e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2024; 14(12); 208-213

Original Research Article

Comparison of Three Different Doses of Intranasal Nitroglycerine in Attenuation of Pressor Response to Laryngoscopy and Intubation - A Randomized, Double Blind, Intervention at SMS Hospital Jaipur

Jitendra Kumar Meena[1], Rajesh Sharma[2], Meena Bhupendra Murarilal[3]

[1]Senior Resident, Department of Anaesthesia, SMS Medical College and Hospital, Jaipur
[2]Senior Professor & HOD, Department of Emergency Medicine, SMS Medical College and Hospital, Jaipur
[3]Senior Resident, Department of Anaesthesia, SMS Medical College and Hospital, Jaipur

Received: 18-10-2024 / Revised: 21-11-2024 / Accepted: 26-12-2024
Corresponding author: Dr. Jitendra Kumar Meena
Conflict of interest: Nil

Abstract:

Background: Laryngoscopy and endotracheal intubation are associated with a transient but marked sympathoadrenal response, manifested by increases in heart rate and blood pressure. Excessive hemodynamic stress can precipitate complications in susceptible individuals. Various pharmacological interventions, including opioids, local anesthetics, and vasodilators, have been investigated to blunt this response. Nitroglycerine (NTG) administered intranasally may attenuate this pressor response via rapid absorption and vasodilatory effects.

Methods: In this randomized, double-blind, interventional study, 138 normotensive adult patients undergoing elective surgery under general anesthesia were allocated into three groups (46 in each). Patients in Group A received 400 µg intranasal NTG, Group B received 800 µg, and Group C received 1200 µg. Hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure) were recorded from baseline to 10 minutes post-intubation. Incidence of adverse events (tachycardia, hypotension, nausea) was also noted.

Results: All three groups showed an increase in heart rate at laryngoscopy and intubation. The group receiving 1200 µg demonstrated a higher peak heart rate compared to those receiving 400 µg or 800 µg. Conversely, systolic, diastolic, and mean arterial pressures decreased more pronouncedly with the 1200 µg dose compared to the lower doses. By 10 minutes post-intubation, blood pressure in the 1200 µg group was reduced by approximately 18–28% from baseline, while it was 10–21% and 13–24% in the 400 µg and 800 µg groups, respectively. The highest incidence of tachycardia (10.8%) and hypotension (8.7%) occurred with the 1200 µg dose; however, these events were easily managed without significant morbidity.

Conclusion: Intranasal nitroglycerine effectively attenuates the pressor response to laryngoscopy and intubation. The 1200 µg dose offers the most pronounced attenuation of blood pressure but carries a higher incidence of side effects. The intermediate dose (800 µg) may provide a favorable balance between efficacy and tolerability.

Keywords: Intranasal nitroglycerine, Laryngoscopy, Intubation, Pressor response, Hemodynamics.

Introduction

Laryngoscopy and endotracheal intubation are integral to modern anesthetic practice, ensuring a secure airway for patients undergoing various surgical procedures [1]. However, these maneuvers are associated with reflex sympathetic stimulation leading to tachycardia and hypertension—collectively termed the "pressor response" [2]. In patients with limited cardiovascular reserve, this exaggerated hemodynamic fluctuation can precipitate myocardial ischemia, arrhythmias, and even cerebrovascular events [3]. As a result, anesthesiologists have explored a variety of pharmacological strategies to mitigate these untoward responses, including beta-blockers, opioids, local anesthetics, and vasodilators [4]. Nitroglycerine (NTG) is a potent vasodilator primarily acting on venous capacitance vessels, resulting in decreased venous return and reduced cardiac preload. Additionally, at higher doses, NTG also dilates arterial vessels and lowers afterload [5]. Compared to intravenous or sublingual administration, intranasal NTG confers a rapid onset of action and comparatively reliable absorption [6]. This makes it an attractive option

