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CLINICAL INVESTIGATIONS

Effect of an upper respiratory tract infection on upper airway reactivity

N. NANDWANI, J. H. RAPHAEL AND J. A. LANGTON

Summary

Patients presenting for elective anaesthesia and surgery may be suffering with, or recovering from, a recent upper respiratory tract infection (URTI). It is a frequent clinical problem as to whether to postpone surgery in such patients as they may be more likely to suffer adverse respiratory events related to administration of general anaesthesia. Using dilute ammonia vapour as a chemical stimulus, we measured upper airway reactivity in 11 healthy volunteers (six males), mean age 39.8 (range 30–58) yr, who had symptoms of an URTI. Volunteers were recruited 24–72 h after symptoms first began, and followed-up at regular intervals for the next 8 weeks. Measurements of upper airway reactivity were made on the following days (±24 h) after commencement of URTI symptoms: 3, 6, 9, 15, 20 and 27. Additional measurements were obtained 56 days after symptoms first began, and these were regarded as baseline measurements. Upper airway reactivity was increased on days 3, 6 and 9 compared with baseline measurements ($P<0.01$, Wilcoxon). There was no significant change in airway reactivity from day 15 onwards, by which time 10 of the 11 subjects were completely devoid of symptoms. All subjects were asymptomatic by day 20 and remained so until the study ended on day 56. We conclude that upper airway reactivity was increased during the acute phase of an URTI, and that this appeared to be related to the presence of symptoms. (*Br. J. Anaesth.* 1997; **78**: 352–355).

Key words

Airway, reflexes. Infection, respiratory tract. Complications, respiratory. Complications, infection.

Most adults suffer at least one upper respiratory tract infection (URTI) per year. The incidence increases to 5–6 episodes per year in children. Therefore, many patients presenting for elective surgery and anaesthesia may either be suffering with, or recovering from, a recent URTI.

The decision whether or not to anaesthetize such a patient is a common clinical dilemma. In the past it has been routine practice to postpone anaesthesia and surgery in patients suffering from an URTI, but this may have medical, social and financial consequences. There have been relatively few studies investigating this important clinical area and these have focused on the incidence of adverse respiratory events associated with anaesthesia in children. In a large prospective study, Cohen and Cameron studied 1283 children with symptoms of an URTI and 20 876 children without any symptoms who were undergoing elective surgery.[1] They found that children suffering from an URTI were three times more likely to suffer an adverse respiratory event; the risk increased 11-fold if tracheal intubation was performed. In 1992, Levy and colleagues[2] found that children with an acute or recent URTI had an increased likelihood of transient hypoxaemia in the perioperative period. There has also been a well documented case report of laryngospasm resulting in death in a child recovering from a recent URTI.[3] It has even been suggested that an anaesthetist may be negligent for anaesthetizing a child while suffering from an URTI.[4]

At present there are few studies which have investigated adult patients with symptoms of an URTI undergoing anaesthesia. There is however evidence of increased bronchial reactivity in adults suffering from an URTI; Empey and co-workers demonstrated a 200% increase in airway resistance in response to inhaled histamine in subjects with colds compared with a 30% increase in controls.[5] There is however little evidence to demonstrate that anaesthesia in adult patients with an URTI leads to an increased incidence of respiratory complications.

We are able to measure upper airway reactivity in subjects by using dilute ammonia vapour as a chemical stimulus to the upper airway.[6] The aim of this study was to determine the sensitivity of upper airway reflexes during an URTI and to record the duration of any possible changes and the relationship of these changes to the presence of symptoms.

Subjects and methods

After obtaining Ethics Committee approval and written informed consent, we studied 12 volunteers,

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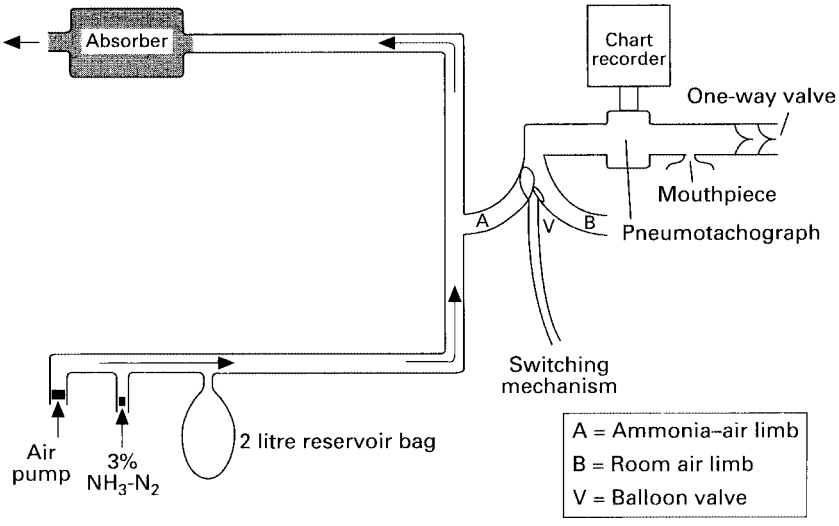

Figure 1 Schematic diagram of the equipment used to measure upper airway reactivity.

