Can a simple forced inspiratory maneuver help identify subjects at risk for sleep-disordered breathing?

Poate o manevră simplă de inspir forțat să identifice pacienții cu risc de tulburări respiratorii în timpul somnului ?

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Abstract

Application of a negative pressure has been utilized in experimental settings to demonstrate abnormal upper airways compliance. We hypothesized that a simple forced inspiratory maneuver could be used as a screening test for this abnormality in an epidemiological setting.
277 men and women, aged 30 years or more, who attended a Preventive Medicine Centre, volunteered for completing a sleep questionnaire, having standard anthropometric measurements, a non-invasive upper airways examination, and for performing an oronasal peak inspiratory maneuver.
The peak inspiratory flow (PIF) of 127 females was significantly less compared to that of the 137 males (211±47 vs. 269±59 l.min-1). PIF was significantly inversely related to age in both sexes; a positive correlation with height was found in males only. Males with enlarged soft palates had a significantly lower PIF (256±54 vs. 277±62 l.min-1 ; p=0.04). No difference in PIF was found in subjects who stated that they experienced breathing pauses during sleep. Habitual snoring males had a significantly lower PIF as compared to the non-snorers (251±59 vs. 282 ±57 l.min-1; p=0.003); after adjustment for age, this difference was borderline significant (p=0.06).
A forced inspiratory flow maneuver yielded a PIF which was different between genders, was age-dependent in both sexes, and related to height in males. PIF did not identify male subjects with breathing pauses during sleep, but was associated with a larger soft palate and was borderline decreased in habitual snoring males. The present results suggest that, with further validation, the PIF test could represent a simple means to indirectly explore upper airways compliance.
Keywords: *sleep apnea, snoring, peak inspiratory flow, sceening test*

Rezumat

Aplicarea unei presiuni negative a fost folosită experimental pentru a demonstra complianța anormală a căilor aeriene superioare. În acest studiu am plecat de la ipoteza că o manevră simplă de inspir forțat ar putea fi utilizată ca test de depistare a acestei anomalii în condiții epidemiologice.
277 subiecți de ambe sexe, de cel puțin 30 de ani, participând la un examen de medicină preventivă au acceptat completarea unui chestionar de somn, măsurători antropometrice, efectuarea unui examen simplu al căilor aeriene superioare și efectuarea unei manevre de inspirație oronazală forțată.
Debitul inspirator de vârf (PIF) a fost diferit între cele două sexe (127 de femei : 211±47, bărbați 269±59 l/min) și a scăzut cu înaintarea în vârstă. O relație pozitivă cu talia a fost prezentă numai la bărbați. Bărbații cu un văl palatin mărit au avut PIF semnificativ redus (256±54 vs. 277±62 l.min-1 ; p=0.04). În grupul de subiecți declarând apnei de somn nu s-au găsit reduceri ale PIF. Bărbații declarând sforăit frecvent au prezentat o scădere a PIF (251±59 vs. 282±57 l.min-1; p=0.003); după luarea în considerare a vârstei, această diferența a devenit semnificativa doar la limită (p=0.06).
O manevră de inspirație forțată a arătat diferențe între sexe, o relație inversă cu vârsta și o relație pozitivă cu talia la bărbați. PIF nu a identificat subiecții cu pauze respiratorii în timpul somnului, dar a fost semnificativ redus la bărbații cu văl palatin mărit și redusă la limita semnificației la bărbații cu sforăit frecvent.
Rezultatele de față sugerează ca, după validare pe un grup mai numeros, PIF ar putea reprezenta un mijloc simplu de detectare a unor anomalii ale căilor respiratorii superioare.
Cuvinte-cheie: *apnee în somn, sforăit, debit inspirator de vârf, test screening*

Introduction

Because of their frequency and their severe consequences, sleep apneas are considered a major public health problem. In an active US population, Young et al. found 24% apnea-hypopnea (defined as more than 5 events per hour of sleep) in men and 9% in women[1]. These authors estimated that a large majority (over 80%) of subjects with moderate to severe sleep apnea had not been clinically diagnosed[2]. The reference procedure for the diagnosis of obstructive sleep apneas (OAS) is polysomnography (PSG). Performed in sleep laboratories, this is a time-consuming and expensive procedure, inducing long waiting lists, stress for the putative patient, and important expenses for the insurance companies. Screening for ignored cases, or prioritizing the patients addressed by the attending physician for evaluation at the sleep laboratory, is therefore desirable.