for attenuating the hemodynamic surges during laryngoscopy without the delay of slower administration routes. The choice of an appropriate NTG dose is critical, given the potential for both inadequate control of blood pressure and excessive reduction leading to deleterious hypotension [7]. The relationship between dose, efficacy, and side effects in intranasal NTG remains an important area of investigation. Although several studies have shown that single-dose NTG can attenuate the pressor response, it remains unclear which specific dose offers the optimal therapeutic window for reducing complications while preserving stable hemodynamics [8]. This randomized, double-blind, interventional study was undertaken to compare three different doses of intranasal NTG—400 µg, 800 µg, and 1200 µg—for attenuation of pressor responses in normotensive patients undergoing elective surgery. The primary objective was to assess the proportionate differences in changes in heart rate (HR) and blood pressures (systolic, diastolic, and mean arterial pressure) across the three dosing regimens. Secondary objectives included evaluation of side effects such as tachycardia, hypotension, and nausea.[9,10] We hypothesized that all three doses would attenuate the hemodynamic response to laryngoscopy; however, higher doses might provide a stronger effect at the expense of more frequent adverse events. The findings from this study can help clinicians choose a dose that balances effective attenuation of hemodynamic surges with an acceptable safety profile, particularly in those with underlying cardiovascular risks.

Materials and Methods

Study Design and Setting: This hospital-based, double-blind, randomized interventional study was conducted at the Department of Anaesthesiology, Sawai Man Singh Medical College and its affiliated hospitals in Jaipur, Rajasthan. Approval from the Institutional Ethics Committee was obtained (No: 1229/MC/EC/2021) prior to patient recruitment.

Study Population and Duration: Adult patients (age 20–55 years), belonging to ASA physical status I or II, scheduled for elective surgeries under general anesthesia, were considered. Recruitment continued until a total of 138 participants were enrolled (46 in each of three groups), fulfilling the calculated sample size requirement. Patients with anticipated difficult airway, hypertension, IHD, arrhythmias, hepatic/renal dysfunction, pregnancy, or a known allergy to nitroglycerine were excluded.

Randomization and Blinding: A simple randomization via opaque sealed envelopes was used. A total of 138 envelopes (46 per group) were prepared, each specifying one of the three dosing regimens. A colleague opened the envelope, and patients were allocated to one of the following groups:

- **Group A:** Intranasal NTG 400 µg
- **Group B:** Intranasal NTG 800 µg
- **Group C:** Intranasal NTG 1200 µg

This was a double-blind study in which neither the participant nor the medical personnel (including anesthesiologists and operating room staff) were aware of the dose being administered. The study drug was prepared by a member of the research team not involved in the clinical management. Unblinding occurred only in the event of a severe adverse incident.

Anesthetic Protocol

1. **Pre-Anesthetic Checkup:** Included thorough medical history, physical examination, and routine investigations (hematological profile, renal and liver function tests, ECG, and chest X-ray).
2. **Informed Consent:** Written informed consent was obtained after explaining the study and anesthesia procedure.
3. **Monitoring:** Standard noninvasive monitors (ECG, NIBP, pulse oximeter) were attached upon arrival in the operating room. Baseline hemodynamic parameters were noted.
4. **Premedication:** Intravenous (IV) metoclopramide (10 mg), ondansetron (4 mg), midazolam (1 mg), and glycopyrrolate (0.2 mg) were administered.
5. **Administration of Study Drug:** According to the allocated envelope, patients received a single intranasal dose of NTG (400 µg, 800 µg, or 1200 µg). This was followed by 3 minutes of preoxygenation.
6. **Induction:** IV thiopentone (5 mg/kg) and succinylcholine (2 mg/kg) were administered to facilitate laryngoscopy. Direct laryngoscopy and endotracheal intubation were performed at 5 minutes after intranasal NTG administration.
7. **Maintenance and Reversal:** Anesthesia was maintained with 50% N2O + 50% O2, 0.2–1% sevoflurane, and intermittent doses of atracurium (0.5 mg/kg loading, 0.1 mg/kg as needed). At the conclusion, reversal was achieved with neostigmine (0.05 mg/kg) and glycopyrrolate (0.008 mg/kg). Patients were extubated upon recovery of protective airway reflexes and transferred to the recovery area.

Outcome Measures

- **Primary Outcomes:** Heart rate (HR) and blood pressures (systolic, diastolic, and mean) recorded at baseline, immediately after study drug administration, during intubation, and 1, 3, 5, 7, and 10 minutes post-intubation.
- **Secondary Outcomes:** Incidence of adverse effects including tachycardia, hypotension, and nausea.

