

Gastro-oesophageal reflux and nocturnal asthma

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ABSTRACT: Gastro-oesophageal (GO) reflux is believed to be a possible cause of nocturnal asthma. The aim of this study was to see if there is any correlation between the incidence of GO-reflux at night and nocturnal asthma. Thirty-seven adult patients with a history of nocturnal asthma for more than one hundred days a year and of reflux disease were evaluated using 24 h pH-monitoring of the oesophagus and measurement of peak expiratory flow (PEF) rate every hour when awake. Half of the patients suffered from severe GO-reflux at night, whilst the other half had no nocturnal reflux. Respiratory symptoms and inhalation of beta-2 agonists were recorded during the night and PEF was recorded when the patients awoke in the morning. A significant correlation was found between reflux at night and the degree of bronchial obstruction in the early morning, but not between night-time reflux and nocturnal respiratory symptoms. It would appear that GO-reflux in most asthmatics is neither a strong nor immediate trigger factor in nocturnal asthma, although it does seem to influence bronchial obstruction during the night as was demonstrated by a low morning-PEF value.

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A high incidence of gastro-oesophageal (GO) reflux or GO functional disturbances has been noted in asthmatics [1, 2] and has been suggested as a possible trigger factor for nocturnal asthma [3-5].

Nocturnal attacks of asthma may be caused by reflux in the recumbent position, either because of aspiration of stomach contents or because of stimulation of acid-sensitive receptors in the oesophagus, resulting in vagally mediated bronchoconstrictor reflexes or increased bronchial hyperreactivity [6-12]. If GO-reflux during the night is a general and important trigger factor for nocturnal asthma, it is reasonable to suggest that asthmatic patients with nocturnal reflux should have more nocturnal respiratory symptoms or more pronounced bronchial obstruction in the early morning than asthmatic patients who are free from nocturnal reflux. The correlation between reflux at night as measured by long-term pH-monitoring in the oesophagus, nocturnal respiratory symptoms, and the first morning-PEF value was, therefore, studied in patients with a history of nocturnal asthma and reflux disease.

Patients and methods

Fifty-one adult patients with a history of nocturnal asthma for more than one hundred days per year and a history of reflux disease, *i.e.* heartburn and regurgitation, gave informed consent for enrolment in this investigation. The diagnosis of asthma was based on the criteria established by the American Thoracic Society [13]. The patients were evaluated by oesophageal pH-monitoring and PEF-recordings over a

period of 24 h. Patients with nocturnal reflux >0% of the recorded time but less than 1% were excluded from the study. The study was comprised of eighteen patients with nocturnal reflux \geq 1% of the recorded time (group A) and nineteen patients with no nocturnal reflux (group B). Age and sex distribution, as well as the medication used in the two groups of patients, are shown in table 1. No patients received anticholinergic medication.

Acid reflux was recorded for 24 h, with antimony pH-electrodes placed 5 cm above the lower oesophageal sphincter. Details of the technique are given by JOHANSSON *et al.* [14]. Pathological GO-reflux is considered to be a pH of less than 4 for more than 1% of 24 h [15]. The patients were asked to record any respiratory symptoms experienced during the night (10.00 pm-6.00 am) and any use of a beta-2 agonist metered dose inhaler. All patients received a special acid-free diet three times a day. The patients were not allowed to drink coffee or other soft drinks containing caffeine or to eat snacks between meals.

Forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were performed prior to insertion of the pH-electrode using a vitalograph (Maids, Moreton, House, UK). The highest value of three consecutive attempts was recorded.

Peak expiratory flow (PEF) was measured by Wright's peak-flow meter. The highest value of three repeated tests was recorded. PEF was performed every hour during the day until the patients went to bed. The first PEF in the morning was recorded

Table 1. - Demographic data and anti-asthmatic medication during the pH recording day in asthmatics with pathological night-time reflux (Group A) and without any reflux at night (Group B) (mean \pm SEM or range).

	Group A n=18	Group B n=19
Age, yrs	57.8(33-73)	57.2 (25-73)
Male/Female	12/6	10/9
Asthma duration, yrs	15.7(2-50)	15.7 (1-66)
Oral beta-2 agonist, mg/day	10.5 \pm 1.2 (n=14)	12.7 \pm 0.9 (n=12)
Oral theophylline, mg/day	740 \pm 106 (n=6)	644 \pm 51 (n=7)
Oral prednisolone, mg/day	8.8 \pm 2.0 (n=6)	8.5 \pm 2.9 (n=3)
Inhaled steroids, μ g/day	907 \pm 77 (n=14)	845 \pm 71 (n=11)
Body weight, kg	77.5 \pm 2.7	75.4 \pm 2.5

before the patients took any anti-asthmatic medication.

The Mann-Whitney U test was used for comparison between groups of patients with and without pathological nocturnal GO-reflux.

This study was approved by the Human Research Ethical Committee.

