Does Aspiration of Saliva Trigger Nocturnal Asthma?

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Abstract

Five adult asthmatics with nocturnal symptoms (mean FEV1 2.31 1; 2mean P020 histamine 1.5 unmoles), 5 asthmatics with no nocturnal symptoms (mean FEV11 2.97 1: mean P020 Histamine 3.7 umoles) and 5 non-asthmatic control subjects (mean FEV1 3.631; mean PD2ohistamine 78 umoles) were challenged with nebulised solutions of their own saliva or isotonic saline in a double blind crossover study to Investigate whether the inhalation of saliva during sleep could cause noctumal asthma. The maximum % fall in FEV I with saliva was -26.6, -6.5 and -4.1 for the nocturnal, non-nocturnal and control groups respectively. The corresponding values for the maximum % fall in FEV1 with saline was -12.4, -5.5 and -3.6. The difference in maximum % fall In FEV1 with both saliva and saline was significant ($p<0.01$) for the nocturnal asthmatics when compared to the non-nocturnal asthmatics. These results lend support to the hypothesis that noctumal symptoms in asthmatic patients may be triggered by Inhalation of saliva during sleep (JPMA 44:60, 1994).

Introduction

Nocturnal asthma is common and can be difficult to treat. The mechanism of nocturnal bronchoconstriction is not well characterised. Suggested mechanisms have included allergy to feathers or dust in the bedding, airway cooling, circadian falls in circulating corticosteroids and catecholamine concentrations and gastric acid reflux into the lungs during sleep[1] but an all, encompassing cause for every case is unlikely. We investigated the possibility that a trigger for nocturnal asthma my be the inhalation of saliva during sleep.

Subjects and Methods

We studied 5 asthmatics with persistent nocturnal symptoms for at least 2 weeks before the start of the study, 5 asthmatics with no nocturnal symptoms during the study and 5 normal subjects, matched for age (mean ages 42.2,45.2 and 44.8years respectively) and sex (4 males in each group). All asthmatics were taking regular inhaled beta2 agonist (salbutamol or terbutaline) and an inhaled prophylactic agent (inhaled steroids, 9; nedocromil sodium, 1). One patient in each group of asthmatics was taking a slow release theophylline preparation, but none, oral steroids. In a randomised, double blind, placebo controlled manner, each subject received 2 ml of their own saliva diluted in 1 ml of isotonic saline or 3 ml of saline delivered by a nebuliser on 2 separate study days. At least 5 ml of saliva was collected immediately before each study, without stimulation, after washing the mouth out with water. The asthmatic patients had refrained from beta2 agonist inhalers for 6 hours and theophylline preparations for 24 hours prior to each study day. FEV1 and peak expiratory flow (PEF) were measured before, immediately after and at 5, 10, 15, 20, 25, 30, 40, 50 and 60 minutes after nebulisation. For each subject, baseline FEV1 was within 200 ml on each study day which were at least one week apart. PD2O to histamine was measured on a third visit using the Yan technique[2]. For each visit the maximum percent fall in FEV1 compared to baseline level was calculated. Paired testing was used to compare the maximum percent fall in FEV1 to saliva and to saline within and between each group.

Results

Baseline FEV11 was significantly lower in the nocturnal group [mean(SD) 2.31(1.31)] compared to normals [3.63(0.53)](PcO.005) but was similar to the non-nocturnal asthmatics [2.97(1.47)I(NS). The maximum percent fall in FEV1 after saliva was -26.6% (nocturnal), -6.5% (non-nocturnal) and -4.1% (normal) (Figure),

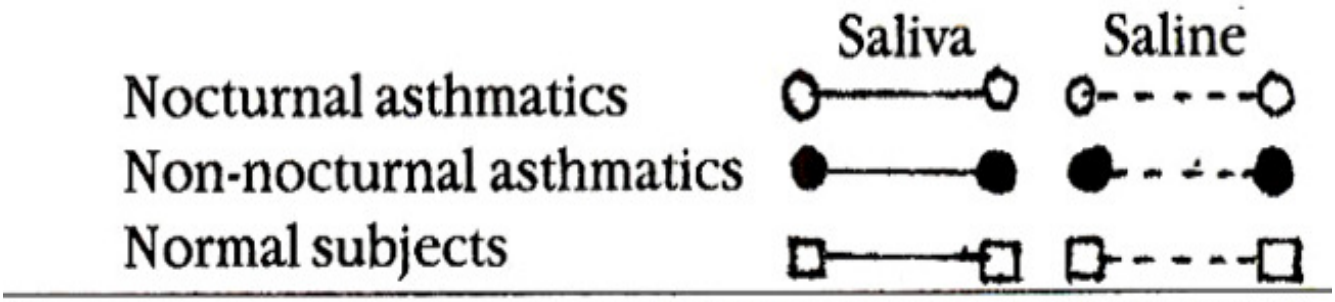

Figure. Time course of the change in FEV1with time to saliva and to saline in the three study groups.

the effect lasting for the duration of the study. After saline the values were -19.3%, -5.9% and -2.2% respectively. The difference in maximum fall to saliva and to saline was significant for nocturnal compared to non-nocturnal asthmatics (P). The equivalent figures for PEF were, for saliva, -16.8, -5.0 and -4.7: for saline, -12.4, -5.5 and -3.6. Mean PD20 histamine for the three groups was 8 umoles (normal), 3.7 umoles (non-nocturnal) and 1.5 umoles (nocturnal).

Discussion

Our study shows that saliva when delivered via nebulizer causes airway narrowing in patients with nocturnal asthma. However, these patients also showed' airway narrowing, although to a lesser degree, with nebulised isotonic saline. This suggests that non- specific airway responsiveness is increased in nocturnal asthmatics which is supported by the trend in histamine reactivity in our study. Other workers have shown that hypotonic saline, dextrose and water can all cause airway narrowing in asthmatics but not in normal subjects indicating that the osmolarity of the solution may be an important determinant of the response[6]. We have no data on the osmolarity or the ion content of the saliva of each individual as this study was an initial study designed to determine whether an effect existed. Nevertheless, inhaled saliva appears to trigger at least an equivalent degree of airway narrowing in those patients with heightened bronchial responsiveness in the laboratory. However, this finding would only be of relevance if it could be demonstrated that saliva can get into the tracheo-bronchial tree during sleep. Gastro-oesopbageal reflux has been suggested as a cause of nocturnal asthma, but there have been conflicting reports as to whether this is an important factor[7]. Studies with nasal instillation of indium III have shown aspiration of the isotope during sleep in 48% of normal subjects[3], so it is likely that saliva can also enter the tracheo-bronchial tree during sleep. We believe that saliva could, therefore, be implicited in nocturnal asthma, although the mechanism is not clear. Salivary output is very low at night, but as broncho constriction is more likely to occur' during REM sleep[4] when dreaming occurs, an appropriate dream could increase salivary output. The pH of saliva is 6.2-7.4 and normal saliva contains an elastase and an amylase. However, in an asthmatic's saliva, there are increased amounts of histamine and lysozyme[5] which may act as mediator(s) of any airway narrowing. Parotid and submandibular saliva are different in their biochemical constituents, but at present we can only

speculate as to the important mediators in this reaction. In summary, we have shown that nebulized saliva can cause marked airway narrowing in patients with nocturnal asthma and histamine hyper-responsiveness, to a greater degree than saline, neither causing any narrowing in normal or non-nocturnal asthmatics. Further work should investigate the characteristic(s) of saliva which may cause nocturnal asthma.

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