Statistical Analysis: Data were entered into a Microsoft Excel spreadsheet and analyzed using

appropriate statistical software. Continuous variables (HR, BP) are presented as mean ± standard deviation, and intergroup comparisons were performed using one-way ANOVA with post-hoc analyses. Categorical data (incidence of adverse events) were analyzed using chi-square or Fisher's exact test. A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 172 patients were screened; 22 were excluded for not meeting inclusion criteria, and 12 declined participation. Finally, 138 patients (46 per group) were enrolled and randomized into Groups A, B, and C, receiving 400, 800, and 1200 µg intranasal NTG, respectively.

Overall Findings: In general, administration of intranasal nitroglycerine significantly blunted the pressor response to laryngoscopy and intubation across all three groups. However, the magnitude of attenuation, as well as the incidence of side effects, varied by dose.

Participant Demographics (2–4 Paragraphs): Overall, the demographic and anthropometric parameters including age, gender distribution, weight, height, and body mass index (BMI) were comparable across the three groups. The mean age ranged between 35.8 and 38.5 years, and about half of the participants were male. Most participants had a normal BMI, and the distribution of ASA Grades I and II was similar in each group, indicating well-matched cohorts without statistically significant differences. A notable proportion of participants fell in the 31–50 years age range, ensuring a relatively healthy adult population suitable for evaluation.

Nearly 60–67% of each group were classified as ASA Grade II, reflecting the presence of mild systemic disease in some patients but without significant compromise. As these variables did not differ significantly among the groups, any differences in outcomes can be attributed more confidently to the dosing strategies rather than demographic confounders.

Hemodynamic Changes: Hemodynamic parameters were recorded at baseline, after administering the study drug, at laryngoscopy (intubation), and at 1, 3, 5, 7, and 10 minutes post-intubation.

1. Heart Rate (HR):

- At baseline, mean HR was comparable (≈81–82 bpm) across all groups (Table 1).
- Post-drug, HR increased modestly in Groups B and C, with the highest surge (≈90 bpm) observed in Group C.
- At intubation, HR peaked in all groups (Group A: 89.8 bpm, Group B: 93.5 bpm, Group C: 94.7 bpm). By 3 minutes post-intubation, HR remained elevated, especially in Group C (≈24% above baseline), while Group A showed a relatively smaller increase (≈16.7%).
- By 10 minutes, HR in Group A nearly returned to baseline, while Groups B and C maintained higher residual elevations (+4.5% and +9.6%, respectively).

2. Systolic Blood Pressure (SBP):

- Baseline SBP was similar (≈123–125 mmHg).
- Immediately following drug administration, SBP dropped more in Group C (112.8 mmHg) than in Groups A or B (118.9 and 115.2 mmHg, respectively).
- At intubation, all groups demonstrated a transient rise; however, Group A returned closer to baseline while Group C remained below baseline despite the upward trend.
- Over the subsequent 10 minutes, SBP in Group C declined the most, reaching nearly 18% below baseline at 10 minutes, followed by Group B (13% below) and Group A (10% below).

3. Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP):

- A similar pattern was noted for DBP and MAP, with Group C exhibiting the largest initial drop and sustaining the greatest reduction relative to baseline during the post-intubation period.
- By 10 minutes, MAP in Group C fell by ≈28% from baseline, while Groups A and B showed reductions of ≈21% and ≈24%, respectively.
- Table 1 and Figure 1 (below) summarize these heart rate changes, and Table 2 and Figure 2 illustrate the systolic blood pressure trends over time.

Table 1: Heart Rate (bpm) at Key Time Points

Table 1. Heart Rate (bpm) at Key Time Points	Group A	Group B	Group C
Baseline	82.1 ± 6.6	82.4 ± 5.7	81.6 ± 5.9
Post-Drug	84.4 ± 5.6	89.8 ± 5.3	90.1 ± 6.3
Intubation	89.8 ± 5.0	93.5 ± 5.3	94.7 ± 5.0
3 min	94.7 ± 6.2	100.1 ± 6.0	104.9 ± 6.3
5 min	90.3 ± 6.4	94.6 ± 6.1	97.3 ± 6.4
10 min	81.8 ± 9.0	88.4 ± 7.4	92.7 ± 8.0

