

Sensitivity of the cough reflex in young and elderly subjects

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Abstract

Objective: to compare the sensitivity of the cough reflex - which is said to be normal in elderly people - in elderly and young subjects.

Subjects: 20 elderly (14 female) subjects, mean (SEM) age 83 (1) years and 20 young (nine female) subjects, mean (SEM) age 27 (1) years, who were all non-smokers. None of the subjects was taking antitussive drugs and none suffered from clinically evident lung, cardiac or neurological disease. Five elderly subjects were unable to perform adequate spirometry and were excluded from analysis.

Design and outcome measures: each subject inhaled 10 ml of nebulized distilled water and isotonic saline (as placebo) for 30 s, 10 min apart in a randomized double-blind crossover fashion. The cough frequency induced with each treatment was recorded on a click counter.

Results: cough frequency on inhaling distilled water was significantly lower in the elderly group than in the younger group, with a difference of 9.53 (95% confidence intervals: 3.63, 15.4; $P < 0.001$). None of the subjects coughed when inhaling placebo solution, resulting in significant differences in cough frequencies between distilled water and placebo of 5.87 (2.82, 8.92; $P < 0.05$) for the elderly group and 15.4 (11.0, 19.8; $P < 0.0005$) for the younger group.

Conclusions: the sensitivity of the cough reflex appears to be significantly reduced in elderly subjects. This may increase the risk of aspiration and bronchopulmonary infection in old age, even in the absence of respiratory disease.

Keywords: cough reflex, elderly people, sensitivity

Introduction

Cough is one of the commonest, yet least well understood of respiratory symptoms [1]. It is a reflex action, mediated by the vagus nerve [2] and as such can be regarded as physiologically protective, preventing lung inundation [3]. Coughing can be artificially induced when either mechanical or chemical stimuli [4, 5] are applied to laryngeal or tracheal epithelium [6, 7]. Chemical stimuli of more peripheral airways may also elicit cough [8].

There are few published data on the cough reflex in old age. One study has demonstrated that in elderly people the cough reflex to inhaled ammonia gas is reduced [9]. However, more recent studies [10, 11] have suggested that the cough reflex in older people is normal, although in one of these studies [10] discrepancies in the comparative groups result in difficulties in data interpretation. The aim of the present study was to compare the sensitivity of the cough reflex in young and elderly subjects.

Subjects and methods

Twenty elderly subjects (14 females), mean (SEM) age 83 (1) years, and 20 young subjects (nine females), mean (SEM) age 27 (1) years, were recruited following written informed consent to the study, which had been approved by the local ethics committee. The elderly subjects were recruited from local volunteer groups (Women's Royal Volunteer Service; $n = 2$) and residential homes ($n = 18$; 12 females) in the city of Aberdeen. The young volunteers were members of the hospital staff.

All subjects were lifelong non-smokers and none was taking antitussive medication. None of the subjects had a cough or suffered from a recent upper respiratory tract infection. In the elderly group, most subjects were not taking any medication. However, three subjects were on regular benzodiazepine therapy (temazepam 10 mg) for night sedation, three were taking regular paracetamol for joint pains and one was taking an antibiotic (trimethoprim) for a urinary tract infection. The subjects undergoing regular benzodiazepine therapy were asked

to withhold this therapy on the night before the study day for adequate washout. In the elderly group, who underwent a physical examination prior to entry into the study, none of the subjects suffered from clinically evident pulmonary, cardiological or neurological disease.

In order to exclude unsuspected airways obstruction, all volunteers underwent spirometry to record forced expiratory volume (FEV₁) according to American Thoracic Society criteria [12] using a Vitalograph spirometer (Vitalograph Ltd, Buckingham, UK). Forced expiratory manoeuvres were performed from total lung capacity to residual volume and the best FEV₁ value was taken from the highest value of three consistent forced expiratory curves [12]. Five subjects in the elderly group were unable to perform technically adequate spirometry and were excluded from subsequent statistical analysis. Mean (SEM) FEV₁ (as percentage of predicted) was 98 (4%) for the elderly group (*n* = 15) and 104 (2%) for the young group (*n* = 20). Predicted normal values for the elderly group were calculated according to Enright *et al.* [13].

