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Hemodynamic and Humoral Response to Intubation with Double-lumen Endotracheal Tubes *Versus* Single-lumen Tubes Combined with an Endobronchial Blocker: A Randomized Clinical Trial

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Abstract

Introduction: Insertion of endotracheal tubes, especially large and relatively inflexible double-lumen tubes, provokes cardiovascular and humoral responses which can cause complications. Bronchial blockers, combined with conventional single-lumen tubes (SLT), serve as alternatives to double-lumen tubes (DLT) and may provoke less hemodynamic response.

Methods: Forty adults scheduled for elective thoracic surgery requiring single-lung ventilation were randomly assigned to DLT or SLT combined with EZ-Blocker (EZ), a bronchial blocker. Heart rate and arterial blood pressure were recorded before induction of anesthesia, before laryngoscopy, after laryngoscopy, and one minute after intubation. Epinephrine, norepinephrine, and cortisol serum concentrations were assessed one minute after intubation.

Results: Pre-laryngoscopy values were comparable in both groups. Mean arterial pressure significantly increased in both groups during intubation. The maximum value during intubation was significantly higher with DLT (121 ± 17 mmHg), compared to bronchial blocker (105 ± 18 mmHg, P=0.022). Heart rate increased significantly during intubation in both groups (DLT from 68 ± 9 to 86 ±11, P<0.001, bronchial blocker from 72 ±11 to 87 ± 16, P=0.002), but the increase did not differ between the groups (P=0.76). Epinephrine, norepinephrine, and cortisol serum concentrations did not increase significantly from baseline values and did not differ between the treatment groups.

Conclusion: Insertion of DLT increases blood pressure more than placement of a SLT combined with bronchial blocker. However, the difference is probably not clinically important. Furthermore, there were no significant differences in heart rate or catecholamine concentrations. Clinicians should consider other factors when choosing between airway options for single-lung ventilation.

Keywords: Anaesthesia; Cardiovascular response; Bronchial blocker; Catecholamines; Stress reaction; Single lung ventilation

Introduction

Single-lung ventilation is necessary in several types of pulmonary, thoracic, and cardiac surgery. Double-lumen tubes which allow separate ventilation of each lung are the most common approach [1,2]. However, double-lumen tubes are larger and relatively inflexible than conventional single-lumen tubes; therefore insertion is more difficult and may trigger an increased hemodynamic response and stimulate the sympathetic nervous system exceedingly [3,4]. A consequence is perioperative tachycardia and hypertension, with consequent risk of myocardial ischemia and infarction [5,6].

Patients undergoing surgery requiring single lung ventilation are often elderly, have diminished physiological reserve, alterations in autonomic function, and a high incidence of coexisting cardiovascular diseases such as coronary atherosclerosis and hypertension [7,8]. In this context, intensive hemodynamic responses might be dangerous for the patients and lead to cardiovascular complications.

An alternative to double-lumen tubes are bronchial blockers, such as Univent torque control blocker [9], wire-guided endobronchial Arndt Blocker [10,11], Cohen Flex-tip Blocker [12], Coopdech Blocker [13], and the EZ-Blocker [14]. Bronchial blockers are easier to insert than double-lumen tubes [15] and thus presumably provoke a smaller stress response and less autonomic system activation.

Previous studies demonstrate that laryngoscopy causes cardiovascular and humoral response [16]. Other studies also demonstrated that the time required for laryngoscopy with a double-lumen tubes — and presumably the resulting autonomic stress — is greater than with single-lumen tube [7,14]. We therefore tested the primary hypothesis that endotracheal intubation with a conventional single-lumen tube combined with a bronchial blocker provokes less hypertension than intubation with a conventional double-lumen tube. Our secondary hypotheses were that endotracheal intubation with a conventional single-lumen tube combined with a bronchial blocker

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triggers less tachycardia and a smaller neuro-endocrine response than intubation with a conventional double-lumen tube.

Methods

With approval of the local Ethics Committee of the Medical University of Vienna, and written informed consent, we enrolled 40 adults scheduled for elective thoracic surgery with single-lung ventilation in this prospective, randomized clinical trial. All patients were American Society of Anesthesiologists physical status 1-3 and aged between 18 and 90 years. We herein report an analysis of secondary outcomes from a previously published study (NCT01171560) [14]. Although initially planned and blood samples were taken, funding for blood analyzes was granted after publication of the initial report.

