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Original Research Article

# Biochemical markers and haemodynamic changes of stress response after intubation with direct laryngoscopy versus video laryngoscopy versus fiberoptic intubation: A comparative study

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ABSTRACT

**Background:** Laryngoscopy and intubation leads to stimulation of pharyngeal and tracheolaryngeal nociceptors resulting in haemodynamic stress response (HDSR). Stress response is regulated by two primary neuroendocrine systems- the hypothalamus pituitary adrenocortical (HPA) and sympathetic adrenomedullary (SAM) system. Salivary alpha-amylase (SAA) level can be used as an index of the SAM activity, and serum cortisol as an index of HPA activity. This study was aimed to compare three different intubation techniques namely Macintosh laryngoscope, Video laryngoscope and Fiberoptic bronchoscope to observe stress response.

**Materials and Methods:** This prospective, comparative and observational study was carried out at 120 patients undergoing various elective surgeries under general anaesthesia. Patients were allocated after randomization into three study groups- Group D (Direct laryngoscope), Group V (Video laryngoscope) and Group F (Fiberoptic bronchoscope) with 40 patients in each. Saliva and venous blood samples were collected before inducing the patients and 5-minutes after intubation. Blood pressure, heart rate and saturation were monitored at fixed intervals.

**Results:** A significant difference was observed in the post-intubation values (p=0.0001) of salivary alpha amylase levels by direct laryngoscopy and fiberoptic laryngoscopy, while it was insignificant in video laryngoscopy (p=0.919). Post intubation cortisol level was significantly high in all three groups. However, on group comparison of mean differences of serum cortisol levels, a significant mean difference was seen between D vs V group (p=0.0001), and V vs F group (p=0.0001), while it was not significant in D vs F group (0.157). In addition, changes in mean arterial pressure and heart rate, at 1- and 5-min post- intubation were least in group V.

**Conclusions:** Video laryngoscopy is a safe, and reliable technique. Moreover, it causes lesser stress response to patients in comparison to direct laryngoscopy and fiberoptic groups.



## 1. Introduction

Direct laryngoscopy and endotracheal intubation are considered among the most invasive stimuli of the practice of general anesthesia which leads to stimulation of pharyngeal and tracheolaryngeal nociceptors resulting in haemodynamic stress response (HDSR).[1,2] Stress response is regulated by two primary neuroendocrine system—the hypothalamus pituitary adrenocortical (HPA) and sympathetic adrenomedullary (SAM) systems.[3] Salivary alpha-amylase (SAA) level can be used as an index of the SAM activity, and serum cortisol as an index of HPA activity. In our study we compared three different intubation techniques Macintosh laryngoscope, a rigid video laryngoscope (VL) and fiberoptic technology to observe stress response. Many studies have done previously

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to study for HPA, SAM and haemodynamic response but no study compare the three technique (DL, VL, FOB) of intubation with help of salivary alpha amylase and serum cortisol measurement.

## 2. Materials and Methods

This prospective, comparative and observational study was carried out at 120 patients admitted to Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow between 2018-2019, undergoing various elective surgery under general anaesthesia. Patients between 18-60 years of age having ASA physical status 1 and 2, with MPG 1 and 2 were included who had been operated in the morning from 8 am till 12 noon. Patients having reactive airway disease, current upper airway infection and patients on beta adrenergic blockers or anticholinergics drug were excluded from study. Randomization was done using computer generated random number table and patients were allocated into three study groups- Group D (Direct laryngoscope), Group V (Video laryngoscope) and Group F (Fiberoptic bronchoscope) with 40 patients in each. All patients were intubated with inj. midazolam 0.03 mg/kg, inj. fentanyl 2 mcg/kg, inj. propofol 2 mg/kg and vecuronium 0.1 mg/kg and maintained with isoflurane 1-1.5 vol% and N2O:O2(60%:40%) and vecuronium 0.02 mg/kg as needed. All intubations were conducted by the same anesthesiologist. Saliva and venous blood samples were collected before inducing patient and after 5-minute after intubation. Blood pressure, heart rate and saturation were monitored at fixed intervals.

