Effect of acute cigarette smoking on gastric contents in regular smoker volunteers. A prospective randomized cross-over study

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Abstract

Background: The authors sought to assess the effect of acute smoking on gastric contents in regular smoker volunteers. The primary endpoint was the variation in antral area during the 120-min study period after cigarette smoking.

Methods: Regular smoker volunteers were included in this prospective randomized single blind cross-over study. Volunteers attended two separate study sessions: Control and Smoking sessions. The study started with an initial ultrasound measurement of the antral area, immediately followed by a 30-min periods of waiting (Control session) or of two-cigarettes smoking (Smoking session). Ultrasound measurements of the antral area were then performed 30, 60, 90 and 120 min after the initial ultrasonography, allowing for the calculations of the variation rates in antral area during the periods 0–30, 0–60, 0–90 and 0–120 min in both sessions.

Results: The variation in antral area during the period 0–120 min was equivalent in both sessions, as the difference in the variation rates between both sessions was −1.2%, with 90% confidence interval of the difference including 0 and lying entirely within the range of equivalence of −10% to 10%. No equivalence was found for the periods 0–30, 0–60 and 0–90 min, because of a non-significant decrease in antral area in the Smoking sessions during these periods.

Conclusions: Preoperative acute smoking did not affect the variation in the gastric volume in regular smoker volunteers during the study period. These results allow for the suggestion that acute preoperative smoking does not probably change the risk of pulmonary aspiration of gastric contents in healthy regular smokers.

Clinical trial registration: NCT 02080598.

Key words: anaesthesia, general; gastrointestinal contents; smoking; volunteers
Preoperative fasting is one of the main preventive measures recommended for minimizing the risk of pulmonary aspiration of gastric contents, one of the most feared complications as a result of general anaesthesia.\(^1\)-\(^4\)

In clinical practice, anaesthetists are regularly faced with patients who have smoked before arriving in the operating room. Indeed, 4% of hospitalized smokers may not abstain from tobacco during their hospital stay,\(^5\) while 15% of regular smokers may continue to smoke within an h of surgery.\(^6\)

Cigarette smoking may be associated with increased cardiac and pulmonary morbidity and with increased incidence of complicated postoperative healing.\(^7\)-\(^9\) However, these complications are efficiently reduced by refraining from cigarette smoking at least eight weeks before general anaesthesia.\(^7\)-\(^10\)-\(^11\)

In healthy patients (i.e. in patients without any history of cardiac or pulmonary disease), the main feared complication related to acute cigarette smoking immediately before general anaesthesia, remains pulmonary aspiration of gastric contents. In regular smokers, acute cigarette smoking may lead to either unchanged, decreased, or accelerated gastric emptying of solids or liquids.\(^12\)-\(^14\)

Acute cigarette smoking may also briefly make the gastro-oesophageal sphincter incompetent, and back to normal within eight min after the end of smoking.\(^15\)-\(^17\) However, there is a lack in clear data as concerns the effect of acute cigarette smoking on the gastric volume in fasted regular smokers.

This non-inferiority prospective randomized cross-over trial aimed to assess the effect of acute smoking on gastric contents in healthy fasted habitual smokers, through using real-time ultrasonographic measurement of the antral area, a well-described non invasive technique, allowing reliable assessment of gastric contents during the preoperative period.\(^18\)-\(^19\) The primary endpoint was the variation in antral area during the 120 min study period, whether healthy volunteers had smoked two cigarettes or not. We hypothesized that the variation in antral area would be <2% and would be equivalent during the 120-min period in both study sessions.

**Methods**

This prospective randomized trial was registered at the French National Agency for Medicines and Health Products Safety (ANSM, N° 2014-A00127-40) on January 22, 2014, and in the public registry ClinicalTrials.gov No NCT 02080598. It was approved by an Institutional Ethics Committee (Comité de Protection des Personnes Sud-Est IV, N°L14-12, Lyon, France). All volunteers provided written informed consent before enrolment.

Regular adult smokers (i.e. volunteers smoking more than five cigarettes a day for more than one year), were included in this cross-over single blind study. The criteria for exclusion from the study were upper gastrointestinal tract diseases, previous gastrointestinal surgery, history of diabetes mellitus, pregnancy and use of medication affecting gastric motility. Volunteers attended two separate study sessions, each at least two weeks apart. In this study, volunteers were randomly allocated by coded envelopes to the following study sessions: control (no cigarette smoked during the study period) or Smoking (two cigarettes smoked over 15 min after the first ultrasound measurement of antral area). Randomization was performed using a computer-generated list. Allocation concealment was ensured by the use of coded, sealed opaque envelopes.

All tests were carried out after an overnight fast and after the volunteers had abstained from smoking for a 12-h period.

