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Research Article

Effect of fiberoptic intubation on myocardial ischemia and hormonal stress response in diabetics with ischemic heart disease

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KEYWORDS

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c-Peptide

Abstract *Background:* Diabetic patients with ischemic heart disease can greatly benefit from decreasing the stress response to intubation with its metabolic sequelae. The use of fiberoptic bronchoscopy will eliminate the response to direct laryngoscopy while lubrication of ETT with lidocaine gel 2% will decrease the response to endotracheal intubation. This study was conducted to compare the stress response hormones (glucose, cortisol and c-peptide) and the hemodynamic responses to intubation between direct laryngoscopy and fiberoptic bronchoscopy in diabetic ischemic patients.
Patients and methods: Forty-four adult diabetic patients with ischemic heart disease, ASA II, with a blood glucose level between 120 and 180 mg/dL, requiring orotracheal intubation under general anesthesia were divided into 2 equal groups. The laryngoscopic group ($n = 22$) and the fiberoptic group ($n = 22$). Ovassapian airway was used to facilitate fiberoptic intubation with avoidance of jaw thrust maneuver. Blood glucose, cortisol and c-peptide were recorded before induction and 10 min after intubation and compared between both groups. The hemodynamic parameters were recorded and compared between both groups. Automated ST segment monitoring was used to detect ischemia.

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Results: There was statistically significant increase in HR, SBP and DBP in laryngoscopic group than in fiberoptic group. However, the incidence of ECG ST-segment changes was comparable with no statistically significant difference between groups. There were no statistically significant differences regarding glucose, cortisol and c-peptide levels between the study groups pre and post-induction. The intubation time in the fiberoptic group showed a statistically significant increase in comparison with the laryngoscope group (39 ± 12.04 vs. 29.3 ± 8.54 s; $P < 0.05$).

Conclusion: The optimum use of fiberoptic bronchoscope with avoidance of jaw thrust maneuver attenuates the hemodynamic response to intubation which is beneficial in diabetic patients with ischemic heart disease. Stress response hormones showed no statistically significant difference between groups.

1. Introduction

Diabetes mellitus is a major chronic disease affecting the vital organs and the autonomic nervous system [1,2]. Stress response with secretion of many anabolic and catabolic hormones (cortisol, epinephrine, glucagon and growth hormone) resulting in alteration in plasma glucose, ketone bodies, blood urea nitrogen, lactate, free alanine, pyruvate, C-peptide and electrolytes [3,4]. In response to stress; blood glucose and cortisol rise while insulin secretion is biphasic. This means suppression of insulin secretion occurs first followed by a normal secretion. C-peptide is a useful marker of endogenous insulin production. In a non-diabetic there is endogenous insulin secretion to utilize the fuel produced by the stress hormones and thus glucose homeostasis is maintained but this compensatory role of insulin is less possible in diabetics.

In diabetics; abnormal metabolism of carbohydrates, proteins and fats as well as electrolyte disorders exists. If the stress response is prolonged, the continuous hypermetabolic state may cause loss of essential components of the body such as glucose, fat, protein and minerals leading to increased mortality and morbidity [1].

Diabetics are twice liable for heart disease or stroke. High blood glucose for a long time leads to an increase in fatty materials deposits inside the blood vessel walls leading to atherosclerosis and ischemic heart disease [5]. In general: myocardial ischemia during tracheal intubation has been reported in more than 11% of patients with myocardial disease [6]. So, tracheal intubation in diabetics represents a greater burden to the ischemic myocardium.

Fiberoptic bronchoscope is an important instrument for difficult airway management. The mechanical stimulus to oropharyngeal structures is reduced by fiberoptic intubation and it is likely to attenuate the hemodynamic response and the stress response during orotracheal intubation which may be of great benefit in diabetics with ischemic heart disease.

Some relevant studies [7–10] have investigated the hemodynamic response and catecholamine release to fiberoptic intubation in healthy individuals and the results were conflicting. No study was done on diabetic patients with ischemic heart disease.

The present study was designed to investigate the effect of fiberoptic intubation on the hemodynamics and stress response hormones (glucose, C-peptide, cortisol) in diabetics with ischemic heart disease in comparison with direct laryngoscopic intubation.