Table 2: Systolic Blood Pressure (mmHg) Over Time

Table 2. Systolic Blood Pressure (mmHg) Over Time	Group A	Group B	Group C
Baseline	123.8 ± 6.7	123.2 ± 6.2	125.0 ± 6.6
Post-Drug	118.9 ± 6.0	115.2 ± 5.6	112.8 ± 5.7
Intubation	125.8 ± 4.6	122.3 ± 4.9	120.0 ± 4.9
3 min	117.2 ± 5.8	112.9 ± 6.6	109.2 ± 5.9
5 min	115.7 ± 6.0	110.9 ± 6.6	107.6 ± 7.1
10 min	110.9 ± 6.1	106.2 ± 6.3	102.0 ± 7.1

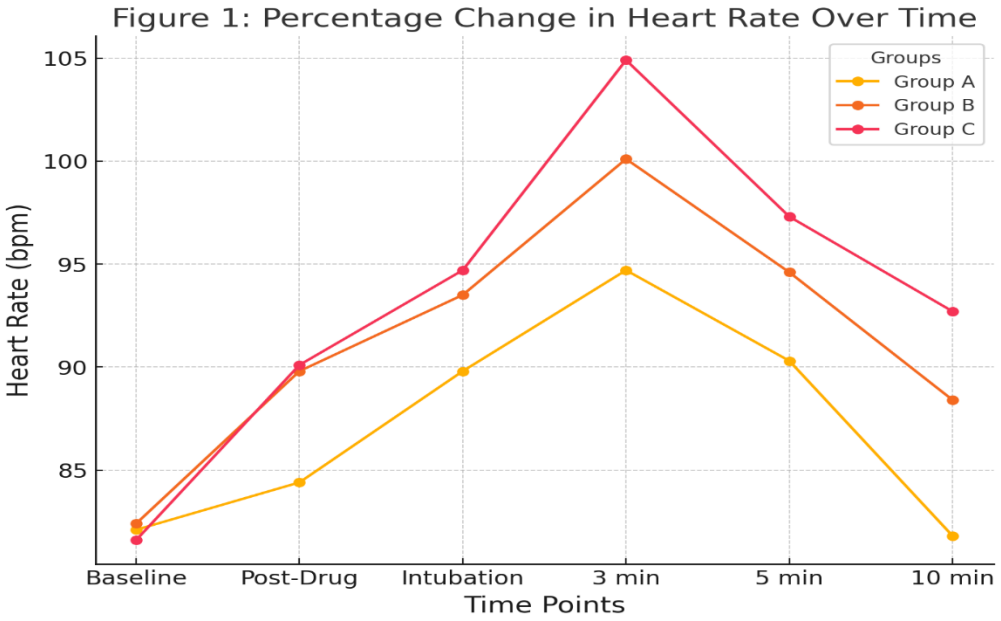

Figure 1: Percentage Change in Heart Rate over Time

Figure 1 shows the percentage change in heart rate from baseline to various time points post-intervention for Groups A, B, and C.