24–72 h after symptoms of an URTI first began. All volunteers were non-smokers and not receiving any medication. Exclusion criteria included a history of asthma or an URTI in the previous 3 months.

URTI was defined according to similar criteria as used by Tait and Knight.[7] Symptoms were divided into three categories: nasal—discharge, obstruction, sneeze; throat—sore throat, non-productive cough; systemic—malaise, muscular ache, temperature less than 38°C.

Subjects were recruited into the study if they had at least one symptom from each category and were deemed to be asymptomatic only when all symptoms had completely disappeared. Subjects were not studied if they had a temperature greater than 38°C, productive cough or evidence of lower respiratory tract infection.

All subjects were followed-up at regular intervals over the next 8 weeks. Measurements of upper airway reactivity were made on the following days (±24 h) after commencement of URTI symptoms: 3, 6, 9, 15, 20 and 27. Additional measurements were obtained 56 days after symptoms first began and these were regarded as baseline measurements. The presence or absence of symptoms was also recorded.

Upper airway reflex sensitivity was measured using a previously described method which uses low concentrations of ammonia vapour as an irritant chemical stimulus to the upper airway during inspiration.[6] Briefly, the subject was asked to breathe through a close-fitting mouthpiece while wearing a noseclip and to exhale to atmosphere via a one-way valve (fig. 1). The mouthpiece was attached to a pneumotachograph which records airflow onto a chart recorder. A pneumatic two-way balloon valve was situated between limbs A and B of the breathing circuit. This balloon valve allowed the investigator to switch rapidly between room air and dilute ammonia vapour. Subjects wore dark goggles and listened to music through headphones so that they were unaware of the switching of the pneumatic valve.

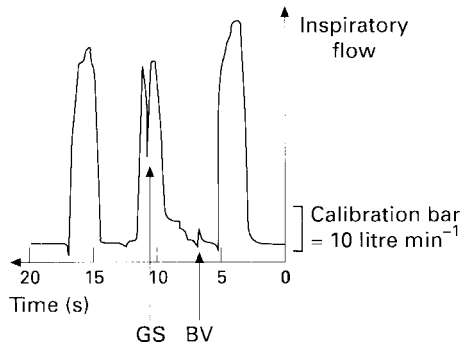

Figure 2 Example of a glottic stop recording. GS = Glottic stop, BV = switching of the balloon valve, allowing the subject to take a single breath from the ammonia–air limb.

In this way the subject's upper airway was exposed to single intermittent breaths containing small concentrations of ammonia vapour and the threshold concentration (NH_3TR) required to elicit glottic closure was recorded. We defined glottic closure as a rapid decrease in inspiratory flow, the flow decreasing by at least 25% of peak inspiratory flow, followed by a swift recovery, and the whole event lasting less than 0.5 s (fig. 2). Low values for NH_3TR are associated with increased sensitivity of the upper airway, high values represent depression of upper airway reflex sensitivity.

Ammonia was supplied via a Rotameter from a 3% ammonia–nitrogen cylinder supplied by the British Oxygen Company. This was added to room air 10 litre min^{-1} to deliver accurate concentrations of ammonia vapour in the range 0–3500 ppm. Calibration of the system has been described previously.[6] By altering the flowmeter settings by increments of 50 ml min^{-1}, corresponding to mean (range) changes in ammonia concentration of 171 (125–235) ppm, we were able to determine the minimum concentration of ammonia vapour required to elicit glottic closure (NH_3TR).

Results

Eleven subjects (six males), mean age 39.8 (range 30–58) yr, completed the study. One subject was completely devoid of symptoms by day 6, five by day

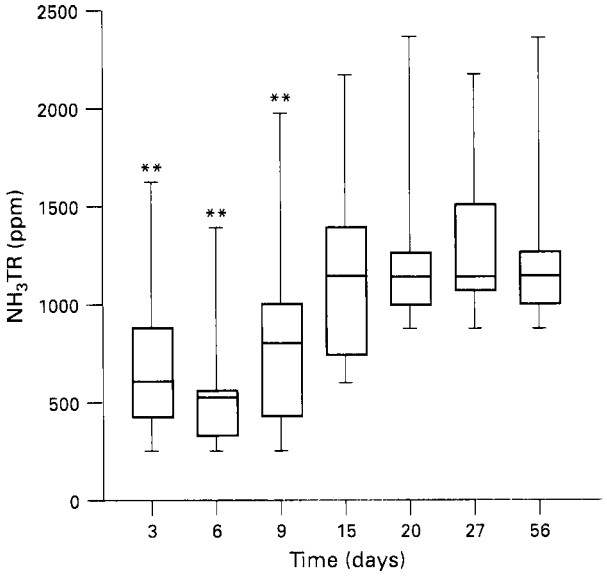

Figure 3 Ammonia threshold concentration (NH_3TR) in volunteers with an upper respiratory tract infection (URTI) showing the median, interquartile range and 10th and 90th percentiles. $^{**}P<0.01$ (Wilcoxon).