2. Patients and methods

After Institutional Ethics Committee Approval and informed consent, forty-four controlled diabetic patients (type II) with ischemic heart disease, ASA physical status II, within a target range of (120–180 mg/dl) blood glucose level [11] were included in the study. They were admitted to Kasr Al-Ainy hospital, scheduled for elective surgery under general anesthesia requiring orotracheal intubation. Types of surgery range from minor to moderate surgery: breast mass, inguinal hernia, laparoscopic cholecystectomy, varicose veins, lipomas and lymph node biopsy. Assessment of the patients' airway was done. They were randomly allocated to two equal groups (each 22 patients) using computer generated number and concealed using sequentially numbered, sealed opaque envelope technique. **Exclusion criteria**: ASA physical status III or IV, age less than 20 or more than 70, uncontrolled diabetics with blood sugar more than 180 mg/dl or less than 100 mg/dL (to avoid the risk of hyperglycemia and hypoglycemia), glycosylated Hb more than 7% , patients with autonomic neuropathy, unstable angina, patients with ejection fraction less than 45%, patients with difficult airway (El-Ganzouri score [12] more than 4), body mass index >30, gastro-oesophageal reflux, hyperactive airway disease, ENT surgery, upper airway abnormalities.

Patients were fasted for 6 h prior to surgery. They were on regular insulin adjusted by sliding scale [11]. Medications were continued till the day of surgery (Table 1b) except acetylsalicylic acid (ASA) or clopidogrel (Plavix) which were stopped one week before surgery. N.B: B blockers are avoided in diabetics because they may mask the symptoms of hypoglycemia. Instead, they used calcium channel blockers to control HR.

At the preoperative room: an 18 gauge intravenous cannula was inserted and baseline samples for blood glucose, cortisol and C-peptide were taken. Midazolam 0.02 mg/kg was given intravenously. No atropine or glycopyrrolate was given before induction. **Monitoring:** Noninvasive systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate {baseline, post-induction and 1 min after intubation} were recorded {the maximum hemodynamic changes appear 1 min after tracheal intubation} [13]. These parameters were recorded and compared between both groups by another anesthesiologist. Oxygen saturation was continuously monitored. Continuous 5-lead ECG recording (Datex, Helsinki, Finland) was connected before induction of anesthesia. It automatically stored all 5-lead ECG complexes every minute and measured the absolute and relative ST-segment deviation at 60 ms after the J point in all leads compared with their preoperative baseline [14].

Induction of Anesthesia: After 3 min of pre-oxygenation, anesthesia was induced with I.V. fentanyl 2 μg/kg, propofol 2 mg/kg and atracurium 0.5 mg/kg. Saline infusion was running during induction. When neuromuscular blockade was complete (absence of response to train of four stimulus), tracheal intubation was done by either the Macintosh laryngoscope (Group L) or by fiberoptic bronchoscope (Group F). In both groups: well lubricated cuffed (PVC) ETTs with 2% lidocaine gel with I.D. 7 mm and 7.5 mm were used for female and male patients, respectively.

In Group L (22 patients): In the sniffing position; intubation was done under direct vision using a Macintosh laryngoscope (size 3).

In Group F (22 patients): In the sniffing position; intubation was done by fiberoptic bronchoscope (Pentax) with an outer diameter of 5.1 mm. The lens was adjusted, the insertion cord was lubricated with lidocaine gel 2% together with the outer surface of an ordinary 7 mm or 7.5 mm I.D. ETT. The light source and suction were checked. The ETT was put in hot water to be malleable. The bronchoscope with the tube over it was advanced through a specialized incubating oral airway (Ovassapian airway). No jaw thrust maneuver was used. If failed first attempt or oxygen saturation decreased below 95%, direct laryngoscopy was used and the patient was excluded.

In both groups: confirmation of ETT position was done by bilateral breath sounds auscultation and by capnography. Ventilation was continued with fresh gas flow of 3 L/min. Anesthesia was maintained with 1.5% isoflurane, 100% oxygen and top-up doses of atracurium. For cases that show ST segment deviation: infusion of 1 μg/kg/min nitroglycerine according to the blood pressure.