Methods

Study participants.

Subjects were community dwellers attending a Regional Preventive Medicine Centre serving about 2 million people in North-Eastern France for a medical check-up. Subjects 30 years and older were informed by the research team of the purpose and nature of the study, the noninvasive character of the measurements, and confidential treatment of the data, in order to obtain informed consent. 308 subjects of both sexes were approached in consecutive order of the Centre electronic files; 282 of them accepted to participate (participation rate : 91.5%). On the basis of clinical data (pregnancy, history of significant respiratory disease) or incomplete questionnaire, 5 of them were excluded.

Data collection.

Sleep questionnaire. A French version of the Wisconsin University Sleep Questionnaire (1992)[1] was self-completed by the participants with aid from their spouse, when relevant. Most questions on frequency of symptoms offered answers on a 5-point scale, from "never-or rarely" to "every night", plus a "don't know" answer. In the present study, we were interested in the respiratory symptoms influenced by sleep, essentially snoring and sleep apneas. Subjects reporting snoring at least 3 nights per week were considered habitual snorers[1,3]. For the three questions on sleep-related breathing pauses (question no. 8: "According to what others have told you, how often do you gasp, choke, or make snorting sounds during sleep?"; question no. 9: "How often do you wake up suddenly with the feeling of gasping or choking?", and question no. 10 "According to what others have told you, how often do you seem to have momentary periods during sleep when you stop breathing or you breathe abnormally?") the positive answers were "at least once a week" or "very often". The reliability and reproducibility of the responses to the French version of the questionnaire have been previously tested by our team and found satisfactory. For example, the Cronbach alpha statistic was 0.67 for the questions on snoring and 0.81 for the questions on sleep apnea[4].

Anthropometry. Age was recorded from the computer files, and height and weight were measured by the usual methods. The body mass index (BMI) was calculated as $kg.m^{-2}$. Neck, waist, and hip-girth were measured; the waist-to-hip ratio (W/H) was computed as an index of central obesity.

Nose-throat examination. Any invasive methods being excluded in this epidemiological study, we limited the instrumental examination of the upper airways to a tongue blade for evaluation of the nose permeability and aspect of the soft palate, uvula, palatine tonsils and tongue following the proposals of Wilms et al.[5]. All subjects were examined by the same physician.

Peak inspiratory flow rate (PIF). A forced inspiratory maneuver was used to measure oronasal peak inspiratory flow with a Youlten-type peak inspiratory flow meter ("In-check", Clement Clarke International, Respiratory Division, Harlow, UK) fitted with an oronasal mask. Each subject was given a careful explanation and demonstration of the maneuver, followed by one or more "blank" trials to check for accurate performance. Then, at least three, and up to six attempts were performed, with the aim of obtaining at least two results corresponding to maximum efforts; all measurements were done by one investigator, blinded to the rest of the data. The mean of two or three attempts was recorded in $l.min^{-1}$ ATPS; subjects with only one satisfactory result were excluded from the analysis.

Statistical analysis.

The differences between mean values of continuous variables were assessed by analysis of variance (ANOVA) and the Student t test if similar variances, or a non-parametric (Kruskall-Wallis) test if the variances differed significantly. Correlations between PIF and anthropometric variables were assessed by Pearson or Spearman tests; adjustment for differences in age were done by linear regression. The statistical analyses used the Stata version 5.0 software[6].

