Left ventricular ejection fraction during anaesthetic induction: comparison of rapid-sequence and elective induction

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A randomized clinical trial was conducted in 14 women, aged 24–60 years, to compare the effects of rapid-sequence induction of anaesthesia and elective induction on heart rate, blood pressure and left ventricular ejection fraction (LVEF). None of the patients suffered from heart or lung diseases, and all were scheduled for hysterectomy. Cuff blood pressure was measured repeatedly by an automatic recording device, and heart rate and LVEF were monitored by a portable nonimaging nuclear probe. In seven patients, a rapid-sequence induction was performed following preoxygenation and with simultaneous injection of thiopentone (5 mg·kg^{-1}) and succinylcholine, without starting manual ventilation until the airway was secured with the endotracheal tube. In another seven patients, elective induction was carried out by sequential administration of the same drugs.

Forty seconds after laryngoscopy and intubation mean blood pressure had increased by 38 per cent and heart rate by 29 per cent from preintubation values in the rapid-sequence induction group, compared to 30 and 12 per cent respectively, in the elective induction group ($p < 0.05$). Similar decreases in LVEF was observed in both groups, from 0.60 to 0.42 in the elective induction group, and from 0.60 to 0.41 in the rapid-sequence induction group.

The equal depression of LVEF indicates that laryngoscopy and intubation produce, with both induction regimens, sudden impairment of cardiac function. The more pronounced hypertension and tachycardia observed during rapid-sequence induction suggests a higher myocardial oxygen consumption which may represent a serious additional burden for the poorly perfused heart.

Key words
ANAESTHETIC TECHNIQUES: rapid-sequence induction, elective induction; BLOOD PRESSURE: hypertension; HEART: heart rate, tachycardia; INTUBATION, ENDOTRACHEAL: complications; RADIONUCLIDE CARDIOGRAPHY: ejection fraction.

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Presented in part at the 8th World Congress of Anaesthesiologists, Manila, Philippines, January 1984.

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Rapid-sequence induction of anaesthesia and intubation are often employed in emergency surgery to minimize the risk of aspiration in nonfasting patients. This induction regimen is a procession of rapidly occuring events designed to reduce the interval from loss of consciousness to securing the airway with the endotracheal tube. However, the question may be raised whether the precautions taken to avoid pulmonary aspiration are obtained at the expense of inducing greater circulatory changes than is caused by elective induction.

The aim of the present investigation was to assess and compare in a randomized clinical study the effects of rapid-sequence induction versus elective induction on blood pressure, heart rate and left ventricular ejection fraction (LVEF).

Methods

Fourteen female patients (median age 37 years, range 24–60 years) scheduled for elective hysterec-

tomy were investigated. None had a history of heart and lung diseases and all had normal findings on physical examination, ECG, and chest *x*-ray. Besides premedication, none of the patients were receiving any preoperative medical treatment. The study protocol was approved by the Copenhagen County Scientific-Ethic Committee, and informed consent was obtained from each patient. All investigations were performed in an anaesthesia preparation room, with the patient in the supine position.

Anaesthetic techniques

All patients were premedicated with diazepam ($0.3\ mg \cdot kg^{-1}$) PO two hours before surgery. By the use of random numbers they were allocated to two groups.

In seven patients a rapid-sequence induction was performed. These patients started breathing 100 per cent oxygen. After one minute, pancuronium ($0.015\ mg \cdot kg^{-1}$) was administered for defasciculation. Three minutes later, sleep was induced by thiopentone ($5\ mg \cdot kg^{-1}$) IV, followed immediately by succinylcholine ($1.5\ mg \cdot kg^{-1}$). Laryngoscopy and endotracheal intubation were performed with a MacIntosh blade laryngoscope and a 7.5 mm tube. Both drugs were given as quickly as possible in rapid succession, and intubation took place one minute after the injection was completed. Not until the cuff was inflated was manual ventilation started with nitrous oxide–oxygen 6:3 $L \cdot min^{-1}$ and halothane one per cent inspired concentration. The end-expired CO_2 concentration was kept within narrow limits for each patient and in the range of 4.5–5.5 per cent.

The other seven patients had an elective induction sequence, without preoxygenation. All intravenous medications were given in the same dosages. Two minutes after defasciculation with pancuronium sleep was induced with thiopentone given over 15 seconds. When the eyelash reflex had disappeared, ventilation was controlled manually using a mask with nitrous oxide–oxygen 6:3 $L \cdot min^{-1}$. One minute after the injection of thiopentone succinylcholine was given. Laryngoscopy and intubation were performed one minute after the injection of succinylcholine. Following cuff inflation, halothane one per cent inspired concentration was added. The endotracheal tube was placed in all 14 patients by the same anaesthetist in a maximum of 20 seconds of laryngoscopy.