The study period started with an initial ultrasound measurement of antral area for each volunteer laying down in a semi-upright position, with the head of the bed elevated to 45°. Then, volunteers had to go outside for 30 min. During this time, according to their session, volunteers had to smoke two cigarettes from their usual consumption over 15 min (Smoking session) followed by 15 min waiting, or they had to wait 30 min without smoking (Control session). At the end of this first period of 30 min, volunteers had to wear a surgical mask during the study period in order to obscure the smell of recent cigarette consumption and thereby ensure blinding. They were again asked to lay down in a semi-upright position, with the head of the bed elevated to 45° throughout the test, and a second ultrasonographic measurement of antral area was performed, followed by three other measurements, each at 30-min intervals, for a total study period of 120 min.

All measurements of the antral area were performed by a physician (LB) blinded to the session (also wearing a surgical mask), using real-time ultrasonography (SonoSite, Inc., Bothell, WA, S-Nerve™, fitted with a 2-5.5 MHz probe), as previously described.\(^18\)-\(^20\) Longitudinal (D\(_L\)) and anteroposterior (D\(_A\)) diameters of a single section of the gastric antrum in the sagittal plane passing through the aorta were determined, using the abdominal aorta and the left lobe of the liver as internal landmarks to obtain the same standardized scanning level consistently. The measurements of the gastric antrum were performed from serosa to serosa, between antral contractions to provide a measure of the relaxed width of the antrum. These longitudinal and anteroposterior diameters were given verbally to a second physician (SL), who calculated the cross-section antral area at each time using the following formula:

\[
\text{Antral area} = A_{\text{area}} = \pi \times D_1 \times D_2 / 4.
\]

The physician performing the ultrasound measurements of longitudinal and anteroposterior diameters could not access the document containing the values of antral area until the end of the whole study.

The corresponding gastric volume to the measured antral area was estimated at each time by using the equation that we previously described,\(^18\) which applies to antral area measured in supine position with the head of the bed elevated to 45°:

\[
\text{Volume (ml)} = -215 + 57 \times \log \text{(antral area)} - 0.78 \times \text{age} - 0.16 \times \text{height} - 0.25 \times \text{weight} - 0.8 \times \text{American Society of Anesthesiologists physical status classification}.
\]

The adjusted \(R^2\) value for this model was 0.570.\(^18\)

These repeated measurements of antral area allowed for the calculation of the variation rates in antral area (\(\Delta A_{\text{area}}\)) between the initial measurement and the measurements performed n=30, 60, 90 and 120 min later, using the equation:

\[
\text{VR}_{\text{A}_{\text{area}}} = \left( \frac{A_{\text{final}}}{A_{\text{initial}}} \right) - 1 \times 100.
\]
Statistical analysis

After a Shapiro-Wilk’s W test for normality of distribution of the data, data were expressed as mean(SD) or median (range) when appropriate. Repeated measurements of antral area were analysed by two-way analysis of variance, followed by a post-hoc test (Bonferroni adjusted comparisons) when appropriate, using the Statistica® version 6.0 computer software package (Statssoft, Tulsa, OK, USA). The VRaa0-n were compared between both sessions, using paired Student’s t-test, with applying the Benjamini–Hochberg step-up procedure for multiple hypothesis testing correction. A P<0.05 was considered as statistically significant.

The primary outcome of this study was the variation in the ultrasound measurement of antral area during the study period of 120 min, as expressed by the VRaa0-120 calculated for each patient between the initial ultrasound measurement and the measurement performed 120 min later. Considering that the VRaa0-120 would not exceed 2% in fasted healthy volunteers during the study period, we assumed equivalence if the difference (calculated with the corresponding 90% Confidence Interval) in the VRaa0-120 between both sessions did not exceed 10%, which corresponds to the intraindividual random measurement error for the assessment of the variation in antral area, as previously described. Using Blackwelder’s formula22:

\[ n = \left( \frac{Z_{1-\alpha} + Z_{1-\beta}}{\pi} \right)^2 \frac{[\pi(1-\pi) + ss(1-ns)]}{[\pi^2 - ss]} \]

where \( \pi \) and ss are the true VRaa0-120 for Control and Smoking sessions, \( Z_{1-\alpha} \) and \( Z_{1-\beta} \) are the upper percentage points of the standard normal distribution, and \( \delta \) the critical difference (equivalence margin). The sample size required to demonstrate equivalence between groups with \( \alpha = 0.1 \), \( \beta = 0.05 \), and \( \delta = 0.20 \), was 17 volunteers per session. Because of potential protocol violations, we decided to include 20 volunteers.

Results

Twenty volunteers were included. Two volunteers did not participate in their second session. The analysis was performed on the 18 remaining volunteers: 10 men and eight women, median age 29 yr, range 20–55.

Repeated two-way analysis of variance did not find any Time×Session significant statistical difference as concerns the antral area measured at time 0, 30, 60, 90 and 120 min, and as concerns the corresponding estimated gastric volumes (Figs 1 and 2). The VRaa0-120 did not significantly differ among the sessions, as set out in Table 1.