Results

Of the 277 subjects attempting the PIF test, thirteen (4.6%) failed to produce an acceptable result. Among the 264 subjects with valid results, we found a highly significant difference by *gender*, the PIF of males (n=137) being largely superior to that of females (n=127) (268.9±59.5 vs. 210.7±43.6 $l.min^{-1}$, p=0.00001, Kruskall-Wallis test). All the subsequent analyses were therefore done separately by sex. *Current smoking* had no notable influence on PIF. We found significant negative correlations between PIF and *age* in both males (r=-0.27 p=0.002) and females (r=-0.23, p=0.009); PIF was positively related to *height* in males only (r=0.23, p=0.009). No significant correlations with *weight, BMI, neck-waist- and hip circumferences*, and the *W/H ratio* were found in either sex. We looked at a possible influence of *nose-throat abnormalities* on PIF; no influence was found for females, while males with a *large soft palate* had a significantly lower PIF (256±54 vs. 277 ±62 $l.min^{1}$ p=0.04). Males declaring *breathing pauses during sleep* (n=26) had a PIF similar (264±65 vs. 270±58 $l.min^{-1}$; p=0.64) to subjects giving a negative response; similarly, no difference was found in females. *Habitual snoring* males (n=60) had a significantly lower PIF as compared to their non-snoring (n=74) counterparts (251±59 vs. 282±57 $l.min^{1}$; p=0.003); no difference was found in females. As snorers differed from non-snorers in age among males (46.7 vs. 41.7 years), and as PIF was related to age, an adjustment was done for this covariate. After adjustment, the PIF of snorers was borderline lower (263±60 vs. 282±57 $l.min^{-1}$; p=0.06) as compared to that of non-snorers.

Discussion.

In this population-based study we investigated the possible relation between a decrease in peak inspiratory flow and sleep-disordered breathing. The mean PIF was significantly decreased in males with a larger soft palate, and borderline lower (when age-adjusted) in habitual male snorers, but no difference emerged between subjects declaring and denying breathing pauses during sleep. Nasal peak flows, either expiratory or inspiratory, were extensively used to assess nasal patency[7,8]. A series of factors, such as subject position, vascular tone, time of day, hormonal cycle, etc. were found to influence nasal PIF. These factors modulate the flow by changing the resistance, while driving pressure is generated at "a rate by which the inspiratory muscles convert chemical energy into mechanical energy" as stated by Agostoni and Fenn[9].

Nasal and oral PIF may be measured separately and compared in patients, yielding a "nasal patency index". In a pilot trial, preceding this study we noticed that "blind", healthy subjects found the nasal PIF maneuver uncomfortable and difficult to perform correctly, and consequently opted for, and preferred, the oronasal mask. For the same reason, we favoured the start of the maneuver from functional residual capacity[10] rather than the residual volume level. At the time of the present study, the number of attempts was not standardized in the literature, varying between 2 and 5[11]; to obtain at least two valid results, in some of our subjects we were obliged to record up to 6 attempts.

Recently, Lofaso et al. described a learning effect increasing the sniff nasal inspiratory pressure beyond the tenth attempt in a laboratory setting[12]; this seems to be hardly acceptable in a field survey of volunteers, with implicit acceptability limitations and tight time constraints. No consensus existed in previous research in respect to the final result either: largest value or mean; we analyzed both. To the best of our knowledge, the only report of the nasal PIF use in epidemiological setting is that of Annesi et al.[13]. These authors recorded nasal PIF and FEV1 in a sample of middle-aged men and found the nasal PIF to be normally distributed, with a mean of 155± 54 $l.min^{-1}$, and no correlation with age, height, or weight. The inverse correlation of oronasal PIF with age in our subjects of both sexes is in agreement with the results on oral PIF of Nairn and McNeill[14].

Upper airway obstruction has been explained by a series of factors, the detailed discussion of which is beyond the scope of the present paper. One factor is an *anatomically small pharynx*. In a large series of healthy subjects Brown et al.[15] found larger pharyngeal cross-sectional areas in *males as compared to females* and a negative correlation with *age* in the former. Haponik et al.[16] reported a smaller pharynx in awake upright OSA patients. Rivlin et al.[17] found a significant correlation between the cross-sectional area of the pharynx and the number of apneas in OSA; these results were extended to "simple" snorers by Bradley et al.[18]. In their study, Rodenstein et al. found a similar degree of pharynx area reduction in snorers and OSA patients[19].