Measurements

Left ventricular ejection fraction (LVEF), blood pressure and heart rate were measured at least once every minute. All control values were obtained as the mean of four or five single determinations at the end of an initial control period of 15–20 minutes of rest. Thirty seconds after intubation an arterial blood sample was drawn from all patients for blood gas analysis. Blood pressure was measured indirectly by an automatic recording device (Arterio-Sonde®, Roche). Heart rate and LVEF were recorded by a computerized, mobile nonimaging nuclear probe (Nuclear Stethoscope™, Bios Inc., Valhalla, NY 10595) allowing bedside beat-to-beat monitoring of LVEF by means of the radionuclide technique. The use of this instrument during induction of anaesthesia has been described elsewhere.[1]

Radionuclide measurements were performed using red blood cells labeled with stannous pyrophosphate and 15–20 mCi ^{99m}technetium pertechnetate, using a modified *in vivo* technique.[2] The probe was placed over the chest in a 30° left anterior oblique position with 10° caudal tilt, and LVEF was calculated as the mean of a series of successive heart beats recorded within single intervals of ten seconds. With this procedure we have previously found a satisfactory agreement ($r = 0.90$) between values for LVEF obtained by the nuclear stethoscope and by gamma camera.[3] Following intubation, end-tidal CO_2 was monitored with a Gould Godart Capnograph MK II.

A nonparametric test for paired data (considering also ties)[4] was used within both of the groups to compare each value with a preceding value or with the initial control value. The Mann Whitney U-test was used for comparisons between groups. The level of significance chosen was $2\alpha < 0.05$. All data are given as median values, with ranges in parenthesis.

Results

There were no statistically significant differences between the groups for age, weight, or the control values for mean arterial blood pressure, heart rate and LVEF (Figure). Forty seconds after laryngoscopy and intubation mean arterial blood pressure in the rapid-sequence induction group increased by 38 per cent compared to the preintubation value, and 30 per cent in the elective induction group ($p < 0.05$). Simultaneously, there was in the rapid-

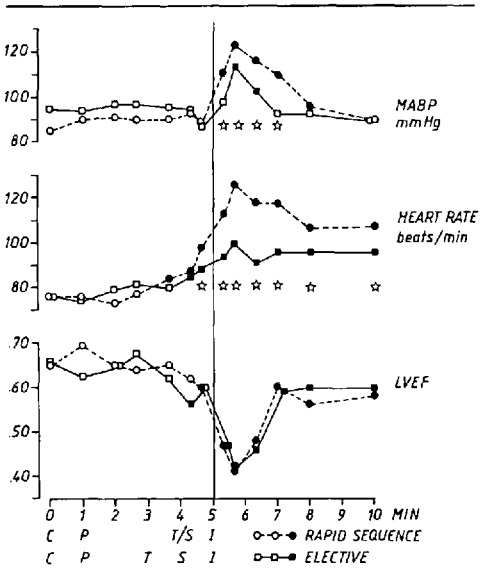

FIGURE Relationship between mean arterial blood pressure (MABP), heart rate, and left ventricular ejection fraction (LVEF) recorded in the rapid sequence induction group (○ - ○ - ●) and elective induction group (□ - □ - ■), respectively. Closed symbols indicate statistically significant changes from control values (C). Stars indicate a statistically significant difference between groups. Abbreviations: P = pancuronium, T = thiopentone, S = succinylcholine, I = laryngoscopy and intubation. For further details see text.

sequence induction group a pronounced increase in heart rate (maximal increase 29 per cent compared to 12 per cent in the elective induction group ($p < 0.05$)). In both groups mean arterial blood pressure returned to control values towards the end of the study period, whereas heart rate remained moderately elevated.