Results

As a group, patients with nocturnal reflux (group A, n=18) had a lower morning-PEF value than the group of patients with no reflux at night (group B, n=19), (table 2). The difference between the morning-PEF values in group A and group B was more pronounced when patients who took beta-2 inhalants

Table 2. - Reflux time, nocturnal respiratory symptoms and lung function in patients with (Group A) and without (Group B) pathological reflux at night (mean \pm SEM).

	Group A n=18	Group B n=19	
Night-time reflux, %	4.2 \pm 0.8	0	
Day-time reflux, %	5.9 \pm 1.1	4.5 \pm 1.5	NS
Nocturnal Respiratory Symptoms.			
No. of patients	7	3	NS
FEV ₁ , %pred	71 \pm 5.1	73 \pm 5.9	NS
FVC, % pred	70 \pm 3.9	72 \pm 6.5	NS
PEF _{mean} , %pred	67 \pm 4.1	70 \pm 4.8	NS
PEF _{high} , %pred	79 \pm 3.7	78 \pm 4.9	NS
PEF _{morning} , % of highest day value	73 \pm 2.9	81 \pm 2.5*	

PEF_{mean} = the mean value of all PEF recordings during the day of study. PEF_{high} = the highest PEF value during the day of study. PEF_{morning} = the first PEF recording in the early morning. *: p<0.05; NS: not significant

at night were excluded (70 \pm 3.4; n=11 and 80 \pm 2.5; n=16, respectively; p<0.03). The patients in group A who woke at night due to respiratory symptoms (n=7) had a mean reflux time during the night of 5.4 \pm 1.2% (SEM) compared to patients in the same group without nocturnal respiratory symptoms (n=11) of 3.5 \pm 1.0% (SEM; NS). Respiratory symptoms and the use of beta-2 inhalants at night were more frequent in group A than group B although the difference was not statistically significant (table 2).

Pathological reflux during the day was of approximately the same magnitude in the group with nocturnal reflux as in the group without (table 2).

The two groups did not differ regarding body weight, severity of asthma as reflected by history, consumption of asthma medicines and daytime lung function (tables 1 and 2).

Discussion

We found a significant relationship between the presence of GO-reflux at night and the degree of bronchial obstruction in the early morning but not between night-time reflux and nocturnal respiratory symptoms. There was no difference in medication use or severity of asthma during the recording day between patients in either study group which could account for the more pronounced reduction in morning-PEF observed in those with nocturnal reflux. It should be noted, however, that the majority of patients with night-time reflux did not report any nocturnal respiratory symptoms, suggesting that GO-reflux is not a strong and instant trigger factor for asthma in most patients. This suggestion is consistent with a study by EKSTRÖM and TIBBLING [16] which showed that reflux episodes do not elicit asthma attacks, and a study by HUGHES *et al.* [17] which did not demonstrate coughing or wheezing during documented episodes of nocturnal reflux. MARTIN *et al.* [4] found, however, that children with a history of nocturnal asthma had more night-time reflux than children without nocturnal symptoms and in a case report described by BENGSSON *et al.* [15] a woman with severe nocturnal asthma and GO-reflux was successfully treated with the H₂-antagonist ranitidine.

These somewhat contradictory reports may depend on whether immediate or delayed influences of reflux on asthma are studied. In agreement with other authors, it seems reasonable to suggest that stimulation of acid sensitive receptors in the oesophagus by GO-reflux may increase vagal bronchomotor tone without eliciting attacks of asthma, and that this stimulation may also increase bronchial reactivity [11, 12, 18]. If so, it is most likely that GO-reflux should be regarded as an aggravating factor, lowering the threshold for other factors which exacerbate a patient's asthma during the night, rather than being a powerful and instant bronchoconstrictor stimulus. This does not exclude the possibility that in a few cases GO-reflux will be the main aetiological factor for nocturnal asthma, especially when aspiration occurs [5].

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RÉSUMÉ: On considère que le reflux gastro-oesphagien est une cause possible d'asthme nocturne. Le but de cette étude a été d'établir s'il y avait quelque corrélation entre l'incidence du reflux gastro-oesphagien nocturne et l'asthme nocturne. Trente-sept patients adultes, dont l'anamnèse révèle un asthme nocturne pendant plus de 100 jours par an, ainsi qu'un reflux, ont été évalués par monitoring du pH pendant 24 h. Au niveau de l'oesophage et par mesure du débit expiratoire de pointe à chaque heure d'éveil. La moitié des patients souffrait d'un reflux gastro-oesphagien sévère la nuit, tandis que l'autre moitié n'avait pas de reflux du tout. Les symptômes respiratoires et l'inhalation de bêta-2-stimulants ont été enregistrés pendant la nuit, et le débit de pointe a été mesuré quand les patients se réveillaient le matin. Une corrélation significative a été établie entre le reflux nocturne et le degré d'obstruction bronchique au petit matin, mais non entre la période de reflux nocturne et les symptômes respiratoires nocturnes. Il semblerait donc que, chez la plupart des asthmatiques, le reflux gastro-oesphagien ne soit pas un facteur déclenchant violent ni immédiat dans l'asthme nocturne, quoiqu'il semble influencer l'obstruction bronchique pendant la nuit comme démontré par une valeur basse du débit expiratoire de pointe matinal.