In both groups: the time was recorded by another anesthesiologist from the moment of insertion of the instrument into the mouth till its removal. Only one attempt was allowed. If a second attempt was needed, the patient was excluded from the study. In Group F: all cases were done by anesthesiologists experienced in fiberoptic bronchoscope according to the established protocol for training in fiberoptic intubation [12].

Other samples for blood glucose, cortisol and c-peptide were taken 10 min after intubation and before surgical incision. Comparison was done between both groups. Glucose oxidase method was used for measuring plasma glucose. Serum C-peptide and cortisol were measured by chemiluminescent based ELISA technique.

3. Statistical analysis

Obtained data are presented as mean ± SD, numbers and percentages as appropriate. Categorical variables were compared using Chi-square (χ^2) test with continuity correction. Comparisons of continuous variables were performed using unpaired Student's *t*-test or mixed-design "two-group univariate repeated measures" analysis of variance (ANOVA) with post hoc Dunnett's test for multiple comparisons against baseline values to further investigate any statistically significant findings. Statistical analysis was performed using computer programs Microsoft® Office Excel 2010 (Microsoft Corporation, NY, USA) and SPSS 16.0 (SPSS Inc., Chicago, IL, USA). P value < 0.05 was considered statistically significant.

4. Results

It was a preliminary study in diabetic patients with ischemic heart disease. In (Group F): one patient was excluded due to failed fiberoptic intubation because of excess secretions (no atropine was given to avoid ischemic manifestations) and one patient who needed a second attempt. In (Group L): one patient required a second attempt and one patient had incomplete laboratory results of stress response hormones. These cases were excluded from the study.

Demographic data were obtained: Sex, age, weight, height and BMI.

The mean values of demographic characteristics of the patients are summarized in Table 1a.

There were no statistically significant differences regarding glucose, c-peptide and cortisol levels between the study groups pre and post-induction (Table 2).

(The incidence of ECG ST-segment changes was comparable with no statistically significant difference between the two groups (10% vs. 5%; $P > 0.05$) (Fig. 1).

The increase in HR was statistically significant relative to the baseline before induction in the laryngoscope group (95.0 ± 15.12 vs. 79.7 ± 14.23; $P < 0.05$). The HR showed

Table 1a Patients' demographic characteristics (mean ± SD).

	Fiberoptic (n = 20)	Laryngoscope (n = 20)
Sex	8 males 12 females	9 males 11 females
Age (years)	51.2 ± 8.649	47.2 ± 8.995
Weight (kg)	73.05 ± 10.85	75.45 ± 8.73
Height (cm)	164.75 ± 8.11	167.95 ± 5.83
BMI (kg/m^2)	26.80 ± 2.47	26.73 ± 2.56

*Statistically significant between-group difference ($P < 0.05$).

Table 1b Medications in both groups.

Cardiac medications	Fiberoptic group n = 20	Laryngoscopic group n = 20
Acetylsalicylic acid (ASA) or Clopidogrel (Plavix)	20	20
Oral nitrates {e.g. Isosorbide Mononitrate: Effox , Isosorbide Dinitrates: Nitromack}	20	20
Calcium channel blocker: e.g. Verapamil.	20	20
Angiotensin converting enzyme inhibitor (ACEI)	15	16
Statins (decrease cholesterol)	17	18
Trimetazidine (Vastarel)	4	5

n = Number of patients.
*Statistically significant between-group difference ($P < 0.05$).

Table 2 Glucose, c-peptide and cortisol levels (mean ± SD).

	Fiberoptic ($n = 20$)	Laryngoscope ($n = 20$)
Glucose (mg/dl)		
Pre-induction	124.4 ± 18.58	119.5 ± 11.36
Post-induction	128 ± 19.21	120.5 ± 10.14
c-Peptide (ng/ml)		
Pre-induction	2.26 ± 0.61	2.8 ± 0.49
Post-induction	2 ± 0.58	2.6 ± 0.51
Cortisol (ug/dl)		
Pre-induction	23.8 ± 3.19	24.9 ± 3.22
Post-induction	25.4 ± 3.11	26.3 ± 2.6

*Statistically significant between-group difference ($P < 0.05$).
†Statistically significant intragroup difference ($P < 0.05$).

