J Clin Monit Comput
DOI 10.1007/s10877-015-9659-x

ORIGINAL RESEARCH

Comparison of the effects of various airway devices on hemodynamic response and QTc interval in rabbits under general anesthesia

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Received: 29 June 2014 / Accepted: 27 January 2015

Abstract In this study, we aimed to compare the effects of various airway devices on QTc interval in rabbits under general anesthesia. The subjects were randomly separated into four groups: Group ETT, Group LMA, Group PLA, Group V-gel. Baseline values and hearth rate, mean arterial pressure and ECG was obtained at the 1st, 5th and 30th minutes after administration of anesthesia and placement of airway device and, QTc interval was evaluated. Difference was observed between ET group and V-gel group in the 5th minute mean arterial pressure values ($p < 0.05$). It was observed that QTc intervals at the 1st and 5th minute in the ET group significantly increased when compared with the other groups ($p < 0.05$). Again, it was observed that QTc interval of ET group at the 15th and 30th minute was longer when compared with PLA and V-gel groups ($p < 0.05$). It was also observed that QTc interval of LMA Group at the 5th minute after intubation significantly increased when compared with V-gel group ($p < 0.05$). It was observed that HR values of ETT group at the 1st, 5th and 15th minutes after intubation increased with regards to PLA and V-gel groups ($p < 0.05$). It was determined that the 30th minute hearth rate of ETT group was higher when compared to V-gel group ($p < 0.05$). Conclusion: In our study we observed that V-gel Rabbit affected both hemodynamic response and QT interval less than other airway devices.

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Keywords Endotracheal intubation · Laryngeal mask airway · Cobra PLA · V-gel Rabbit · Supraglottic airway · QTc · Hemodynamic response

1 Introduction

Airway safety in general anesthesia is obtained by endotracheal intubation or a supraglottic airway device. Various types of laryngeal mask airway (LMA), Cobra Perilaryngeal airway (PLA) and I-gel are used as supraglottic airway devices [1, 2]. V-gel Rabbit is an airway device that recently has come into use and is manufactured from thermoplastic elastomer appropriate for rabbit perilaryngeal anatomy. V-gel Rabbit is similar to I-gel used in humans and it does not use a cuff [3]. While placing these airway devices, various hemodynamic responses, such as hypertension, tachycardia, and arrhythmia, may develop related to the increase in reflex sympathoadrenal activity and plasma catecholamine concentration [4, 5]. This cardiovascular hemodynamic response is affected by various factors such as the type of airway device used, laryngoscopy use and duration, intubation technique, and anesthesia depth [6, 7].

QT interval refers to the period between ventricular depolarization and repolarization as observed on an electrocardiogram. It includes the period which begins at the onset of the QRS complex and concludes when the T wave returns to the isoelectric line. QT interval changes with heart rate (HR) and QT corrected for heart rate is named QTc. It is known that many anesthetic agents, such as sevoflurane and opioids, lengthen the QT interval on an electrocardiogram (ECG). It has also been shown that an increase in QTc interval is related to sudden deaths in cases of ischemic heart disease and even in healthy individuals.

Published online: 31 January 2015

Increase in sympathoadrenal activity and QT distance during laryngoscopy and intubation can cause life threatening ventricular arrhythmia [8, 9].

With this study we aimed to compare the effects of endotracheal tube (ETT) intubation and supraglottic airway device such as Classic LMA, Cobra PLA and V-gel Rabbit on hemodynamic parameters and QTc interval in rabbits.

2 Materials and methods

Twenty-four adult, white New Zealand rabbits that weighed 2.5–3 kg were used in this study. Necessary permission for the experiments was obtained from Canakkale Onsekiz Mart University Animal Experiments Ethics Committee, and the study was performed in Canakkale Onsekiz Mart University Experimental Research Center. Before the study, the rabbits were subjected to clinical examination with regards to behavior, respiration, and cardiovascular system, and no abnormalities were detected in the experiment animals included in the study.

All the experiments were performed between 9 a.m. and 4 p.m. Animals were fed with standard feed during the experiment and they had constant access to water. Temperature of the shelters was around 21 ± 2 °C and light was arranged as 12 h of light and 12 h of dark.

Twenty-four rabbits were randomly separated into four groups:

Group ETT ($n = 6$) The group for which the ETT (Size 3, Bıcakcılar Tıbbi Cihazlar AS. Istanbul, Turkey) was used as the airway device.

Group LMA ($n = 6$) The group for which the Classic LMA (Size 1, La Premiere Plus, Amstrong Medical Ltd. Colerine, North Ireland) was used as the airway device.

Group PLA ($n = 6$) The group for which Cobra PLA (Size ½, Pulmodyne Inc., Indiana, USA) was used as the airway device.

Group V-gel ($n = 6$) The group for which V-gel Rabbit® (R-3, Docsinnovent® Ltd. London, UK) was used as the airway device.