The difference of the VRaa0-120 between both sessions was −1.2%, with 90% CI of the difference ranging from −6.1% to 8.4%. This interval includes 0 and lies entirely within the range of equivalence of −10% to 10% stated above. However, as concerns the periods 0–30 min, 0–60 min and 0–90 min, the 90% confidence interval of the differences of the VRaa0-n between both sessions did not lie entirely within the range of equivalence, as set out in Table 1.

Discussion

Our results showed that the variation in antral area during the 120-min study period was <1.5% and was equivalent in both Smoking and Control sessions. In fasted healthy volunteers, changes in gastric volume during the study period may reflect the balance between gastric secretions and gastric emptying of residual gastric volume. Usual cigarette smoking may lead to both increased basal acid gastric secretion, and basal and stimulated pepsin outputs.24 The effect of acute cigarette smoking on acid gastric secretion remained however uncertain: it was reported that one or two cigarettes smoked transiently decreased acid secretion stimulated by infusion of pentagastrin in volunteers,25 while other authors did not report any significant effect of acute cigarette smoking on stimulated gastric acid secretion.26 As concerns the effect of acute smoking on gastric emptying, conflicting results were also published.15–14 Using scintigraphy, it was reported that acute cigarette smoking delayed both solid and liquid gastric emptying in 15 habitual smokers,14 while other authors found that cigarette smoking accelerated only the gastric emptying of the liquid component of the meal.12 More recently, Sanaka and colleagues13 showed that acute smoking accelerated the later phase of the gastric emptying of solids assessed by a carbon-labelled octanoic acid breath test, in eight male regular smokers. In the same way, acute cigarette smoking did not significantly change the gastric volume and pH, measured after induction and before extubation by suctioning the gastric contents via a nasogastric tube in fasted healthy regular smokers, premedicated with diazepam, given with 50 ml of water one h before the surgery.27 This result suggests that acute smoking did not affect the gastric emptying of water, although the period of time between cigarette smoking and the invasive
assessment of gastric volume and pH was not controlled and could consequently be >1 or 2 h.

In our study, the variation in antral area for the period 0–90 min was not equivalent between the Smoking and the Control sessions, although the 90% confidence interval of the difference of the rates included 0. In fact, the VRaa0-30 was negative during the Smoking session in contrast to the one recorded in the Control session, without however any significant difference between both sessions. As concerns the periods 0–30 and 0–60 min, one can notice that the 90% confidence interval of the difference of the variation rate between both sessions did not include 0 and was entirely positive, as a result of a decrease in antral area in the Smoking session compared with the Control session. However, this equivalence study was not powerful enough to conclude that there were significant differences between both sessions during the periods 0–30 and 0–60 min. Nevertheless, these results tend to corroborate those of some previous studies, reporting that acute smoking did not increase gastric secretions, while probably enhancing gastric emptying of the basal liquid contents present in the stomach, during the first h after cigarette smoking.

Our study is the first to use a real-time non-invasive ultrasound tool for the assessment of the effect of acute cigarette smoking on the gastric volume in fasted regular smokers throughout a study period of 120 min. Ultrasound measurement of antral area was previously used for the assessment of gastric emptying in healthy, diabetic and dyspeptic patients. It was reported that repeated ultrasound measurements of antral area highly correlated with the gold standard scintigraphy after ingestion of a standardized meal, and that measurement of gastric emptying rate, corresponding to the calculation of the variation rate in antral area, was highly reproducible, with inter and intraobserver random measurement error of 10.9% and 9.5%, respectively. Furthermore, the individual measurement of antral area is highly reproducible, with high intra and interrater reliability. In a previous study, we reported that ultrasound measurement of antral area was sensitive enough to detect the presence of small fluid volumes, about 25 ml, in the stomach, with a good performance. This non-invasive tool was therefore particularly appropriate for the assessment of the variation in gastric volume throughout the study period in volunteers.

However, constituting a limitation of this study, variations of the acidity in the stomach could not be studied, and the accurate effect of cigarette smoking on gastric secretion. The lack of standardization of the type of cigarettes, constituted another limitation of this study. One can suppose that the effect of cigarette smoking on gastric contents may differ according to their composition, even if no correlation was previously found between the plasma nicotine level and gastric emptying. At last, our results are valid for healthy regular smokers only. Further studies should be conducted in regular smokers suffering from pathologies affecting gastric secretion and/or gastric emptying.

In conclusion, in fasted regular smokers, acute preoperative smoking did not affect the small (<1.5%) variation in the gastric volume during the period 0–120 min, while not increasing the gastric volume during the periods 0–30, 0–60 and 0–90 min. Consequently, acute smoking does not probably change the risk of pulmonary aspiration of gastric contents. In clinical practice, the postponement of the operation in fasted patients having smoked before their surgery should therefore probably be limited to patients with increased cardiovascular or pulmonary risks. Further studies will be required to assess the effect of acute smoking on the gastric emptying within the first two h after the ingestion of clear fluids in regular smokers, as current preoperative fasting guidelines allow drinking clear fluids till two h before anaesthesia.

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