19 (63.3%) in group B. The gestational age difference was not statistically significant ($p>0.05$) between two groups. Again para of the patients was observed that primi para was found 20 (66.7%) in group A and 23 (76.7%) in group B. Multipara was 10 (33.3%) and 7 (23.3%) in group A and group B respectively. The difference was not statistically significant ($p>0.05$) between two groups. In the weight distribution of the patients was observed that majority patients had weight 50-60 kg in both groups which was 15 (50.0%) in group A and 13 (43.3%) in group B. The weight difference was not statistically significant ($p>0.05$) between two groups. In mallampati of the patients was observed that 20 (66.7%) in group A and 19 (63.3%) in group B. The difference was not statistically significant ($p>0.05$) between two groups and last one the pattern of C/S of the patients was observed that emergency C/S was found 26 (86.7%) in group A and 25 (83.3%) in group B. The difference was not statistically significant ($p>0.05$) between two groups [Table-1]. Mean heart rate- pre induced and pre laryngoscopy were not statistically significant between two groups (P value: 0.519 and 0.460 respectively). However, 1, 3 and 5 minutes after laryngoscopy were statistically significant between two

groups (p<0.05). The mean SAP- pre induced and pre laryngoscopy were not statistically significant between two groups (P value: 0.429 and 0.168 respectively). However, 1, 3 and 5 minutes after laryngoscopy were statistically significant between two groups (p<0.05). The mean DAP - pre induced and pre laryngoscopy were not statistically significant between two groups (P value: 0.166 and 0.177 respectively). However, 1, 3 and 5 minutes after laryngoscopy were statistically significant between two groups (p<0.05). The mean MAP - pre induced and pre laryngoscopy were not statistically significant between two groups (P value: 0.124 and 0.182 respectively). However, 1, 3 and 5 minutes after laryngoscopy were statistically significant between two groups (p<0.05).

Table 1. *Distribute the study people according to the demographic status. (N=60).*

		Group-A		Group-B		P-value
		n	%	n	%	
Age of the patients (years)	≤20	6	20	10	33.3	0.140_{ns}
	20-24	12	40	15	50.0	
	25-30	9	30	5	16.7	
	>30	3	10	0	0.0	
Gestational age (weeks)	36-37	5	16.7	2	6.7	0.225_{ns}
	37-38	15	50.0	19	63.3	
	38-39	7	23.3	3	10.0	
	≥39	3	10.0	6	20.0	
Para	Primi	20	66.7	23	76.7	0.390_{ns}
	Multi	10	33.3	7	23.3	
Weight (kg)	<50	7	23.3	2	16.7	0.528_{ns}
	50-60	15	50.0	13	43.3	
	>60	8	26.7	12	40.0	
Mallampati	I	20	66.7	19	63.3	0.786_{ns}
	II	10	33.3	11	36.7	
Pattern of C/S	Emergency	26	86.7	25	83.3	0.717_{ns}
	Elective	4	13.3	5	16.7	

Table 2. *Different follow up of the study people according to HR, SAP, DAP, MAP. (N=60).*