Exclusion criteria included a body mass index (BMI)>45 kg/m^2; anycontraindications to insertion of a double-lumen tube or bronchial blocker; systemic infection or suspected tuberculosis; thoracic surgery or use of beta-blockade medications, calcium antagonists or ACE inhibitors within the month of surgery; and suspected difficult airway (Mallampati Score 4).

Protocol

Patients were premedicated with 7.5 mg oral midazolam an hour before surgery. A radial arterial cannula was inserted. After two minutes of pre-oxygenation, anesthesia was induced with intravenous midazolam 0.04 mg/kg, fentanyl 2 µg/kg, propofol 1.5 mg/kg, and rocuronium 0.6 mg/kg. Two minutes after rocuronium administration, one of three involved experienced anesthesiologists intubated the patients in supine position. Each was familiar with both techniques and had high level of experience in endotracheal intubation. Participating patients were randomly assigned 1:1 to one of two groups: (a) double-lumen tube; or, (b) conventional single-lumen tube combined with the EZ bronchial blocker. Randomization was based on computer-generated codes kept in sequentially numbered opaque envelopes that were opened just before induction of general anesthesia.

A left-sided double-lumen tube (Bronchocath; Teleflexmedical - Ruesch, Kernen, Germany), size 37 French for women and 39 French for men was used for intubation in the double-lumen tube group. Double-lumen tubes were introduced into the trachea using conventional direct laryngoscopy using a curved Macintosh blade of an appropriate size. After passing the vocal cords, the tube was rotated 90 degrees towards the left and advanced until slight resistance was met. Tracheal and bronchial cuffs were inflated and correct position was verified by fiberoptic bronchoscopy [17].

Patients assigned to the bronchial blocker group were intubated using a conventional single lumen tube (Mallinckrodt, Athlone, Ireland), 7.5 mm intraluminal diameter for women and 8.5 mm for men, using conventional direct laryngoscopy. A multiport adapter was inserted between the tube and the circle system Y piece, and an EZ bronchial blocker (AnaesthetIQ B.V. and IQ Medical Ventures B.V., the Netherlands, Rotterdam) was inserted through an upper port on the multiport adapter with completely deflated cuffs. The EZ bronchial blocker was advanced until slight resistance was met, suggesting the position between the end of tracheal tube and the carina was reached, with the distal ends of the bronchial blocker protruding into the left and right main bronchi. Correct position was verified with fiberoptic bronchoscopy [18]. Each distal cuff on the bronchial blocker was inflated with air and then deflated under direct visual guidance to ensure proper function.

After intubation, patient`s lungs were mechanically ventilated and anesthesia was maintained with propofol, fentanyl and sevoflurane.

Measurements

An independent investigator documented radial arterial pressure, heart rate (HR), electrocardiogram (ECG), and peripheral oxygen saturation (SpO_2) during intubation. The Anesthesiologist responsible for the intubation procedure was not told that hemodynamic parameters serve as an outcome measure. We also recorded the patient's sex, age, weight, height, American Society of Anesthesiologists (ASA) physical status score, and Mallampati score.

Arterial blood was sampled just before starting laryngoscopy and one minute after inflating the cuffs (either of double-lumen tube or bronchial blocker). We sampled blood for catecholamine analysis one minute after intubation because Oczenski et al. reported that mean arterial blood pressure, heart rate, and plasma norepinephrine concentrations were highest one minute after endotracheal intubation [18], an observation that was subsequently confirmed in other settings [19,20].

Blood samples were maintained on ice for no more than 15 minutes before serum was separated by centrifugation at 2000 r.p.m. for 3 minutes. Serum cortisol was analyzed by an electrochemiluminescence immunoassay with a Modular <EEE> automated analyzer from Roche Diagnostics, Mannheim, Germany. The limit of detection was 0.018 µg/dl and the interassay coefficient of variation was 4.2%. Catecholamines were measured in plasma samples with kits from Chromsystems, Graefeling/Munich, Germany. After extraction by alumina oxide the catecholamines were separated on a C18-reverse phase column by high-performance liquid chromatography. Norepinephrine and epinephrine were quantified by an amperometric electrochemical detector (ERC, Riemerling, Germany). Analytical sensitivity was about 20 ng/l and analytical imprecision was 8-13% as reflected by the interassay variation coefficients.