During observation, no manipulations (including movement of head and skin preparation of operating field) were performed on patient. Any patient who required more than one attempt to achieve successful intubation was excluded from statistical analysis of the data.

## 3. Results

This study data showed normal distribution. The results were expressed in mean and standard deviation, frequency, percentages and graphs. The mean and standard deviation values of various biomarkers and haemodynamic variables (continuous variable) was analyzed across the three intubation techniques i.e. direct laryngoscopy, video laryngoscopy and fiberoptic intubation (nominal variable) by using one-way Anova test. Post Hoc analysis was also done to determine the groups showing significant difference. Paired t test and Repeated measures Anova test was used to assess intra-group significance. Two tailed probability (p) was calculated to test statistical significance at the 5% level of significance.

Difference in age and gender of patients of group D, V and F were not found to be statistically significant.

A significant difference was observed in the post-intubation values (p=0.0001) of salivary amylase levels by direct laryngoscopy and fiberoptic laryngoscopy, while it was insignificant in video laryngoscopy (p=0.919).

Post intubation cortisol level was significantly high in all three groups. However, on group comparison of mean differences of serum cortisol levels, a significant mean difference was seen between Direct vs Video Laryngoscopy (p=0.0001), and Video vs Fiberoptic Laryngoscopy (p=0.0001) while it was not significant in DL vs FOB group (0.157)

The mean arterial blood pressure at 1-min post-intubation was significantly raised in all three groups (0.001). On post HOC analysis among groups,1-min post intubation, a significant difference was seen for mean arterial pressure between Direct vs Video Laryngoscopy, and Video vs Fiberoptic Laryngoscopy (p=0.03, p=0.044 respectively). However, it was insignificant between Direct vs Fiberoptic Laryngoscopy (p=0.114).

While comparing mean arterial pressure 5-min post-intubation a significant difference (>0.05) was seen in comparison to pre-intubation value in DL and FOB group. However, it was not significant (<0.05) in VL group. Similarly, on post HOC analysis among groups for blood pressure parameters at 5-min post intubation, a significant difference was seen between Direct vs Video Laryngoscopy, and Video vs Fiberoptic Laryngoscopy (p=0.0006, p=0.04 respectively). However, it was insignificant between Direct vs Fiberoptic Laryngoscopy (p=0.06).

There was no significant difference in the mean SpO2 value across the three types of intubation at 1-min and 5- min post-intubation. The mean intubation time was maximum for fiberoptic laryngoscopy and minimum in case of direct laryngoscopy. There was a significant difference in the mean intubation time across the three groups of intubations (p=0.0001).

## 4. Discussion

Direct laryngoscopy and endotracheal intubation are considered among the most invasive stimuli of the practice of general anesthesia which leads to stimulation of pharyngeal and tracheolaryngeal nociceptors resulting in haemodynamic stress response (HDSR).[1,2] Many research and trials are being done to decrease the HDSR response and for ease of intubation by using different types of devices and different techniques but no study compare the three technique (DL, VL, FOB) of intubation with help of salivary alpha amylase and serum cortisol measurement. The present study was designed for comparison of haemodynamic and biochemical markers of stress response after intubation with direct laryngoscopy, fiberoptic Intubation and by video laryngoscopy and, for this purpose, total 120 patient in the age group of 18 to 60 year were allocated in three different group. All demographic data (age and sex) were comparable in all three group.