9 and 10 by day 15. All were asymptomatic by day 20 and remained so until the study ended on day 56 when the baseline NH_3TR measurements were recorded.

There was a decrease in NH_3TR, corresponding to an increase in upper airway reactivity, from a baseline mean of 1255 (SEM 126) ppm to 674 ppm (116) on day 3, 587 ppm (108) on day 6 and to 806 ppm (170) on day 9 after the commencement of URTI symptoms (fig. 3). Using Friedman two-way ANOVA and Wilcoxon matched pairs signed ranks test, these changes were statistically significant ($P<0.01$).There was no significant change in NH_3TR compared with baseline measurements from day 15 onwards.

Discussion

Upper airway reflex activity is important to the anaesthetist because it is involved in both airway protection and upper airway complications such as cough and laryngospasm. We are able to measure upper airway reactivity using small concentrations of ammonia vapour as a chemical stimulus to the upper airway.[6] Using this technique previous studies have shown that airway reflexes are depressed by administration of oral benzodiazepines[8] and also by topical administration of lignocaine to the vocal cords.[9] It has also been shown that upper airway reactivity decreases with advancing age.[10] In comparison, chronic smokers have significantly greater airway reactivity than non-smokers,[11] an effect that can last for up to 10 days after abstinence from cigarettes.

The exact mechanism responsible for reflex glottic closure has not been fully elucidated. Receptors known to respond to chemical irritants are found in the epithelial and subepithelial layers of the pharynx and larynx. Afferents from these receptors travel mainly in the superior laryngeal nerve and synapse in the brain stem. In adult humans the main response to irritant receptor stimulation is glottic closure and a brief pause in inspiration. Higher concentrations of irritants result in cough. We have used the threshold concentration of dilute ammonia vapour required to elicit glottic closure (NH_3TR) as a measure of upper airway reactivity.

It is thought that the epithelial lining of the upper airway plays an important role in restricting access of inhaled irritants to the subepithelial receptors. It is known that infection of the upper respiratory tract results in mucosal oedema followed by shedding of the epithelial cell layers.[12] Loss of airway epithelium can extend down to the basement membrane and may persist for as long as 3 weeks after the initial infection. Our findings of increased upper airway reactivity during the acute phase of an URTI agree with the findings of Empey and colleagues, who demonstrated that bronchial reactivity in response to inhaled histamine is increased during an URTI.[5] Chronic smokers also develop inflammation and destruction of the protective epithelial barrier[13] and this may account for the increase in upper airway reactivity which has been demonstrated previously.[11]

The diagnosis of URTI is complicated by the fact that a particular clinical syndrome is not always associated with a specific pathogen. The rhinovirus, myxovirus and respiratory syncytial virus are the most common pathogens. We recruited subjects on the basis of the presence of symptoms attributable to an acute URTI.[7] We did not attempt to perform viral cultures as this would have been neither practical nor cost-effective for a self-limiting usually benign condition. In everyday anaesthetic practice the presence of symptoms would be used to assess the need to postpone surgery.

There is some interest in the effect of inhaled anaesthetic agents on the course of an URTI. It has been suggested that after surgery and anaesthesia there may be a decrease in both the severity and duration of certain respiratory symptoms. Tait and Knight[7] found a significantly lower incidence of sore throat, sneezing, malaise and fever in children after general anaesthesia compared with those that were not. Earlier *in vitro* studies examining exposure of several viruses to halothane demonstrated dose-dependant inhibition of viral replication.[14] This effect is thought to result in part from a decrease in synthesis of viral proteins, although these *in vitro* experiments required an exposure time equal to the replicative time of the virus. Nevertheless these studies demonstrate the sensitivity of some viruses to anaesthetic agents which could potentially be reflected in the clinical situation. These findings are of special interest as they add an additional clinical perspective.

An editorial in the *British Journal of Anaesthesia* in 1990[15] highlighted the fact that to date there is little evidence to show that general anaesthesia administered to an adult patient with an URTI results in an increased incidence of adverse respiratory events. Our study has demonstrated that upper airway reactivity was increased during the acute phase of an URTI. In addition, we have shown that this increase appeared to be related to the presence of symptoms. However, the exact relationship between an

increase in the sensitivity of airway reflexes and the incidence of upper airway problems requires further investigation.

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