Statistical Analysis

Maximum hemodynamic response, defined as highest mean arterial blood pressure during intubation was our primary outcome. Secondary outcomes were increases in serum epinephrine, norepinephrine and cortisol concentrations; the change in mean arterial blood pressure from before induction of anesthesia to immediately before laryngoscopy, to after passing vocal cords, and to after inflating the bronchial cuffs.

For descriptive statistics we used Sigmaplot, Version 11.0 (Sytstat Software Inc., Chicago, Illinois, USA). Statistical analysis was performed using Mann-Whitney Rank Sum Test for non-parametric data and the student t-test for parametric data. Results are presented as means ± SDs; $p<0.05$ was considered to be significant.

A power analysis and sample-size estimate was made for the previously published data. However, a study population of 40 patients (20 per group) allowed us to detect a difference in maximum mean arterial blood pressure of 20 mmHg between the two groups with a power of 0.85 and an alpha error of 5%.

Results

Forty patients, twenty in each group, were enrolled and randomized. One patient who was randomized to the EZ bronchial blocker group was excluded before intubation because placement of arterial cannula proved impossible; this subject was therefore excluded from analysis. Baseline intraoperative characteristics of the study groups are shown

	Double-lumen tube (n=20)	Bronchial blocker (n=19)	P Value
Sex (m/f)	12; 8	8; 11	
Age (yr)	62 ± 14	54 ± 20	P=0.109
Weight (kg)	79 ± 19	74 ± 13	P=0.407
Height (cm)	173 ± 11	170 ± 9	P=0.409
ASA physical status (number)			
1	5	2	
2	9	10	
3	6	7	
Mallampati score			
1	2	4	
2	13	12	
3	5	3	
Cormack and Lehane			
1	13	14	
2	7	5	
Indications			
Lung biopsy	2	1	
Lobectomy	8	5	
Segmentectomy	6	7	
Pleural decortication	4	6	
Midazolam (total in mg)	3.2 ± 0.8	3.0 ± 0.5	P=0.422
Fentanyl (total in mg)	0.2 ± 0.4	0.2 ± 0.3	P=0.603
Rocuronium (total in mg)	47.6 ± 11.7	44.5 ± 8.1	P=0.439
Propofol (total in mg)	119 ± 29.2	111 ± 20.3	P=0.415

Values are means ± SDs or number of patients.

Table 1: Morphometric and demographic characteristics.