		Group-A (n=30)	Group-B (n=30)	P value
		Mean±SD	Mean±SD	
HR- Heart Rate (beat/min)	Pre induction	92.4±7.2	93.7±8.3	0.519_{ns}
	Pre laryngoscopy	93.2±5.1	94.3±6.3	0.460_{ns}
	1 min after laryngoscopy	95.3±2.1	99.1±3.2	0.001_{s}
	3 min after laryngoscopy	96.2±5.1	99.2±6.1	0.043_{s}
	5 min after laryngoscopy	97.1±3.5	99.8±3.2	0.002_{s}
SAP- Systolic arterial blood pressure (mmHg)	Pre induction	134.9±6.7	135.8±7.2	0.429_{ns}
	Pre laryngoscopy	133.2±3.2	134.3±2.9	0.168_{ns}
	1 min after laryngoscopy	128.0±3.4	130.7±6.3	0.043_{s}
	3 min after laryngoscopy	126.3±3.1	129.8±5.6	0.004_{s}
	5 min after laryngoscopy	125.9±4.0	130.5±3.2	0.001_{s}
DAP- Diastolic arterial blood pressure (mmHg)	Pre induction	93.5±5.3	95.2±4.0	0.166_{ns}
	Pre laryngoscopy	92.3±3.8	93.8±3.5	0.117_{ns}
	1 min after laryngoscopy	88.5±4.3	91.3±3.0	0.004_{s}
	3 min after laryngoscopy	87.5±5.7	90.1±3.6	0.039_{s}
	5 min after laryngoscopy	85.2±2.9	91.8±3.3	0.001_{s}
MAP- Mean arterial blood pressure (mmHg)	Pre induction	106.4±6.1	108.7±5.3	0.124_{ns}
	Pre laryngoscopy	106.1±5.6	107.9±4.7	0.182_{ns}
	1 min after laryngoscopy	103.2±2.4	106.3±3.1	0.001_{s}
	3 min after laryngoscopy	100.3±3.1	104.7±4.6	0.001_{s}
	5 min after laryngoscopy	98.1±3.7	101.3±3.1	0.001_{s}

5. Discussion

This randomized control trial study was carried out with an aim to compare the effectiveness of intravenous nitroglycerine and intravenous hydralazine in preventing increase heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) after laryngoscopy in women with severe preeclampsia undergoing caesarean delivery under general anaesthesia.

A total of 60 patients with severe preeclampsia and gestational age of more than 30 weeks, who presented for elective or urgent cesarean delivery under general anaesthesia in Dhaka Medical College Hospital, Dhaka during October 2014 to March 2015 were included in this study. Patients who received 50 mcg nitroglycerine intravenously and patient who received 5 mg hydralazine intravenously were considered as Group A (n=30) and Group B (n=30) respectively and patients were selected randomly by lottery method using sealed envelope. Patients have blood pressure>160/110 mmHg, patient with gestational age of

more than 36 weeks and patients who had contraindications for spinal anaesthesia were enrolled in this study.

In this present study it was observed that majority patients were belonged to age 20-24 years in both groups. The mean was found 25.8±5.26 years varied from 17 – 33 years in group A and 24.15±3.69 years varied from 18 – 31 years in group B. P value was reached from chi square test and it was 0.140, so that the mean age difference was not statistically significant (p>0.05) between two groups. Safavi et al. [25] observed the mean age was 28.1±4.7 years in Nitroglycerine-treated (GROUP A) group and 27.0±5.1 years in Group B (Hydralazine-treated group). Similarly, in another study Channaiah et al. [27] found the mean age was 37.63±12.28 years in Nitroglycerine-treated group. The higher mean age and age range obtained by the above authors may be due to geographical variations, racial, ethnic differences, genetic causes, different lifestyle, and increased life expectancy. All these factors may have significant impacts on sever preeclampsia. In this study the mean gestational age was found 37.6±2.3 in group A and 37.8±1.6 weeks in group B. The mean gestational age difference was not statistically significant (p>0.05) between two groups. Similarly, Safavi et al. [25] showed the mean gestational age was 36.4±1.1 weeks in Nitroglycerine-treated group and 36.7±0.85 weeks in Hydralazine-treated group. Thus, this study supports the present study. In this present study it was observed that primi para was found 66.7% in group A and 76.7% in group B. Multipara was 33.3% and 23.3% in group A and group B respectively. The difference was not statistically significant (p>0.05) between two groups. Safavi et al. [25] showed primi para was found 62.5% in Nitroglycerine-treated group and 70.0% in Hydralazine-treated group. Multi para was found 37.5% in Nitroglycerine-treated group and 30.0% in Hydralazine-treated group. In another study Iftikhar et al. [26] study revealed that parity distribution 28 patients (56%) in group-A and 26 patients (52%) in group-B were primigravidae while 22 patients (44%) in group-A and 24 patients in group-B were multigravidae, which are closely resembled with the present study. Many investigators Conde-Agudelo and Belizan [28], Lee et al. [29]; Marviel et al. [30] reported that obese women are a risk factor for development of severe preeclampsia. In this current study it was observed that majority patients had weight 50-60 kg in both groups. The mean weight was found 54.0±9.7 kg in group A and 55.0±10.2 kg in group B. The mean weight difference was not statistically significant (p>0.05) between two groups. Similarly, Channaiah et al. [27] showed the mean weight was 54.81±14.11 kg in nitroglycerine-treated group, which is consistent with the present study. On the other hand Safavi et al. [25] found the mean weight was 84.4±5.1 kg in Nitroglycerine-treated group and 85.7±5.6 kg in Hydralazine-treated group, which is higher with the current study. In this study it was observed that mallampati I was found 66.7% in group A and 63.3% in group B. The difference was not statistically significant (p>0.05) between two groups. In this present study it was observed that emergency C/S was found 26 (86.7%) in group A and 25 (83.3%) in group B. The difference was not statistically significant (p>0.05) between two groups. Similarly, Safavi et al. [25] showed emergency C/S was found 87.5% in Nitroglycerine-treated group and 80.0% in Hydralazine-treated group. Elective C/S was found 12.5% in Nitroglycerine-treated group and 20.0% in Hydralazine-treated group, which is closely resembled with the present study.