2.1 Method

In order to obtain ECG records of the rabbits, the areas where the crocodile type electrodes would be placed on the anterior and posterior extremities were shaved. Rabbits were not given food for 12 h prior to the procedure. In order to avoid loss of temperature during anesthesia, a 39 °C blanket was laid. ECG (Digital ECG system Poly-Spectrum-8/E, Neurosoft Ltd. 5, Voronin str., Ivanovo, Russia) traces taken on admission to the unit were recorded. Rectal temperature was measured. Invasive blood pressure follow-up was monitored (PETAŞ® KMA 800, Ankara, Turkey) by insertion of a 24-Gauge catheter (Bıcakcılar Tıbbi Cihazlar AS, Istanbul, Turkey) through the left main auricular artery. Approximately 30 min of general anesthesia was planned for the rabbits and 5 mg/kg of xylazine (Rompun®, Bayer Healthcare LLC) and 30 mg/kg of ketamine (Ketasol, Richter Pharma AG) was administered to the rabbits via the quadriceps femoris muscle. A 26-Gauge catheter (Bıcakcılar Tıbbi Cihazlar AS, Istanbul, Turkey) was inserted from the right ear lateral vein after controlling pedal and palpebral reflexes. 1 mg/kg rocuronium bromide (Esmeron 50 mg/5 ml, Organon Ilac AS. Istanbul, Turkey) was administered intravenously in order to suppress respiration. The rabbit face mask and Mapleson C pediatric ventilation circuit (Morton Medikal San Tic Ltd., Izmir, Turkey) was supplied by a mix of 50 % O_2 and 50 % air. After complete paralysis, the airway devices were placed by the same anesthesiologist to all rabbits. For easy placement of the airway device, another anesthesiologist pulled the tongue laterally during the procedure.

2.2 ECG recording

ECG records were obtained according to the method reported by Uzun et al. [10]. Baseline and the 1st, 5th, 15th and 30th minutes measurements after the placement of airway device were repeated by the electrodes attached to the extremities. ECG records were recorded digitally and I, II, III, aVR, aVL, and aVF derivations were recorded with 1 mV = 20 mm, speed 50 mm/s and open (35 Hz) filter. QT duration was determined by measuring the time span from the onset of Q wave to the end of T wave. The adjusted QT interval was measured according to the formula designated by Bazett [11].

2.3 Anesthesia maintenance

All experimental animals were connected to an anesthetic machine (Anesthesia Machine w/O_2 Flush Model M3000PK Parkland Scientific Lab and Research Device. Florida, USA) and were manually ventilated. Anesthesia maintenance was ensured with 1.15 % isoflurane as 50 % Oxygen and 50 % air mixture. Rabbits were ventilated manually by the same anesthesiologist under approximately 15 cm H_2O pressure (approximate 10 ml/kg) for approximately 40 min so that the respiration rate would be appropriate to rabbit physiology. Mean arterial pressure (MAP), HR and I, II, III, aVR, aVL and aVF derivations in ECG were recorded at baseline and 1st, 5th, 15th and 30th minutes after placement of airway device. Rabbits

that began spontaneous respiration after 30 min, were administered 0.05 mg/kg of neostigmine iv + 0.02 mg/kg of atropine iv. Rabbits with sufficient respiratory effort were extubated.

2.4 Statistical analysis

Findings were evaluated by MINITAB statistical software 12.1 (Minitab Inc., Pennsylvania, USA). Groups were compared using One-way ANOVA (Tukey's *t* test) test with regards to baseline values and HR, MAP, blood gas values, and QTc intervals at the 1st, 5th, 15th and 30th minutes after placement of airway device.

3 Results

The mean weights of rabbits in the different groups included in the study were similar (Table 1). No significant difference was observed between MAP values of the rabbits in all four groups at baseline and the 1st, 5th, 15th and 30th minutes after intubation during the experiment. However, a significant difference was observed with regards to MAP value at the 5th minute between the ETT group and the V-gel group (Fig. 1). Moreover, no statistically significant difference was observed between the blood gas values of the groups at baseline, the 10th, and the 30th minute.

QTc intervals at baseline and 1st, 5th, 15th and 30th minutes post-intubation were compared in the study. No significant difference was observed between the rabbits of the four groups with regards to baseline QTc intervals. It was observed that QTc intervals at the 1st and 5th minutes increased in the ETT group compared to other groups ($p < 0.05$) (Fig. 2). Statistically, there was no significant increase between the ETT group and the LMA group in QTc intervals at the 15th and 30th minutes. However, when the ETT group was compared with the PLA and V-gel groups at the 15th and 30th minutes for QTc intervals, we detected a significant increase ($p < 0.05$) (Fig. 2). It was also observed that the QTc interval of the LMA group at the 5th minute was significantly higher than in the V-gel group ($p < 0.05$) (Fig. 2).