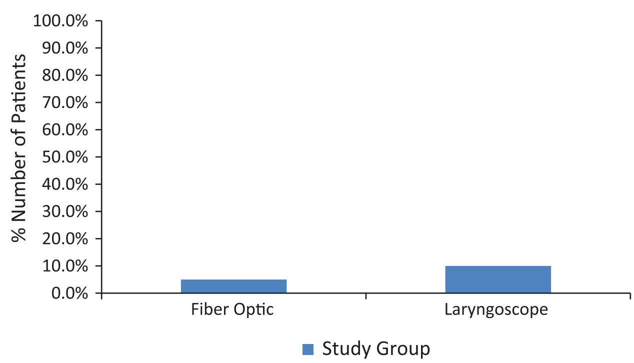

Figure 1 ECG ST-segment changes in response to induction and intubation in both groups.

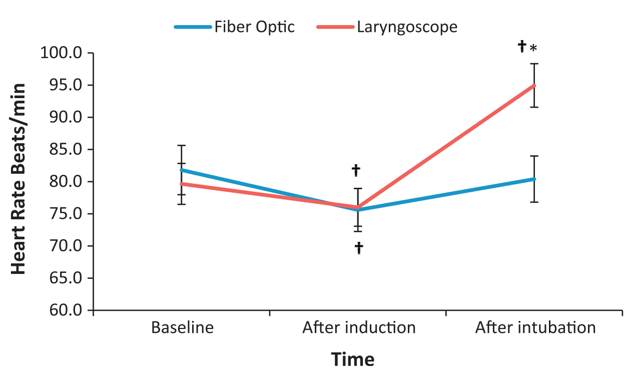

Figure 2 Heart rate throughout the observation period. $^{*}P < 0.05$ vs. the other group. $^{\dagger}P < 0.05$ vs. baseline. Error bars represent ±1 SE.

also a statistically significant increase in comparison with the fiberoptic group after intubation (95.0 ± 15.12 vs. 80.4 ± 16.05; $P < 0.05$) (Fig. 2).

Regarding the changes in ABP, there were statistically significant increases in SBP and DBP in the laryngoscope group after intubation relative to the baseline values (SBP 143.8 ± 16.39 vs. 133.2 ± 12.74; DBP 84.1 ± 15.09 vs. 77.1 ± 9.48; $P < 0.05$).

Also, both SBP and DBP in the laryngoscope group showed statistically significant increases after intubation in comparison with the corresponding values of the fiberoptic group (SBP 143.8 ± 16.39 vs. 128.3 ± 12.67; DBP 84.1 ± 15.09 vs. 73.5 ± 13.38; $P < 0.05$) (Figs. 3,4).

The intubation time in the fiberoptic group showed a statistically significant increase in comparison with the laryngoscope group. (39 ± 12.04 vs. 29.3 ± 8.54 s; $P < 0.05$) (Fig. 5).

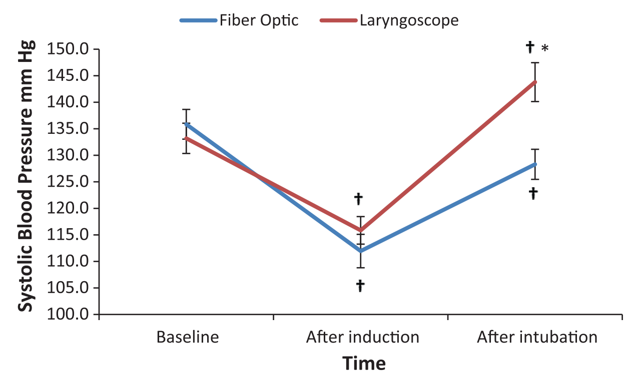

Figure 3 Systolic blood pressure throughout the observation period. $^{*}P < 0.05$ vs. the other group. $^{\dagger}P < 0.05$ vs. baseline. Error bars represent ±1 SE.