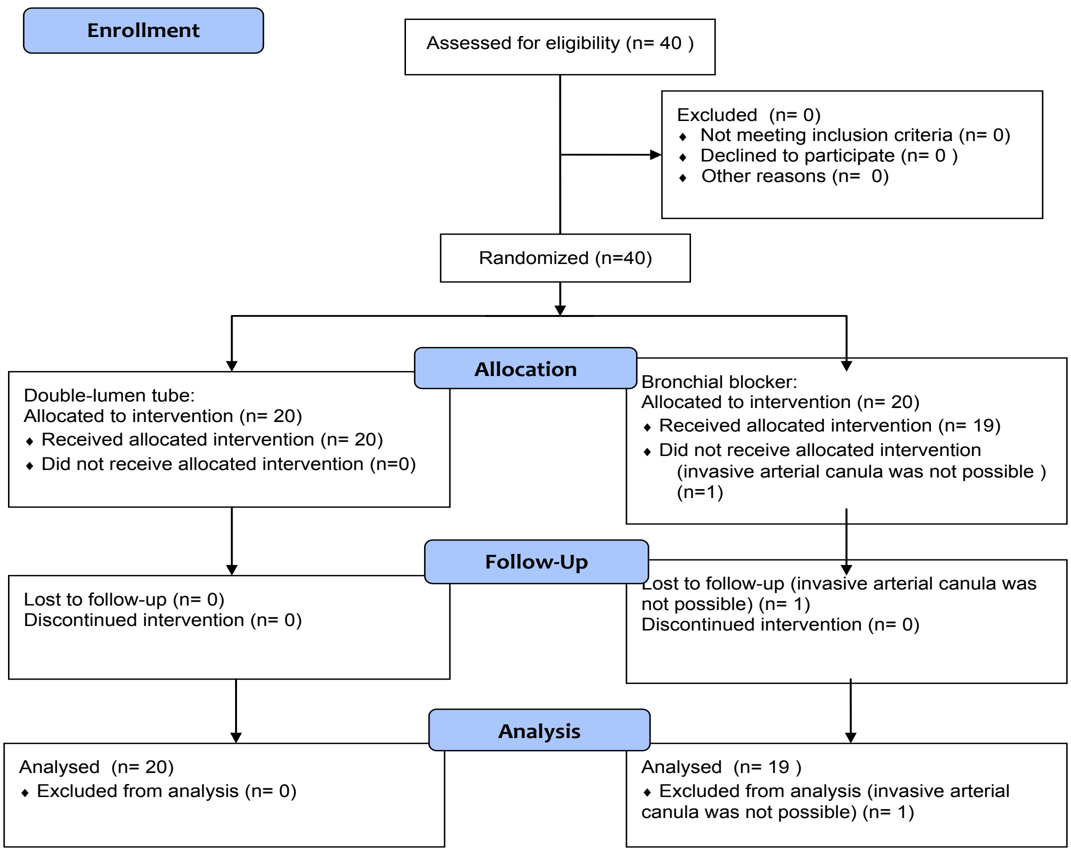

Figure 1: Difference between the mean induction doses of Propofol. Bar A is for Group K, Bar B is for Group M.

in Table 1. Patients randomized to the double-lumen tube group, by chance, were slightly heavier, taller, older, and more likely to be male. However, these differences were neither statistically significant nor clinically important. No supplemental fentanyl was given until at least one minute after intubation. Each endotracheal intubation was successful on first attempt and no tube misplacement occurred (Figure 1).

Endotracheal intubation using double-lumen tube took 85 seconds (range 166 s) and was significantly faster than endotracheal intubation using conventional single lumen tube combined with the bronchial blocker (192 s, range 379 s, p<0.001).

Blood pressure increased during intubation in both groups. The highest mean arterial pressure during intubation was significantly greater than before induction of anesthesia in both groups (double-lumen tube from 96 ± 23 to 121 ± 17 mmHg, P=0.002 and bronchial blocker from 92 ± 12 to 105 ± 18 mmHg, P=0.013). Mean arterial blood pressure before induction of anesthesia, before start of laryngoscopy and after passing vocal cords did not differ significantly between both groups [Table 2], whereas difference after inflating the bronchial blocker cuffs (P=0.008, double lumen tube 113 ± 25 mmHg and bronchial blocker 87 ± 12 mmHg) and highest score during intubation procedure (P=0.022, double lumen tube 121 ± 17 mmHg and bronchial blocker 105 ± 18 mmHg) differed significantly.

The highest heart rate during intubation was significantly greater than before induction of anesthesia in both groups (double-lumen tube from 68 ± 9 bpm to 86 ± 11 bpm, P ≤ 0.001 and bronchial blocker from 72 ± 11 bpm to 87 ± 16 bpm, P=0.002). Heart rates were comparable in both groups at all times [Table 2].

Epinephrine, norepinephrine, and cortisol serum concentrations did not increase significantly from baseline values, and did not differ between the treatment groups [Table 2].

	Double-lumen tube (n=20)	Bronchial blocker (n=19)	p-value
Mean arterial blood pressure (mmHg)			
Before induction of anaesthesia	96 ± 23	92 ± 12	0.588
Prior to start of laryngoscopy	86 ± 18	79 ± 12	0.230
After passing vocal cords	98 ± 27	92 ± 18	0.431
Inflating bronchial cuffs	113 ± 25	87 ± 12	0.008
Highest value	121 ± 17	105 ± 18	0.022
Average maximum change	28 ± 21	20 ± 16	0.376
Heart rate (beats/min)			
Before induction of anaesthesia	68 ± 9	72 ± 11	0.220
Prior to start of laryngoscopy	70 ± 13	71 ± 12	0.765
After passing vocal cords	73 ± 12	81 ± 18	0.172
Inflating bronchial cuffs	85 ± 13	83 ± 14	0.695
Highest value	86 ± 11	87 ± 16	0.757
Average maximum change	19 ± 12	15 ± 11	0.381
Norepinephrine (ng/l)			
Before laryngoscopy	224 ± 144	207 ± 101	0.669
One minute after intubation	223 ± 135	234 ± 120	0.633
Epinephrine (ng/l)			
Before laryngoscopy	60 ± 52	43 ± 20	0.227
One minute after intubation	28 ± 25	30 ± 40	0.876
Cortisol (µg/dl)			
Before laryngoscopy	13 ± 7	13 ± 8	0.998
One minute after intubation	12 ± 7	12 ± 8	0.946

Values are means ± SDs.

