Cough threshold after upper abdominal surgery

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Abstract

The effect of upper abdominal surgery under general anaesthesia on the cough threshold was studied in 26 patients, on the basis of the concentrations of capsaicin and citric acid causing cough. Cough threshold was determined after administering doubling doses of nebulised aerosols of capsaicin and citric acid before operation and on the first and fourth postoperative days. There was an increase in cough threshold (decrease in cough sensitivity) in response to both inhaled irritants on the first postoperative day from the preoperative day and a return towards preoperative values by the fourth day after surgery. The increase in cough threshold on the first postoperative day correlated with the time since opiate administration ($r = 0{\cdot}7$ for capsaicin, 0·52 for citric acid). These results show that the threshold concentration of chemical irritants causing cough is increased on the first postoperative day after upper abdominal surgery.

Cough is a major defence reflex of the airways and is necessary for the effective clearance of excess bronchial secretions.[1] Suppression of cough in the postoperative period, it has been suggested, may help to cause pulmonary complications of surgery, but there have been no studies of the cough reflex in the perioperative period. We have studied the effect of upper abdominal surgery under general anaesthesia on the cough response to two inhaled chemical irritants (capsaicin and citric acid) and examined the relation between cough threshold and the interval from opiate analgesic administration.

Methods

Fifty consecutive patients undergoing elective upper abdominal surgery were interviewed over five months; 26 patients consented to the cough study, which was approved by the Frenchay District ethical committee, and informed written consent was obtained. Patients were assessed clinically by a physician (JPD) and the day before operation the presence of cough, smoking, sputum production, and chest signs was noted. A posteroanterior chest radiograph was obtained and the forced expiratory volume in one second (FEV_1) measured by spirometry (Vitalograph). The duration and type of operation were recorded; clinical assessment was repeated on the first and fourth postoperative days and a further posteroanterior chest radiograph was obtained on the second postoperative day. The timing of all postoperative opiate analgesia was recorded.

COUGH THRESHOLD

Cough was stimulated by giving doubling doses of a nebulised aerosol of two chemical irritants (capsaicin and citric acid) by means of a single vital capacity inhalation.[2] The concentration of irritant at which the first cough was induced (the cough threshold) was determined on the preoperative day and on the first and fourth postoperative days. Measurements were made at the same time of day to avoid any diurnal variation.[2] Subjects were informed about the study in general terms—"We are testing airway reflexes" and "You may cough"—but were not told that the study of cough was the primary objective. The subjects wore a nose clip and were trained to breathe through a mouthpiece, exhale to residual volume, and then inhale to total lung capacity over five seconds at a constant flow rate, during which period the irritant was administered via a Wright's nebuliser. Capsaicin dissolved in absolute alcohol made up in normal saline was given at one minute intervals in doubling concentrations increasing from $1{\cdot}5 \times 10^{-7}$ to 96×10^{-7} mol/l until the cough threshold was determined. The study was repeated immediately in an identical manner with citric acid monohydrate dissolved in distilled water in concentrations from 0·125 to $2{\cdot}0 \times 10^{-1}$ mol/l.

STANDARDISATION OF OTHER VARIABLES

The anaesthetic regimen was standardised, all patients receiving intravenous induction with thiopentone, neuromuscular blockade with a non-depolarising agent, and intermittent positive pressure ventilation with a Bromptom-Manley ventilator. General anaesthesia was maintained with a mixture of nitrous oxide and oxygen with enflurane or isoflurane. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate. Atropine, doxapram, and regional anaesthesia were avoided. Postoperative analgesia consisted of intermittent, intramuscular, on demand opiates (1·5 mg/kg pethidine or 0·25 mg/kg papaveretum). By the fourth day paracetamol was the only analgesic prescribed and no patients had received opiate analgesia for at least 16 hours before measurement of cough threshold. All patients received the same

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Accepted for publication 21 November 1989