It was observed in this study that pre induction mean heart rate was found 92.4±7.2 beat/min in group A and 93.7±8.3 beat/min in group B. Mean SAP was found 134.9±6.7 mmHg and 135.8±7.2 mmHg in group A and group B respectively. Mean DAP was found 93.5±5.3 mmHg in group A and 95.2±4.0 mmHg in group B. Mean MAP was found 106.4±6.1 mmHg and 108.7±5.3 mmHg in group A and group B respectively. It was observed that there is no statistically significant difference in pre induction HR, SAP, DAP and, MAP between two groups. Similarly, Safavi et al. [6] observed that the mean heart rate was 93.3±7.6 beast/min in Nitroglycerine-treated group and 89.0±15.6 beats/min in Hydralazine-treated group. The mean SAP was found 165.3±7.8 mmHg in Nitroglycerine-treated group and 169.3±11.1 mmHg in Hydralazine-treated group. The mean DAP was found 107.4±4.2 mmHg in Nitroglycerine-treated group and 109.4±8.9 mmHg in Hydralazine-treated group. The mean MAP was found 126.7±3.8 mmHg in Nitroglycerine-treated group and 129.3±8.1 mmHg in Hydralazine-treated group, which is comparable with the current study.

Safavi et al. [31] study showed that hydralazine was ineffective for attenuation of the stress caused by laryngoscopy during induction of general anesthesia. This may be due to the slow onset and variable duration of action of this drug, as well as compensatory tachycardia, which makes it difficult to titrate its action against the hypertensive response. [32, 33] In another study Hill et al. [34] showed that intranasal nitroglycerine can prevent an increase in BP following laryngoscopy and intubation. On the contrary, magnesium sulfate and lidocaine did not have significant effect on the hemodynamic changes following intubation. Further, in a study by Mikawak et al. [35], it was shown that administration of a single dose of intravenous nitroglycerine was a safe and effective method for attenuation of the hypertensive response following intubation. In a study performed in Greece [36, 37] women were enrolled to receive nitroglycerine before induction of anesthesia, and it was found that nitroglycerine effectively attenuated the increase in BP after laryngoscopy. These results are all in agreement with the success rates observed in the current study.

Limitations of the study

Our study wasn't a blinded study so patient bias was present along with observer bias in subjective recording and the study population was selected from one selected hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the country. The present study was conducted at a very short period of time. Small sample size was also a limitation of the present study. Therefore, in future

further study may be under taken with large sample size.

6. Conclusion and Recommendations

Overall, this can be concluded with the observation that women with severe preeclampsia who were preoperatively treated with intravenous nitroglycerine for blood pressure control, their haemodynamic response to laryngoscopy was more effectively attenuated than the group treated with intravenous hydralazine. Intravenous nitroglycerine provided a safe and more effective prophylaxis for patients with severe preeclampsia undergoing cesarean delivery under general anaesthesia in attenuating haemodynamic responses to laryngoscopy. Further studies can be undertaken by including large number of patients.

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