Heart rates at baseline and the 1st, 5th, 15th and 30th minutes after intubation of each of the four groups were statistically compared. No significant difference was observed between the baseline heart rates of the rabbits in the four groups. While there was no significant difference in heart rate values at the 1st, 5th and 15th minutes after intubation between the ETT group and the LMA group, it was observed that the heart rate values of the ETT group were significantly higher than those of the PLA and V-gel groups ($p < 0.05$) (Fig. 3). It was observed that the heart rates of the ETT group at the 30th minute after intubation were significantly higher than those of the V-gel group ($p < 0.05$) (Fig. 3).

It was observed that heart rate in the LMA group was significantly higher than the PLA group and the V-gel group respectively at the 1st and 5th minute after intubation; it was also significantly higher than both the PLA group and V-gel group at the 15th and 30th minutes after intubation ($p < 0.05$) (Fig. 3).

Table 1 Demographic data between groups

	Group ETT	Group LMA	Group PLA	Group V-gel	*p* value
kg	3.05	2.95	2.90	3.00	$p > 0.05$

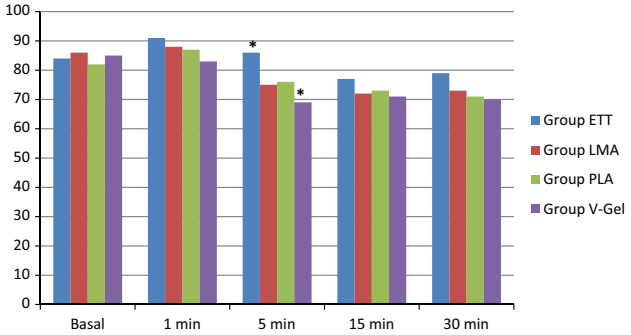

Fig. 1 Between groups in mean arterial pressure values (mmHg). *Asterisk* significant difference was observed between ET group and V-gel group ($p < 0.05$)

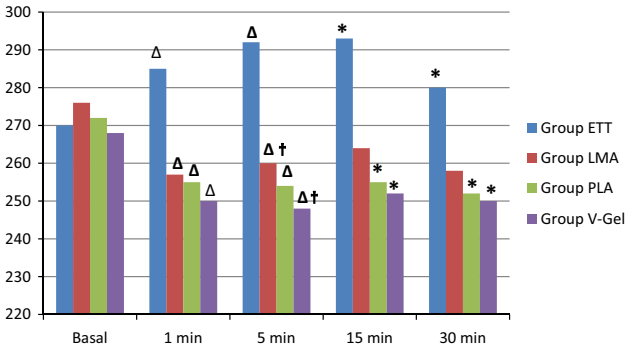

Fig. 2 Between groups in QTc interval values (ms). *Open triangle* QTc intervals increased in ETT group compared to other groups ($p < 0.05$). *Dagger* QTc interval of LMA group was significantly higher than V-gel group ($p < 0.05$). *Asterisk* QTc intervals increased in ETT group compared to PLA and V-gel groups ($p < 0.05$)

4 Discussion

In this study, we observed that endotracheal intubation increased QTc interval when compared with supraglottic

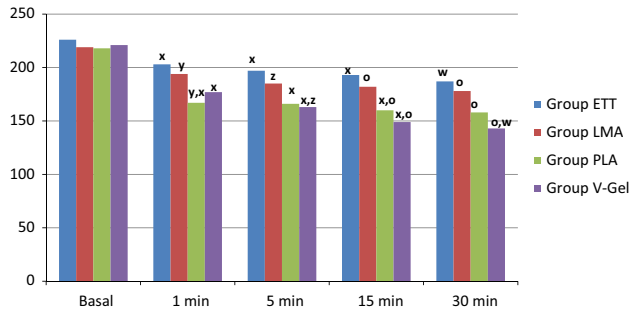

Fig. 3 Between groups in heart rate values (bpm). *x* HR increased in ETT group compared to PLA and V-gel groups ($p < 0.05$). *y* HR increased in LMA group compared to PLA and V-gel groups ($p < 0.05$). *z* HR of LMA group significantly higher than V-gel group ($p < 0.05$). *o* HR increased in LMA group compared to PLA and V-gel groups ($p < 0.05$). *w* HR of LMA group significantly higher than V-gel group ($p < 0.05$)

airway devices. In supraglottic airway devices, we observed that the V-gel affected QTc interval less when compared with Cobra PLA and Classic LMA. We detected that the ETT increased MAP when compared to the V-gel Rabbit, and also, the ETT increased heart rate when compared to Cobra PLA and V-gel Rabbit.