Upper airway permeability is also influenced by *posture* and *wake state*. *Airway compliance* is an important determinant of upper airway configuration, along with surface adhesive forces, tissue elasticity, and pharyngeal muscular forces. A simple means to assess pharynx compliance was the measurement of cross sectional area using the acoustic reflection technique either during a slow expiration[14] or during gradual inspiratory or expiratory maneuvers against an occluded airway[20]. In the latter study, an *increased compliance in snorers*, with *or without OSA*, as compared to normal subjects was reported. In animal or human laboratory experiments, more sophisticated methods of pharynx compliance assessment have been utilized. Applying *negative* (-40 cm H_2O) *pressures* to the nose of normal sleeping subjects, Schwartz at al. obtained flow limitation and noticed the appearance of audible snoring[21]. Van Meerhage et al.[22] reported a correlation between the expiratory flow limitation induced by the negative expiratory pressure and the apnea-hypopnea index.

The third mechanism of upper airway closure is a *less efficient or untimely contraction of pharyngeal dilator muscles*[23]. Even if not too invasive, application of negative pressure to the upper airway through the mouth or the nose is tedious, time-consuming, and necessitates a perfect co-operation of the subject, thus appears unsuited in field surveys. In the present epidemiological setting, we evaluated the usefulness of a simple respiratory maneuver - the peak inspiratory flow test -, as an easy means to explore upper airway collapsibility. For acceptability and feasibility reasons, after having noticed some difficulty in performing the nasal inspiration, we opted for the oronasal peak inspiratory flow, which was easily performed by more than 95% of the participants . Care was paid to avoid neck flexion or glottis contraction during the performance, as these represent methodological bias. It must be stressed that we found no indications on the performance or normal values of the oronasal PIF in the literature.

The oronasal PIF was significantly (22%) less in females as compared to males; this may be explained by both a larger pharyngeal cross-sectional area[15] and a higher muscular force[9] in the latter. The results were negatively related to age in both sexes and positively related to height in males. The comparison with the results of the nasal PIF reported by Annesi et al.[12] suggest that the higher flows recorded by us were predominantly oral flows. Except age and height, we found no correlation with anthropometric data. In males only, a *large soft palate* was associated with a significantly lower PIF (p=0.04) confirming the role of the former in controlling the inspiratory flow[24].

The aim of the present study was to ascertain if a decrease in PIF (maneuver generating an abrupt drop of upper airways pressure) is associated with symptoms suggesting sleep-disordered breathing. The PIF of males declaring *breathing pauses* were not significantly decreased. Several facts, along with the limited number of subjects[26] may explain this negative result: a) the symptom was self-declared, (no polysomnograms were recorded); b) our subjects were awake and standing, while in most previous studies an increase in pharynx compliance was found in supine patients or during sleep[20,21]; c) morphological differences in pharyngeal cross-sectional shapes have been described by Rodenstein et al.[19] between "simple snorers" and OSA patients; d) interestingly, higher suction pressures were found in snorers, as compared to OSA patients[25]. In agreement with the rhinometry data of Young et al.[26] we found the oronasal PIF in *habitual snoring males* to be decreased (p=0.003) as compared to that of non-snorers; no difference was found in females. As PIF was related to age, and snorers were 5 years older, an adjustment had to be applied; after adjustment, snorers' PIF was borderline decreased.

No preliminary evaluation of the sample size was possible for our study, as no previous PIF data were available at the start. Based on the results obtained in this study, an *a posteriori* computation indicated that at least 53 subjects were necessary to validate the observed difference between snorers and non-snorers with an alpha error of 0.05 and a power of 0.80.

Our study had weak points which should be acknowledged. First, breathing pauses during sleep and snoring were "self-declared", as no polysomnograms or sound recordings could be obtained. Second, no elaborate ENT examination or cephalograms to evaluate the upper airways anatomy were included in the protocol, for ethical reasons. Third, the PIF maneuver was designed to produce a brief negative airway pressure, but this pressure was not measured. The study strengths were the first evaluation of a simple respiratory test, supposed to influence upper airways caliber, in a community sample of "study blind" men and women with a high participation rate, using a validated structured sleep questionnaire, with 95% success rate.

Conclusion

Because of these somewhat ambiguous results, obtained in a middle-aged population, we believe the present preliminary study deserves duplication in a larger population sample including older ages, with a more elaborate protocol including measurements of peak inspiratory pressure and objective recordings of snoring sounds and sleep apneas, in order to definitely assess the value of a simple peak inspiratory effort as a screening test. With such confirmation of its validity, inclusion of the PIF test in one of the future clinical prediction rules for sleep-disordered breathing[27] could be considered.

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