**Table 1:** Comparison of pre-intubation and post-intubation salivary alpha amylase levels on the basis of intubation technique (N=120)

| Salivary alpha amylase levels (U/ml) | Intubation Technique | | | f Value | p Value # |
|---|---|---|---|---|---|
| | Direct Laryngoscopy | Video Laryngoscopy | Fiberoptic Laryngoscopy | | |
| **Pre-Intubation** | 50.51±9.37 | 47.58±9.31 | 50.36±10.73 | 1.123 | 0.329 |
| **Post-Intubation** | 70.61±11.00 | 47.41±5.00 | 61.89±11.83 | 57.575 | **0.0001*** |
| **p Value @** | 0.0001* | 0.919 | 0.0001* | | |

# one-way Anova, @ Paired t test, *p<0.01, highly significant

**Table 2:** Comparison of pre-intubation and post-intubation serum cortisol levels on the basis of intubation technique (N=120)

| Serum cortisol levels (mcg/dL) | Intubation Technique | | | f Value | p Value # |
|---|---|---|---|---|---|
| | Direct Laryngoscopy | Video Laryngoscopy | Fiberoptic Laryngoscopy | | |
| **Pre-Intubation** | 11.12±4.25 | 9.87±2.17 | 10.14±3.07 | 1.6125 | 0.204 |
| **Post-Intubation** | 16.72±6.95 | 11.97±2.63 | 18.65±3.13 | 21.813 | 0.0001* |
| **p Value @** | 0.0001* | 0.0002 | 0.0001* | | |

#one-way Anova, @Paired t test, *p<0.01, highly significant

**Table 3:** Post HOC analysis for mean serum cortisol levels

| Serum Cortisol levels | Mean difference | 95% Confidence Interval | | p Value |
|---|---|---|---|---|
| | | Lower | Upper | |
| Direct vs Video Laryngoscopy | -4.75 | -7.2211 | -2.2789 | **0.0001*** |
| Direct vs Fiberoptic Laryngoscopy | 1.93 | -0.5411 | 4.4011 | 0.157 |
| Video vs Fiberoptic Laryngoscopy | 6.68 | 4.2089 | 9.1511 | **0.0001*** |

**Table 4:** Comparison of blood pressure parameters pre-intubation and 1-min and 5-min post-intubation

| Blood pressure parameter | Intubation Technique | Pre-intubation | 1-min/ 5-min post-intubation | p-value(1-min/5-min) |
|---|---|---|---|---|
| **Mean Arterial Pressure** | Direct laryngoscopy | 93.18±11.64 | 109.88±17.84 / 95.45±18.66 | <0.001 / >0.05 |
| | Video laryngoscopy | 88.60±11.36 | 105.18±6.56 / 83.70±11.11 | <0.001 / <0.05 |
| | Fibre optic laryngoscopy | 91.25±13.30 | 101.83±10.61 / 87.45±9.81 | <0.001 / >0.05 |

#one-way Anova, *p<0.01, highly significant

**Table 5:** Post HOC analysis of mean blood pressure parameters at 1-min and 5-min post-intubation

| | | | | | |
|---|---|---|---|---|---|
| **Mean arterial pressure at 1-min** | **Direct vs Video Laryngoscopy** | **-7.70** | **-11.3712** | **1.9712** | **0.03** |
| | Direct vs Fiberoptic Laryngoscopy | -8.05 | -1.3788 | -14.7212 | 0.114 |
| | Video vs Fiberoptic Laryngoscopy | -7.35 | -10.0212 | 3.3212 | 0.044 |
| **Mean arterial pressure at 5-min** | Direct vs Video Laryngoscopy | -11.75 | -19.0529 | 4.4471 | 0.0006* |
| | Direct vs Fiberoptic Laryngoscopy | -8.00 | -15.3029 | -0.6971 | 0.068 |
| | Video vs Fiberoptic Laryngoscopy | 10.75 | -3.5529 | 11.0529 | 0.04 |