Following elective induction with thiopentone there was a decrease in LVEF from 0.68 to 0.56 (−18 per cent) (Figure). The slight recovery (to 0.60) observed after the injection of succinylcholine was followed by a decrease to 0.42 (−30 per cent) after laryngoscopy and intubation. Rapid-sequence induction was accompanied by a small decrease in LVEF from 0.64 to 0.60 (−6 per cent) with a further decrease to 0.41 (−32 per cent) following laryngoscopy and intubation. Thus, the maximum decrease in LVEF was similar in the two groups, with the minimum value being observed in both at about 40 seconds after intubation. LVEF did not reach control values in any of the groups during the remainder of the investigation. Blood gas analyses 30 seconds after intubation revealed the following median values with ranges in parenthesis: rapid-sequence induction: pH 7.36 (7.33–7.38), P_aO_2 32.8 kPa (28.4–34.4) and P_aCO_2 5.3 kPa (5.2–5.6); elective induction: pH 7.38 (7.36–7.41), P_aO_2 22.8 kPa (17.2–25.4) and P_aCO_2 5.4 kPa (5.3–5.7). the difference between groups for P_aO_2 was statistically significant.

Discussion

The period of laryngoscopy and intubation is considered one of the highest risk intervals during anaesthesia and operation,[5] much attention being paid to problems concerning pulmonary aspiration of gastric contents during anaesthetic induction.[6] Maintenance of haemodynamic stability is another important issue. In healthy subjects the reported haemodynamic reactions to common types of elective anaesthesia induction are tachycardia, arterial hypertension,[1,7–11] and apparent depression of left ventricular performance.[1,11] In patients with cardiovascular or cerebrovascular diseases these haemodynamic changes are potentially dangerous and may eventually, in combination with other predisposing factors, lead to either perioperative myocardial infarction or cerebrovascular haemorrhage.[12–14]

We therefore wanted to examine whether rapid-sequence induction would increase the untoward circulatory reactions, thereby amplifying the possibility of causing serious complications in high-risk patients.

The mechanisms responsible for the circulatory reaction to anaesthetic induction have been difficult to clarify. In anaesthetized cats, the haemodynamic changes following mechanical stimulation of the upper respiratory tract occur in the presence of enhanced neuronal activity in the cervical sympathetic fibres.[15] In man, the observed increases in blood pressure after laryngoscopy and intubation are accompanied by an increase in plasma norepinephrine concentrations, suggesting increased sympathetic activity.[16–19]

Present study

With our study design, we were not able to examine the effects of each single intervention. Instead, we wanted to mimic the daily clinical routine by monitoring the cumulative haemodynamic changes following a series of both pharmacological and

mechanical interventions.[20] The increases in mean arterial blood pressure and heart rate observed after laryngoscopy and intubation were larger in the rapid sequence induction group than in the elective induction group (Figure). In both groups, the increase in heart rate was began before the increase in blood pressure took place. At the same time, immediately prior to laryngoscopy and intubation, the first decreases in LVEF were observed in the two groups, suggesting – in the absence of an afterload increase at this particular point of time (Figure) – myocardial depression caused by thiopentone. This was in accordance with our previous observations in normal female patients,[1] and was further sustained by the observation that LVEF started to decrease somewhat earlier in the elective induction group than in the rapid sequence induction group receiving thiopentone one minute later (Figure). In both groups, peak values for mean arterial blood pressure and heart rate coincided with the maximum depression of LVEF recorded within the first minute following laryngoscopy and intubation.

Previous reports

The increases in blood pressure and heart rate in the elective induction group were similar with those observed by others during elective induction,[9,10,18] although study design and presentation of results differ considerably. The changes in LVEF were of approximately the same magnitude as previously reported by Giles *et al.*,[11] who used diazepam ($0.3\ mg \cdot kg^{-1}$) IV for induction of sleep. In their study, the median interval from laryngoscopy and intubation to recovery of LVEF was two minutes, with a tendency for persisting depression in patients with coronary artery disease. In healthy noncardiac patients, the recovery of left ventricular performance preceeded the recovery of blood pressure and heart rate. In contrast, in our patients, receiving thiopentone instead of diazepam, LVEF never returned to the control level.

Two reports describe the haemodynamic changes evoked by rapid-sequence induction.[21,22] Both were randomized clinical trials dealing with the possibility of preventing the hypertensive and tachycardic response to rapid-sequence induction. Neither compared rapid-sequence with elective induction. However, the haemodynamic changes in the control groups of both studies were very similar to those recorded in our patients who received the rapid-sequence induction. Cork *et al.*[21] demonstrated that preloading with fentanyl ($5\ \mu g \cdot kg^{-1}$) before a sleep induction dose of thiopentone ($2\ mg \cdot kg^{-1}$) minimized the increases in heart rate and blood pressure and prevented possible elevation of plasma concentrations of norepinephrine. Safwat *et al.*[22] found that an interval of five minutes between propranolol pretreatment and tracheal intubation was optimal for attenuating increases in heart rate, blood pressure and rate pressure product during rapid-sequence induction with thiopentone and succinylcholine.