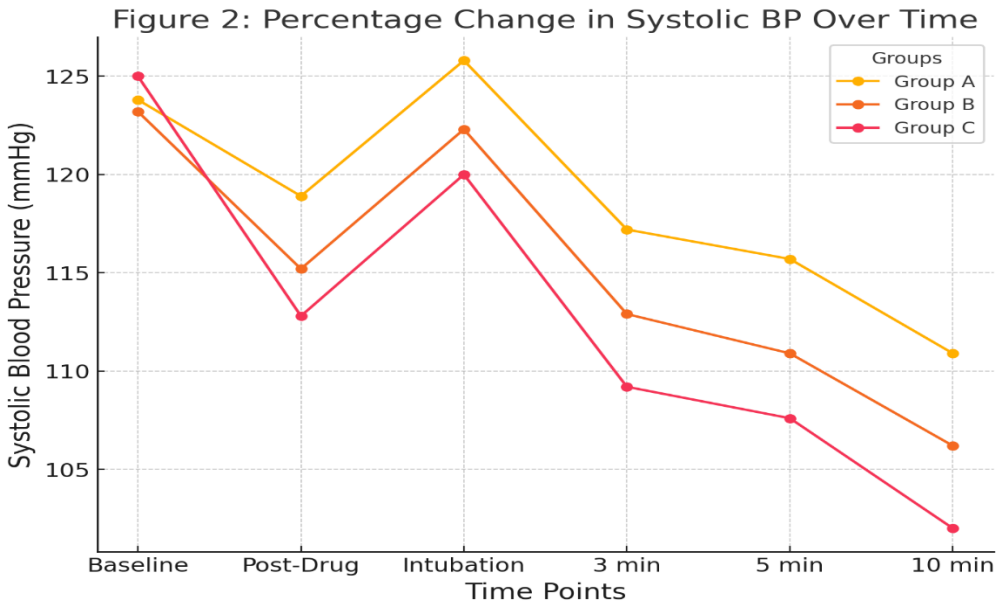

Figure 2: Percentage Change in Systolic BP over Time

Figure 2 illustrates the percentage change in systolic blood pressure over the same time intervals for the three groups.

Side Effects: The incidence of tachycardia, hypotension, and nausea was highest in Group C (10.8%, 8.7%, and 13%, respectively) and lowest in

Group A (4.3%, 2.1%, 6.5%, respectively). Intermediate values were observed in Group B. Most of these events were self-limiting or easily managed with standard interventions (e.g., fluid bolus, anticholinergics, and antiemetics).

Discussion

Attenuation of the pressor response to laryngoscopy and endotracheal intubation is a critical component of perioperative cardiovascular stability, particularly in patients with coexisting cardiovascular disease [11,12]. In this study, we evaluated three different doses of intranasal nitroglycerine (400, 800, and 1200 µg) for their efficacy in suppressing this hemodynamic surge. The findings indicate that while all three doses demonstrate significant attenuation, the highest dose (1200 µg) elicited the largest and most sustained reduction in arterial pressures—albeit with a concomitantly higher incidence of side effects.

Our results corroborate earlier literature documenting the benefits of vasodilators like NTG, which decrease both preload (via venodilatation) and afterload (via arterial dilation at higher doses) [13,14]. Intranasal delivery offers a rapid and reliable route, avoiding extensive first-pass metabolism seen with oral preparations and the invasive requirements of intravenous dosing [15]. In the present study, Group C (1200 µg) showed the greatest suppression of systolic, diastolic, and mean arterial pressures, consistently outperforming the other two groups in attenuating the peak intubation response.

However, an important observation is that the largest drop in blood pressure also translated into a modestly higher risk of hypotension, which occurred in nearly 8.7% of patients in Group C. Similarly, tachycardia was more frequent, possibly reflecting reflex sympathetic activation due to pronounced systemic vasodilatation [16]. By contrast, lower doses (400 and 800 µg) provided adequate attenuation of the intubation response for many patients, with fewer hemodynamic complications. For instance, Group A demonstrated only a mild and transient rise in heart rate, returning to near-baseline values by 10 minutes post-intubation, suggesting a gentler effect on preload and afterload [17].

In comparing previous work on intravenous or sublingual NTG with our intranasal approach, the timeframe and magnitude of response differ. Intranasal administration offers a relatively rapid onset, approaching that of the sublingual route, but with the advantage of ease of administration and less oropharyngeal irritation [18]. It is worth noting that, in clinical practice, tailoring the dose of NTG to a patient's cardiovascular reserve is imperative. While higher doses provide stronger attenuation, they also raise the possibility of troublesome hypotension, dizziness, or reflex tachycardia, all of which can be risky in certain populations.

Overall, this study highlights that 800 µg intranasal NTG may strike a balance between maintaining a stable hemodynamic profile and minimizing side effects. Nevertheless, dosage decisions should be individualized based on each patient's comorbidities and anesthetic risk profile. Future multi-center studies with larger patient cohorts might further refine these dosing thresholds and validate any subgroup benefits, such as in the elderly or those with underlying cardiovascular pathology.

Conclusion

Intranasal nitroglycerine is a valuable pharmacological tool for attenuating the pressor response associated with laryngoscopy and endotracheal intubation. In this study, all three tested doses (400, 800, and 1200 µg) effectively blunted the hemodynamic surge. Although the 1200 µg dose provided the most substantial reduction in arterial pressures, it was accompanied by a higher rate of side effects such as hypotension and tachycardia. The 800 µg dose appeared to offer a more favorable balance of efficacy and tolerability. Clinical judgment remains paramount in selecting the optimal dose for each patient's cardiovascular risk profile.