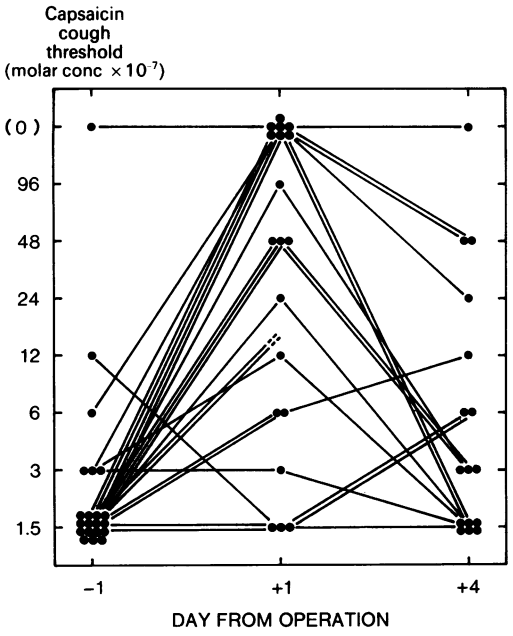

Figure 1 Cough threshold with inhaled capsaicin in the perioperative period. (0)—Cough assumed to occur at 192×10^{-7} molar; --cough assumed to occur at 24×10^{-7} molar.

preoperative antibiotic regimen of a single dose of intravenous cefuroxime 1·5 g at induction. A single dose of intravenous metronidazole 500 mg was given in addition to the two patients who underwent gastric surgery. No routine antibiotics were administered after operation. The physiotherapy regimen was identical for each patient except for the five developing signs of infection postoperatively.

STATISTICAL METHODS

Differences between cough thresholds on the preoperative and the first and fourth postoperative days were compared by the Wilcoxon matched pairs test. Patients who did not cough in response to the range of concentrations of irritants used were assumed to have coughed at the next doubling dose for the purposes of analysis. The log change in cough threshold between the preoperative and the first postoperative day was examined in relation to the time from opiate administration (Spearman rank correlation).

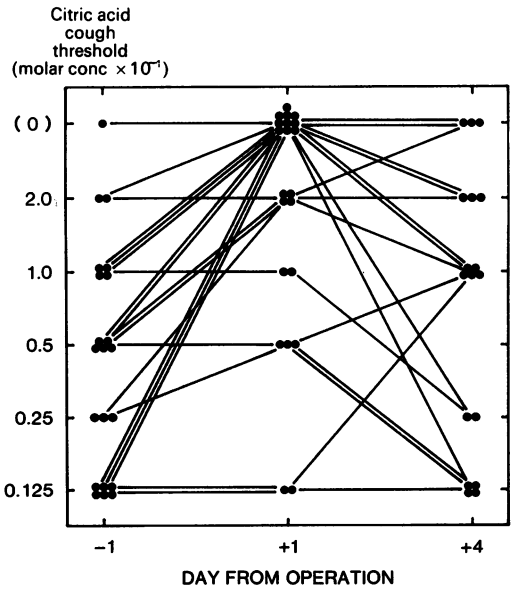

Figure 2 Cough threshold with inhaled citric acid in the perioperative period. (0)—Cough assumed to occur at $4{\cdot}0 \times 10^{-1}$ molar.

Results

We studied 12 men and 14 women. Twelve were smokers and six had evidence of respiratory disease, with chronic sputum production or airflow obstruction, or both. Median FEV_1 was 2·55 (range 1·6–3·8) l for the men and 2·25 (range 1·5–2·9) l for the women. Twenty three patients underwent cholecystectomy, two gastric surgery, and one splenectomy. The median duration of surgery was 1·25 hours (range 0·5–3·0 hours). None of the patients was diabetic or had cough syncope or bronchiectasis, and none was using an angiotensin converting enzyme inhibitor. No patient had had a respiratory tract infection within the previous six weeks.