Rapid-sequence versus elective induction

The reason for the observed depression of global left ventricular function is not known. It may be a consequence of myocardial depression caused by thiopentone[1] with the added negative effect on LVEF of the later increase in afterload elicited by laryngoscopy and intubation (Figure).

Theoretically, it cannot be excluded that tracheal instrumentation and intubation may produce sudden transient ischaemia-like responses, including LVEF depression, even in a study population of young female patients without known heart disease. For example LVEF depression has been observed in normal volunteers during sudden strenuous exercise[23] in the absence of segmental wall motion abnormalities or ischaemic ECG-changes. The mechanism is thought to be development of an unfavourable myocardial supply/demand balance, producing global subendocardial ischaemia. If such an imbalance can occur during laryngoscopy and intubation it may be argued that the greater oxygen supply provided by preoxygenation could explain why the decrease in LVEF was not more pronounced in the rapid sequence induction group in spite of the greater increase in heart rate and blood pressure (Figure). In this connection, it is noteworthy that calculated values for the rate pressure product were above 17,000 following intubation in six of the seven patients in the rapid-sequence induction group, and above 12,000 in six of the seven patients in the elective induction group. These levels are known to be associated with the appearance of ischaemic ECG-changes during intubation before noncardiac elective surgery in patients with coronary artery disease[13] or during the prebypass period of coronary artery surgery.[24]

Furthermore, the higher sympathetic activity, as indicated by the greater increase in heart rate during the rapid sequence induction, might modify the decrease in LVEF.

The administration of succinylcholine immediately after thiopentone during the rapid-sequence induction presumably opposed the decrease in sympathetic activity, caused by thiopentone,[17] more effectively, than when the two drugs were given one minute apart as in the elective induction group. The net outcome was increased sympathetic stimulation during rapid-sequence induction. An indication for this mechanism may be the biphasic course of the LVEF depression observed only in the elective induction group. A small decrease in LVEF following thiopentone was succeeded by a short recovery after succinylcholine and a profound depression after laryngoscopy and intubation (Figure).

The intermittent positive pressure ventilation by face mask may in part be responsible for the less pronounced increase in blood pressure in the elective induction group,[25] and the use of nitrous oxide prior to intubation may add to this effect by further reducing cardiac output as a result of decreases in both heart rate and contractility.[26,27]

Conclusion

With both induction regimens, laryngoscopy and intubation were followed by depression of left ventricular performance as reflected by similar decreases in LVEF. Simultaneous hypertensive and tachycardic changes were more pronounced during rapid-sequence induction, suggesting that with this procedure a higher oxygen demand may present an unwanted additional burden to the poorly perfused heart.

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Résumé

Une étude clinique randomisée a été faite chez 14 femmes âgées de 24 à 60 ans afin de comparer les effets de la séquence rapide d'induction de l'anesthésie et de l'induction élective sur la fréquence cardiaque, la pression artérielle, et la fraction d'éjection du ventricule gauche (LVEF). Aucune des patientes souffraient de maladie cardiaque ou pulmonaire et toutes étaient cédulées pour hystérectomie. La mesure de la tension artérielle par brassard était répétée par un appareil automatique et la fréquence cardiaque et le LVEF étaient surveillés par un probe portatif nucléaire non imagé. Chez sept patientes, une séquence rapide d'induction était faite après préoxygénation et injections simultanées de thiopentone (5 mg·kg^{-1}) et succinylcholine sans ventilation manuelle jusqu'à l'intubation. Chez sept autres patientes, l'induction élective était faite par l'administration séquentielle des mêmes médicaments.

Quarante secondes après laryngoscopie et intubation la pression artérielle moyenne augmenta de 38 pour cent et la fréquence cardiaque de 29 pour cent des valeurs préintubation pour le groupe à séquence d'induction rapide, comparativement à 30 et 12 pour cent respectivement pour le groupe à induction élective ($p < 0.05$). Une diminution similaire du LVEF a été observée dans les deux groupes de 0.60 à 0.42 pour le groupe à induction élective et de 0.60 à 0.41 pour le groupe à induction rapide.

La dépression indentique dans les deux groupes du LVEF nous indique que la laryngoscopie et l'intubation produisent une détérioration soudaine de la fonction cardiaque avec les deux méthodes d'induction. L'hypertension plus prononcée et la tachycardie observée lors de la séquence rapide d'induction suggère une plus grande consommation d'oxygène qui pourra représenter une surcharge additionnelle sérieuse pour le cœur mal perfusé.