Each subject then inhaled, at a normal tidal volume, 10 ml of nebulized distilled water or isotonic sodium chloride using an ultrasonic nebulizer (Monaghan Co., Littleton, CO, USA) and mouthpiece [14]. Each solution was inhaled over a 30 s period in a randomized, double-blind crossover design. Inhalation of the two solutions was separated by a 10 min washout period with the isotonic sodium chloride acting as a placebo control [14]. All subjects were instructed to keep the mouthpiece in the mouth even when coughing in order to inhale the nebulized solution for the full 30 s period. The number of coughs induced by each solution was recorded on a click counter and stored for analysis.

Statistical analysis

The recruitment of 20 subjects to each group was sufficient to detect a 20% difference in cough frequency between the two groups with 80% power at the 5% level (two-tailed). However, in the elderly group, data were analysed on the 15 subjects who were able to perform a technically adequate FEV₁.

Data were analysed as mean values and comparisons made between groups using a statistical software package (Confidence Interval Analysis, BMJ Publishing Group, London, UK) [15]. A *P* value <0.05 was taken as being statistically significant.

Results

There was a significant reduction in cough reflex sensitivity in the elderly group (*n* = 15) compared with the young volunteers (*n* = 20) when inhaling distilled water (mean and 95% CI for the difference): 9.53 (3.63, 15.4; *P* < 0.001; Figure 1). In each of the groups, a significant difference was observed when distilled water was compared with isotonic sodium chloride.

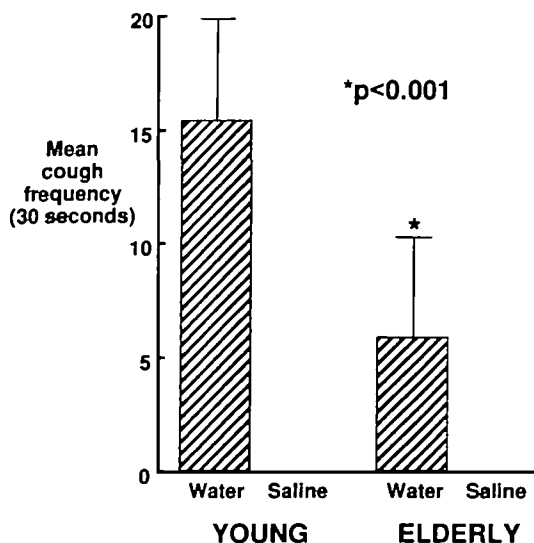


Figure 1. Cough frequency as mean and 95% confidence interval for 20 young and 15 elderly subjects following inhalation of nebulized distilled water and isotonic saline over separate 30 s treatment periods. None of the subjects in either group coughed when inhaling saline. *P* value denotes significance value for comparison between the two age groups.

The mean (and 95% CI) for these differences were 5.87 (2.82, 8.92; *P* < 0.05) for the elderly and 15.4 (11.0, 19.8; *P* < 0.0005) for the young (Figure 1). None of the subjects in either group coughed when inhaling isotonic sodium chloride.

Discussion

The results from this study suggest that the sensitivity of the cough reflex is significantly reduced in the elderly population when compared with young subjects. This may subsequently expose elderly subjects to a greater risk of aspiration or bronchopulmonary infection even when there is no clinical evidence of respiratory disease. In this respect, it has been suggested that patients with aspiration pneumonia may lack a cough reflex [16].