Table 2: Blood pressure, heart rate, catecholamine and cortisol values during intubation.

Discussion

Laryngoscopy is stressful and associated with hemodynamic and humoral responses [3,16]. The stress response is activated by airway receptors which are densest in the proximal portion of the tracheobronchial tree [7]. Shribman et al. demonstrated that the stress response is triggered by laryngoscopy, whereas tracheal intubation *per se* contributes little to the hemodynamic response [16]. In this context, two independent variables seem to be important: duration of intubation and force exerted on the tongue.

Duration of intubation is prolonged when using double-lumen tubes compared with single lumen tubes [7,14]. Grocott et al., for example, demonstrated, that placement of double-lumen tube requires more laryngoscopy attempts compared with single-lumen tube combined with bronchial blocker [15].

We therefore anticipated that endotracheal intubation using single-lumen tube combined with bronchial blocker might be less stressful than endotracheal intubation using a double-lumen tube. Our study confirms that both approaches increase arterial blood pressure compared to baseline. However, the increase was trivial with single-lumen tubes and bronchial blockers. The increase was somewhat larger with double-lumen tubes, but still of questionable clinical importance. Furthermore, heart rates and catecholamine concentrations were essentially unchanged by intubation. We thus conclude that the choice of airway instrumentation for single-lung ventilation should be based on factors other than hemodynamic and autonomic responses.

Our findings confirm prior findings by other researchers. Mizrak et al. compared hemodynamic responses between single-lumen tube, double-lumen tube and laryngeal mask [20]. Hemodynamic response was comparable between single-lumen and double-lumen tube and was highest one minute after intubation, a finding consistent with Yoo et al. [7] Interestingly, our patients showed increase of heart rate and arterial blood pressure, whereas humoral response was not pronounced or absent. This result is consistent with those of Barak et al., who also found little correlation between catecholamine levels and hemodynamic changes during either direct laryngoscopy or fiber optic bronchoscopy [21]. Others, though, do find concordant increases in hormonal and hemodynamic responses. It seems likely that in our patients, the stress was sufficiently brief that it triggered a neurally mediated hemodynamic response without a concurrent hormonal response.

Several studies showed, that double lumen tubes and bronchial blockers are comparable in respect to lung isolation [22]. Insertion of double-lumen tubes is generally faster than positioning bronchial blockers, although introduction is sometimes impossible [23]. In such cases, bronchial blockers are a reasonable alternative [24]. Furthermore bronchial blockers cause less postoperative sore throat and hoarseness than double-lumen tube [25,26].

Our findings are limited to patients with American Society of Anesthesiologists physical status 1-3 and cannot be extrapolated to patients with severe systemic diseases. Device allocation was randomized, but could not be blinded. However, all our outcomes are objective and unlikely to be influenced by bias. The thoracic anesthesiologists who intubated our patients had a high level of experience; practitioners with less skill may have provoked greater hemodynamic or autonomic responses with one or other of the airway approaches [27].

Hemodynamic responses to intubation depend critically on drug choice and dose. Drugs given for anesthetic induction in our study included opioids [4,28], propofol [29,30], sevoflurane [30,31], and midazolam [32] — all of which blunt the hemodynamic and hormonal responses to stressful situations. The response to intubation may have been considerably more impressive with different drugs. Similarly, responses may have been more impressive with lower drug doses.

In summary, insertion of double-lumen tubes increases blood pressure more than placement of a single-lumen tube combined with bronchial blocker. However, the difference is probably not clinically important. Furthermore, there were no significant differences in heart rate or catecholamine concentrations. Clinicians should consider other factors when choosing between airway options for single-lung ventilation.

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