Different phases of anesthesia procedures affect QTc intervals. In particular, changes in QT duration can be affected through the influence of general anesthesia on the autonomic nerve system [12]. Rhythm disorders observed in the electrocardiogram due to fear present before the operation, agents used for anesthesia induction, procedures of laryngoscopy and endotracheal intubation, and hemodynamic and neuroendocrine responses which developed were evaluated in different studies [13, 14].

Endotracheal intubation generally increases arterial pressure, heart rate, and cardiac arrhythmia frequency even in healthy patients [4, 5]. Hemodynamic response to laryngoscopy and tracheal intubation is caused by the catecholamine discharge associated with sympathoadrenal activity [15–17]. On the other hand, Wilson et al. [18] reported that Classic LMA placement caused less catecholamine discharge and hemodynamic response when compared to endotracheal intubation. Classical LMA and Cobra PLA are airway devices with cuffs, and they are inflated under a cuff pressure of approximate 60 cm H_2O [19]. The V-gel is anatomically shaped and made of soft material, so even though it does not have an inflatable cuff, it applies pressure proportionately over the pharynx. Classic LMA and Cobra PLA have inflatable non-anatomically shaped cuffs which means they are more likely to have a greater effect on hemodynamics due to the inappropriate pressure on surrounding structures.

We observed an increase in MAP at the 1st and 5th minutes after tube placement in the ET group and an increase related to hemodynamic response in the LMA and PLA groups. However, we observed no change in the V-gel group. This situation can be explained by the anatomical suitability of V-gel to the perilaryngeal area and the absence of a cuff.

Kihara et al. [6] performed a study by using Trachlight and Fastrach on normotensive and hypertensive patients; they reported that the absence of distortion in extraglottic structures decreased oropharyngeal stimulation. In our study, a decrease in heart rates was observed in all groups at the 1st, 5th, 15th and 30th minutes after intubation. We suppose that this situation is related to the absence of distortion to extraglottic structures, which is also related to the fast metabolism of rabbits and to general anesthesia. A decrease in the oropharyngeal reflex may also be related to administration of rocuronium bromide to all groups. It is well known that endotracheal intubation creates higher hemodynamic stress. In our study, we observed that the increase in heart rate caused by Classic LMA was second only to the increase caused by ETT. This situation may be associated with an increase of oropharyngeal and pharyngolaryngeal stimulation since the Classic LMA has a higher cuff pressure and occupies more space in the mouth than other supraglottic airway devices.

Laryngoscopy and endotracheal intubation may cause an increase in QTc interval related to catecholamine discharge [20, 21]. Therefore, endotracheal intubation causes QTc changes that might cause HR and arterial pressure to increase, various dysrhythmias, and even acute myocardial ischemia [22–24].

Bucx et al. [25] compared plasma catecholamine levels and hemodynamic responses after 3 and 10 s post-laryngoscopy and observed that values at the 10 s mark were higher. Shribman et al. [26] indicated that laryngoscopy duration was longer than expected due to anatomic difficulties encountered in the endotracheal intubation group in the study. This situation might have affected the development of the sympathetic response.

In our study, we observed that QTc intervals were longer at all times in the ETT group when compared with other airway devices. In the LMA group, it was observed that QTc intervals decreased at the 1st minute when compared to the baseline values but later started to increase. We observed that QTc intervals decreased at the 1st minute in the PLA and V-gel groups; there was no significant change at the other time points, but the V-gel group presented the shortest QTc intervals.

This study is the first that compares the effects of endotracheal intubation and supraglottic airway devices on QT interval. In our study, endotracheal intubation caused more sympathetic stimulation than we expected, and QT intervals were significantly longer than they were in other groups. This situation may be related to difficulties encountered during intubation due to the differences in

rabbit anatomy. On the other hand, we observed that the V-gel Rabbit affected both the hemodynamic response and QT intervals less than the other supraglottic airway devices. Perhaps an explanation for this situation could be that the partial ischemia in the perilaryngeal region due to cuff pressures of Classic LMA and Cobra PLA caused more catecholamine stimulation. Consequently, we consider that the sympathetic response may be decreased because the V-gel Rabbit does not have a cuff; The V-gel Rabbit assumes the anatomic form of the region where it is placed, and thus, it applies pressure proportionally to surrounding tissues.

5 Conclusion

In our study, we observed that the V-gel Rabbit had a smaller effect both on hemodynamic response and QT interval when compared to other airway devices. We conclude that the V-gel Rabbit is a good alternative to other airway devices to be used in studies rabbit related studies involving the cardiovascular system. Our results may also have bearing on the comparison between the effects of endotracheal intubation and supraglottic airway devices on QT interval in humans.

Acknowledgments This study was supported by Çanakkale Onsekiz Mart University Scientific Research Project Found with TSA-2013-80 project number. The authors has no financial relationship with the companies that manufactured the materials used in this study.

Conflict of interest The authors declare that they have no conflict of interest.

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