We measured salivary alpha amylase pre-intubation and post-intubation in all three group(Table 1). In direct laryngoscopy group and fiberoptic laryngoscopy group, the mean value of salivary alpha amylase levels has increased from pre-intubation to post-intubation (50.51±9.37 to 70.61±11.00U/ml) and (50.36±10.73 to 61.89±11.83 U/ml) respectively, which was highly significant(p=0.0001). However, there was insignificant change (47.58±9.31 to 47.41±5.00 U/ml) in pre and post intubation values of salivary alpha amylase levels in video laryngoscopic group(p=0.919). Among these devices, a rigid video laryngoscope (VL) uses a blade to retract the soft tissues and transmits a lighted video image to a screen. Video laryngoscope do not require alignment of the oral, pharyngeal, and laryngeal axes for visualization of the glottis and tracheal intubation and causes minimal oropharyngeal and laryngeal stimulation and may hence potentially produce decreased amount of stress response.[4] The fiberoptic laryngoscope facilitates the visualization of the glottis with minimum force, but the need of maneuvers or instruments to clear the airway result in haemodynamic response. Factors like prolonged tracheal stimulation, jaw thrust maneuver in fiberoptic intubation and external neck manipulation also contribute to the haemodynamic response.[5,6] Similarly, the magnitude of the HDSR during Direct laryngoscopy and endotracheal intubation is variable and proportional to the amount of force applied during visualization of the glottis and the degree of tracheolaryngeal manipulation during advancement of ET tube into the trachea.[1,2]Thus, in VL group pre and post-intubation change in level of salivary alpha amylase was insignificant (p=0.919), but it was highly significant(p=0.0001), in DL and FOB group, which shows that Video laryngoscopy causes least neuroendocrine stress response to intubation in comparison to Direct laryngoscopy and Fiberoptic group. Our result was well supported by Natalja et al (2008),[7] who studied comparison of stress response performing intubation by direct laryngoscopy, fiberoptic intubation and the glidescope video laryngoscope and concluded that shorter and more confident intubations with a glide scope produces less nociceptive stimulus and less stress to the patient. In VL patient the SAA level after intubation significantly decreased, but in ML and FOB patients significantly increased. In our study we also found the similar result regarding salivary alpha amylase changes by different techniques. N Jakushenko et al[8] studied whether SAA and cortisol level in saliva and also in plasma were altered by laryngoscopy and endotracheal intubation, and concluded that SAA level significantly increased after intubation. When we compared pre and post intubation serum cortisol (Table 2) on the basis of intubation techniques, a significant difference was observed in the post-intubation values (p=0.0001) in all three groups. The mean value of serum cortisol levels has increased from pre-intubation to post-intubation by direct laryngoscopy (11.12±4.25 to 16.72±6.95 mcg/dl), by video laryngoscopy (9.87±2.17 to 11.97±2.63 mcg/dl) and (10.14±3.07 to 18.65±3.13 mcg/dl) in fiberoptic group. Although cortisol level increased significantly in all three groups, it was least raised in VL group. When post HOC analysis for mean serum cortisol level was performed between all the three groups(Table 3), we found a highly significant (0.0001) differences of serum cortisol levels, between DL and VL group and VL vs FOB group which is probably due to less amount of stress response produced by VL as it causes minimal oropharyngeal and laryngeal stimulation[4]. However, in DL vs FOB groups, it was insignificant (p=0.157) because they both produces a comparable stress response to tracheal intubation.[5] In Direct laryngoscopy, variable amount of force is applied during visualization of the glottis and tracheolaryngeal manipulation during advancement of ET tube into the trachea[1,2] and in FOB, prolonged tracheal stimulation, jaw thrust maneuver and external neck manipulation contribute to the haemodynamic response.[6,7] This again shows that VL group is associated with less stress response comparative to DL and FOB groups. Natalja et al (2008)[7] in their study found that after intubation, the cortisol level in blood serum did not significantly differ between the ML and GS patient groups, but was significantly higher ($P < 0.05$) in the FOB patient group. We also compared HDSR in terms of MAP at different time interval(Table 4). The mean arterial blood pressure at 1-min post-intubation was increased in all three groups and difference was highly significant (0.001). However, at 5 min post intubation there was decrease in MAP in VL group which was significant (0.05), while in DL and FOB group there was increase in MAP value 5 min post intubation but it was not significant. On post HOC analysis of mean arterial pressure at 1-minute and at 5-minute post-intubation between groups(Table 5), a significant difference was seen for mean arterial pressure between Direct vs Video Laryngoscopy, and Video vs Fiberoptic Laryngoscopy. However, it was insignificant between Direct vs Fiberoptic Laryngoscopy. This again shows that VL is associated with lesser pressure response during intubation because of less manipulation of soft tissues[4] when compared with DL and FOB groups. Barak, et al. (2003)[5] compared the stress response following tracheal intubation using direct laryngoscopy to that using fiberoptic bronchoscopy technique. In both groups, blood pressure and heart rate were significantly increased at 1, 2, and 3 min post-intubation and there was no significant difference between the two study groups and further reported that haemodynamic changes disappeared just in 5-min. This shows that haemodynamic response to stress is very fast and the effect is lost very quickly, thus, more precise recording of changes should be made every minute and invasively. They concluded that the use of either direct laryngoscopy