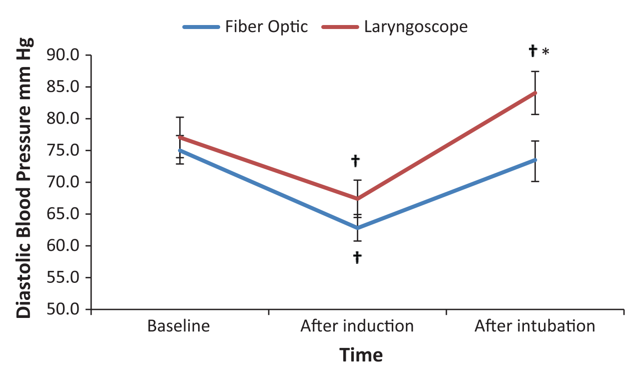

Figure 4 Diastolic blood pressure throughout the observation period. $^{*}P < 0.05$ vs. the other group. $^{\dagger}P < 0.05$ vs. baseline. Error bars represent ±1 SE.

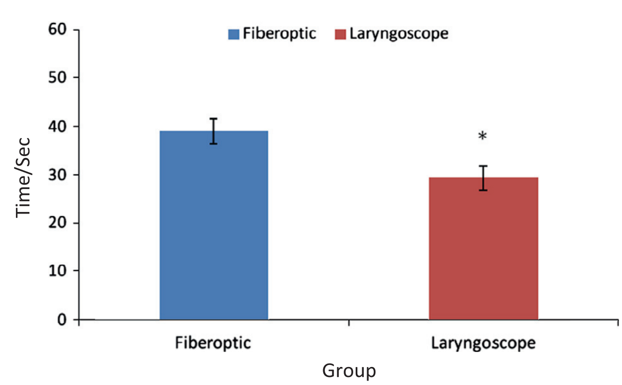

Figure 5 Intubation time in seconds in both groups. (Error bars represent ±1 SE).

5. Discussion

Diabetic patients with ischemic heart disease represent a great challenge to the anesthesiologist. Every effort should be done to make endotracheal intubation smooth and rapid to minimize ischemic sequelae [15,16] and the complications associated with hyperglycemia. This response to intubation is affected by the force applied by the laryngoscope, the intubation time and the degree of anesthetic depth.

Fiberoptic bronchoscope is now more available, and its use becomes easier and more rapid than before with less stimulation to the pharyngeal structures and less stress response.

In this study; the intubation time was shorter with laryngoscopic intubation than with fiberoptic intubation. However, the intubation time in fiberoptic group in this study (39 ± 12.04) seconds is still shorter than previous studies {120 ± 65 s} [15] and (55.0 ± 22.5 s) [17]. This may be explained by the use of the modified oral airways that facilitate fiberoptic intubation with no need for jaw thrust maneuver which is blamed to be the cause for most of the stress response accompanied fiberoptic intubation as will be discussed later.

As the time was shorter in this study in comparison to other studies and jaw thrust wasn't needed, less haemodynamic changes occurred and less stress hormones released. However, no statistically significant difference was recorded between the two groups as regard blood glucose, cortisol and c-peptide.

Jakushenko et al. [15] had studied the comparison between direct laryngoscopy and fiberoptic intubation. They concluded that the hemodynamic changes, blood cortisol, nor epinephrine and salivary alpha amylase level were higher in fiberoptic group than in direct laryngoscopy group. This difference can be explained by the longer time in fiberoptic group (120 ± 65)s than (29 ± 5)s in direct laryngoscopy.

Hawkyard et al. [7] had compared the BP and HR measurements between patients undergoing endotracheal intubation during general anesthesia (Group A), and who had an awake fibreoptic intubation under local anesthesia (group B). They concluded that awake fiberoptic intubation reduces the press or response to endotracheal intubation and it is suitable for use in those patients who are at risk from the pressor response.

On the contrary, Zhang Gue-hua et al. [9] had studied the hemodynamic response to orotracheal intubation by either fiberoptic bronchoscope or direct laryngoscope. They concluded that both techniques cause similar increases in BP and HR. They explained this by the longer intubation time with fiberoptic that leads to hypercapnia which leads to hypertension and tachycardia. Lifting the jaw upward and advancement of the insertion cord of the FOB into the trachea may be added factors.