Five patients refused further testing on the first postoperative day. The remaining 21 patients were much less sensitive to inhaled capsaicin and citric acid—that is, had a higher cough threshold ($p < 0{\cdot}01$ for both irritants; figs 1 and 2). Two patients were reluctant to inhale capsaicin at a concentration above 12×10^{-7} mol/l; they were assumed for the analysis to have coughed at the next concentration of capsaicin. On the fourth postoperative day 17 patients had further tests. Both the capsaicin and the citric acid cough thresholds were significantly lower than on the first postoperative day ($p < 0{\cdot}01$). They were, however, higher on the fourth postoperative day than before operation, though this difference was not quite significant ($p = 0{\cdot}054$ for capsaicin and 0·058 for citric acid).

All patients received opiate analgesia on the first postoperative day. There was a significant relation between the time since opiate administration and the log difference in cough threshold between the preoperative and the first postoperative day (capsaicin: $r = 0{\cdot}7$, $p < 0{\cdot}01$; citric acid: $r = 0{\cdot}523$, $p < 0{\cdot}05$).

Five patients developed a chest infection as judged by purulent sputum, radiological change, and fever. These infections were clinically apparent by the second postoperative day in four patients and on the third day in the other. There was no correlation between cough threshold or change in cough threshold and the development of postoperative chest infection and no relation between cough threshold and smoking, pre-existing respiratory disease, or length or type of operation.

Discussion

Cough is responsible for the expulsion of inhaled foreign bodies and aids mucociliary clearance in the presence of excess bronchial secretions.[1] Postoperative chest infection occurs frequently in patients with chronic bronchitis[3] and suppression of cough at the time of surgery might be an important risk factor.

Cough is initiated by stimulation of airway receptors located in the larynx and major airways. Three types of receptor play a part in the afferent limb of the cough reflex—namely, myelinated, rapidly adapting receptors, smooth muscle receptors, and non-myelinated fibre receptors[4,5]—but the role of each is still not clear. Animal data suggest that capsaicin,

an extract of red pepper, is primarily a C fibre stimulant, whereas citric acid and other inorganic acids act primarily on rapidly adapting receptors. Rapidly adapting receptors may be the principal afferent receptors in the cough reflex[5] and C fibres may have a role in the modification of this response. Both capsaicin[6] and citric acid[2 7] induce a reproducible cough response in man.

The cough threshold was considerably increased on the first day after operation. This is likely to be due, in part at least, to the administration of opiate analgesia, the timing of which was related to the change in cough threshold. Opiate administration, however, is unlikely to be the sole explanation of the change in sensitivity, as the overall shift in the cough threshold is much greater than has been found in previous studies of similar doses of opiates on chemically induced cough.[8] The cough threshold was still somewhat higher on the fourth postoperative day, when no patient was receiving opiates, than before operation. The pattern of change in cough threshold over the perioperative period was similar for capsaicin and citric acid. Using the single breath inhalation technique we have not been able to find tolerance to citric acid,[2] and tolerance to capsaicin has not been reported.[6] The inspiratory efforts our subjects produced appeared to be similar before and after operation. Some reduction in vital capacity may have occurred postoperatively and this would reduce inspiratory flow rate over a five second inspiration. Some data, however, suggest that lower inspiratory flow rates tend to lower the cough threshold[9]—an effect opposite to what we found.

This study does not allow conclusions to be drawn about other factors that could influence the cough threshold by altering the sensitivity of the afferent airway receptors—including anaesthetic agents, endotracheal intubation, and a transient increase in bronchial secretions. Hypoxaemia is well recognised after surgery,[10] and this may have reduced cough by a direct effect on the "cough centre" in the brainstem.[11] Further work to examine these factors is required. The number of patients who developed a chest infection is too small to enable any conclusions to be drawn on the incidence of postoperative infection.

We conclude that most patients undergoing routine surgical procedures display substantial alterations in the cough threshold. There was a significant depression in sensitivity to inhaled irritants on the first day after operation and a return towards preoperative values by the fourth postoperative day. Opiate analgesia may not fully explain this depression. The importance of these data in relation to the risk of postoperative chest infection remains to be determined.

We thank Mr A O Hughes (department of epidemiology, University of Bristol) for assistance with the statistical analysis and the physiotherapy department of Frenchay Hospital. JPD receives a grant from the Stanley Luff bequest.

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