or fiberoptic bronchoscopy produces a comparable stress response to tracheal intubation. We also get similar results in our study groups. Similarly, Sourav, kr Bag et al[9] studied a comparative study between Truview$^{PCD}$laryngoscopy and Macintosh laryngoscopy in viewing glottic opening and ease of intubation: they concluded that the haemodynamic response to intubation was significantly less with the use of Truview$^{PCD}$laryngoscope when compared to that of Macintosh laryngoscope. Kayhan Z et al.(2005)[1] concluded that blood pressure, heart rate, plasma epinephrine, norepinephrine and vasopressin concentrations increased slightly in response to laryngoscopy and intubation, all returning to or below baseline 5-min later with no change in angiotensin converting enzyme activity in normotensive patients. In our study there was no significant difference in the mean SpO2 value across the three types of intubation. Furthermore, no Significant differences were noted in the mean $ETCO_2$ values and mean peak airway pressure values at 5, 15 and 30-min also. Mean intubation time on the basis of intubation techniques, which was maximum for fiberoptic laryngoscopy and minimum in case of direct laryngoscopy. Natalja et al[7] found that endotracheal intubation with a Fiberoptic intubation required the longest time and caused the most pronounced stress response. A significantly longer intubation time in the FOB patient group might be explained by the fact that before the intubation the patients were introduced muscle relaxant. This produced pharyngeal muscle loosening, the tongue and epiglottis pushed towards posterior pharyngeal wall and decreased the volume of pharynx, thus made visualisation difficult. On the other hand, DL and VL techniques allowed to lift the epiglottis, improving the visualisation. Barak et al. (2003)[5] have reported that FOB intubation requires a longer time in comparison to other methods. In fact, the intubation time, although statistically significant, differed only by some seconds in the VL and DL patient groups, while found in the FB patient group being almost twice as long. The Lim et al. (2005)[10] noticed shortest intubation time in the VL patient group. However, Kamewad et al (2016)[11] studied haemodynamic response to endotracheal intubation: direct versus video laryngoscopy and concluded that duration of laryngoscopy and intubation was significantly longer in video laryngoscopy. Moreover, haemodynamic changes did not show any significant differences between the groups.

It is interesting that although in VL group the stress response was statistically less significant than FOB and DL group, it was still present. In VL patient group, post-intubation salivary alpha amylase level did not show any increase while, DL and FOB patient group it was significantly high. Although serum cortisol level was significantly high in all three groups after intubation, it was minimally raised in VL group. This shows that in stress response, both neuroendocrine systems (HPA and SAM) are of importance and can react differently.[3]

Observing the above facts in our study it can be said that intubation with fiberoptic requires the longest time, causing the greatest pressor response[5,6] to the patients while, intubation with video laryngoscopy causes lesser stress response[4,7] to the patients. Thus, the video laryngoscope is a reliable technique for patient's safety.

## 5. Source of Funding

None.

## 6. Conflict of Interest

None.

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