Barak et al. [17] had compared the HR, BP and catecholamine (epinephrine and norepinephrine) blood levels between direct laryngoscopy and fiberoptic groups of patients after intubation. They concluded that no significant difference between the two study groups as regards the hemodynamics or the catecholamines levels. They suggested that general anesthesia of sufficient depth could inhibit the hemodynamic response to intubation and may result in similar results in both groups. Their results can be explained by the prolonged time for fiberoptic intubation (55.0 ± 22.5) seconds.

Newly developed devices that combine the features of fiberoptic bronchoscope and don't require the use of direct laryngoscopy like fiberoptic styletscope and Shikani Optical Stylet were investigated by many [18,10]. They compared the hemodynamic response of using these devices with direct laryngoscopy. They recorded less hemodynamic response with these devices which may be beneficial in patients with ischemic heart disease. Also, the incidence of sore throat was decreased because of elimination of direct laryngoscopy.

As the effect of laryngoscopy and intubation is associated with cardiovascular changes such as hypertension, tachycardia, arrhythmias, myocardial ischemia and an increase in catecholamine levels, Several techniques are used to attenuate these effects [19,20]. If no specific intervention is undertaken; half the patients with coronary artery disease experience episodes of ischemia during intubation [13].

Cardiac troponin which is specific to the myocardium increases after 3–4 h from the occurrence of chest pain in patients with acute myocardial infarction [14]. So, its measurement is of no benefit in this setting. Instead of this; S–T segment analysis together with hemodynamics (especially the heart rate) and catecholamine levels can be indicators of myocardial ischemia. Unfortunately, blood detection of norepinephrine and epinephrine is very complicated and requires instant blood test and immediate freezing of the sample [21]. Catecholamines are excreted also through saliva, but their level in saliva is not correlated with the level in blood. **So, in this study;** the significant decrease in H.R. and blood pressure with fiberoptic bronchoscope in comparison to direct laryngoscopy together with the decreased incidence of ST segment depression were good indicators of its beneficial use in ischemia.

Finally, the importance of avoiding jaw thrust was clarified by Jee et al. [22] who had studied 40 patients under general anesthesia and maintained the patients' airway with jaw thrust for 4 min. The lungs were ventilated through a Patil-Syracuse endoscopy. They concluded that jaw thrust maneuver with adequate force causes significant sympathetic responses during induction of general anesthesia. Nahid Aghdaii et al. [23] found no difference in hemodynamics between fiberoptic intubation with jaw thrust and direct laryngoscopy in ischemic patients undergoing coronary artery bypass graft. They hypothesized that the difference in nociceptive stimulation from the jaw thrust maneuver causes the difference in the circulatory responses between the fiberoptic and laryngoscopic intubation methods.

In summary: the hemodynamic responses to orotracheal intubation have two components; the first response is to laryngoscopy and the second response is to endotracheal intubation. The use of fiberoptic bronchoscopy will eliminate the response to direct laryngoscopy while lubrication of ETT with lidocaine gel 2% will decrease the second response. The use of the modified airways such as Berman, Williams and Ovassapian airways with avoidance of jaw thrust maneuver together with increased training and familiarity with the scope will facilitate fiberoptic intubation and decrease its time.

Limitation of the study: the study wasn't blind as the investigator was aware by the device used.

For future studies: this comparison can be done in patients with difficult airways as the use of direct laryngoscopy may cause more hemodynamic changes with more stress hormones release because of the increased force applied to the pharynx and larynx. Also, in difficult intubation; more external cricoid manipulations may be needed, more attempts may be required, more time may be lost. All these events can be avoided by the use of fiberoptic bronchoscope.

6. Conclusion

The optimum use of fiberoptic broncoscope with avoidance of jaw thrust maneuver attenuates the hemodynamic response to intubation which is beneficial in diabetic patients with ischemic heart disease. Stress response hormones showed no statistically significant difference between groups.

Conflict of interest

We don not have conflict of interest.

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