References

1. Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation-A Comparative Study Between iv Bolus Fentanyl, Lignocaine and Placebo(NS). J Clin Diagn Res [Internet]. 2012 Dec 15 [cited 2023 Jan 20]; 6(10):1749. Available from: /pmc/ articles/PMC3552219/
2. Mohammad A. Cardiovascular Response during Induction, Laryngoscopy, Intubation and Surgery in Normotensive and Controlled Hypertensive Patients Undergoing Abdominal Surgeries under General Anaesthesia. [cited 2023 Jan 20]; Available from: www.ijcmr.com
3. Kanchi M, Nair H, Banakal S, and Murthy K, Murugesan C. Haemodynamic response to endotracheal intubation in coronary artery disease: Direct versus video laryngoscopy. Indian J Anaesth [Internet]. 2011 [cited 2023 Jan 20]; 55(3):260. Available from: https:// journals.lww.com/ ijaweb/Fulltext/2011 /55030/Haemodynamic_response_to_endotracheal_intubation.8.aspx
4. Lakhe G, Pradhan S, Dhakal S. Hemodynamic Response to Laryngoscopy and Intubation Using McCoy Laryngoscope: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc [Internet]. 2021 [cited 2023 Jan 20];

59(238):554. Available from: /pmc/articles/PMC8369551/
5. Ozair E, Ali QE, Siddiqi MMH, Amir SH, Naaz S. A comparative evaluation of dexmedetomidine and fentanyl to attenuate hemodynamic response to laryngoscopy and intubation. Asian J Med Sci. 2018 Jan 1; 9(1):65–72.
6. Bronzwaer A. Cardiovascular Response Patterns to Sympathetic Stimulation by Central Hypovolemia. Br J Anaesth. 2016; 119(1):87–94.
7. Complications of the endotracheal tube following initial placement: Prevention and management in adult intensive care unit patients - UpToDate [Internet]. [Cited 2023 Jan 20]. Available from: https://www.uptodate.com/contents/complications-of-the-endotracheal-tube-following-initial-placement-prevention-and-management-in-adult-intensive-care-unit-patients
8. Endotracheal Tube Intubation Techniques - StatPearls - NCBI Bookshelf [Internet]. [Cited 2023 Jan 20]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560730/
9. Alvarado AC, Panakos P. Endotracheal Tube Intubation Techniques. StatPearls [Internet]. 2022 Jul 13 [cited 2023 Jan 20]; Available from:https://www.ncbi.nlm.nih.gov/books/NBK560730/
10. Heffner JE. Airway management in the critically ill patient. Crit Care Clin. 1990; 6(3).
11. Einarsson O, Rochester CL, Rosenbaum S. Airway management in respiratory emergencies. Clin Chest Med. 1994; 15(1):13–34.
12. Altun D, Ali A, Camci E, Ozonur A, Ozkan Seyhan T. Haemodynamic Response to Four Different Laryngoscopes. Turkish J Anesth Reanim. 2018 Oct 24; 46(6):434–40.
13. Bhardwaj N, Thakur A, Sharma A. A Review of Various Methods for Prevention of Pressor Response to Intubation. Int J Res Rev. 2020; 7(7):7.
14. McNarry AF, Patel A. The evolution of airway management-new concepts and conflicts with traditional practice. Br J Anaesth. 2017 Dec 1; 119:i154–66.
15. Mallick A, Klein H, Moss E. Prevention of cardiovascular response to tracheal intubation. BJA Br J Anaesth [Internet]. 1996 Aug 1 [cited 2023 Jan 20]; 77(2):296–7. Available from: https://academic.oup.com/bja/article/77/2/296/404253
16. Hu D. Implementing the Guideline of the Primary Prevention of Cardiovascular Diseases in China to Daily Practice: Promoting the Transition from “Treatment-Centered” to “People’s Health-Centered.” Cardiol Discov. 2021 Jun; 1(2):68–9.
17. Ease of Intubation While Using Macintosh and (Mccoy’s Type) Laryngoscope Blade Undergoing with Anaesthesiology. Eur J Mol Clin Med. 2020 Apr 1; 7(1).
18. Jaber S, De Jong A, Pelosi P, Cabrini L, Reignier J, Lascarrou JB. Videolaryngoscopy in critically ill patients. Crit Care. 2019 Jun 17; 23(1).