The underlying cause for this reduction in cough reflex sensitivity is not clear, but it is likely to be multifactorial. It is possible that reduction in bronchial smooth muscle tone in elderly people may play a role as muscle tone generally is reduced in old age. The cough reflex is thought to be mediated in part by the vagus nerve [2] and may also involve rapidly adapting vagal receptors (RAR) situated in the larynx and upper airways [3, 6]. Slow phase activity from RAR occurs during respiration when airway tone is increased [17]. Hence, it is conceivable that a converse reduction in airway tone may increase the threshold for inducing cough by inhibiting the respiratory activity of the RARs.

Furthermore, slowly adapting receptors (SAR or stretch receptors) in the airways influence the cough reflex [18, 19]. Bronchoconstriction is known to sensitize the SARs [20] which may reduce the threshold for cough: conversely, bronchodilation would attenuate SAR activity and so lessen cough. This is in agreement with a previous study which has demonstrated inhibition of artificially induced cough by inhaled bronchodilators in healthy volunteers [21].

However, the stretch receptors are known to mediate the tachycardic response and the Hering-Breuer reflex during bronchoconstriction [22]. Previous studies have shown that both responses to bronchoconstriction are reduced in the elderly population [23, 24], which may suggest that the number or the activity of the stretch receptors are reduced in old age. Hence, their role in the cough reflex in older people is not entirely clear cut.

There may be impaired perception of bronchoconstriction in elderly people, both in those with asthma and in healthy subjects [25], which could be linked to an increased cough threshold. In one case study, a reduction in peak expiratory flow rate (PEFR) of 40% was noted to be symptomless in an elderly asthmatic patient [26]; however, this patient was demented and this may have affected her ability to complain about symptoms. Furthermore, in the healthy group in the former study the reduction in FEV₁ was relatively small and may be due to normal variation.

In diabetic patients autonomic dysfunction may result in an altered cough reflex [27]. Impaired autonomic reflexes can occur in elderly patients and this may explain the increased cough threshold seen in our elderly group, although without definitive autonomic reflex investigations this conclusion is hypothetical.

It is important to consider potential central effects in old age which may also play a role in impairing the cough reflex. We attempted to minimize the effects of oral benzodiazepines which were taken by three of our patients by asking them to withhold their medication for 36 h before their study day. This would allow adequate washout for temazepam. However, there are age-related abnormalities in central processing of stimuli, including those relayed to the brain stem, which may occur due to subclinical cerebrovascular disease [28, 29]. Such abnormalities could have influenced the cough reflex in our study.

The reduction in cough frequency in elderly subjects may be due in part to reduced lung function and hence poor inspiration of the nebulized solutions, when compared with the younger population. A proportion (approximately 30%) of elderly patients have increased difficulty in actuating breath-activated inhaler devices due to poor inspiratory effort [30]. However, in our study spirometry demonstrated a mean FEV₁ of 98% of predicted normal, which would suggest that respiratory function was sufficient to inspire the nebulized

solutions adequately. This assumes that to perform normal forced expiration the subject must have comparable inspiration.

The cough response to any stimulus has a subjective component which makes it difficult to study the cough reflex in man. This study was double-blind and randomized and the subjects were not told about the possible occurrence of cough with each solution. Seven of the elderly group did not cough at all with the distilled water while one elderly lady coughed 15 times with the same solution. Those subjects who did not cough did not differ in any particular characteristic from the remainder of the group and the reason for their complete absence in coughing is unclear. Hence, the full range of factors influencing the cough reflex threshold remains to be identified in the elderly population.

In conclusion, the sensitivity of the cough reflex appears to be significantly reduced in old age, although the threshold for coughing varies even within groups. This may increase the risk of aspiration and bronchopulmonary infection in elderly people, even in the absence of respiratory disease. Studies addressing the frequency of respiratory infections in older people would clarify this.

Key points

- There is reduced cough reflex sensitivity in elderly subjects.
 - This may explain the increased risk of bronchopulmonary infection which occurs even when respiratory disease is absent.
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