



Nasal peak expiratory flow and nasal congestion in women: how many subjects are enough?

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Background: Nasal peak expiratory flow is an inexpensive, simple, widely used method to measure changes in nasal congestion. **Objective:** This study was performed in order to define the normal variation in nasal peak expiratory flow and to evaluate and quantify the relationship between subjective scores of nasal obstruction and nasal peak expiratory flow in women. **Materials & methods:** We followed 41 healthy, nonmedicating, normally menstruating women for 3 to 6 months. They registered nasal peak expiratory flow and subjective nasal congestion (scored 0–4) every morning and evening. **Results:** We found that if the aim of a study is to detect a difference in nasal peak expiratory flow corresponding to 1 subjective score step out of 4, different values have to be used for the power calculations, depending on what congestion scores are expected in the study population. If a low score level is expected, more subjects are required.

Conclusion: Our data make adequate power calculations possible for studies in female populations with different degrees of nasal congestion.

Background

Nasal congestion can be objectively quantified by various well established methods that measure the effects of nasal mucosal swelling in different ways, such as airflow, airflow resistance, cross-sectional area and volume, as well as the movement of the mucosa itself. Subjective evaluation of nasal congestion can be presented as subjective scores, for example, 4 to 5 levels, or a continuous visual analog scale.

Nasal (n) peak expiratory flow (PEF), using a PEF meter and an anesthetic mask, is an inexpensive method, which is easy for the subject to handle in most settings, making repeated measurements possible for prolonged periods of time. It is also a practical tool for the non-rhinologist, especially in asthma studies, when the PEF meter is already in use. As the concept of the united airways gained acceptance [1], nasal measurements in asthma studies became desired. In 1973, Taylor and colleagues published the first description of nPEF, performed with a mouth–nose mask [2]; however, since then it has been used mostly with a nose mask in at least 60 studies. We are yet to find relevant data on normal variations related to subjective values of nasal congestion.

As men and women differ in many ways, it is important to study each sex separately; for example, regarding reactions to different medications or exposure to other agents. To be able to do so, normal variations in each sex need to be established.

The aim of this study was to evaluate and quantify the relationship between subjective scores of nasal obstruction and objectively registered nPEF and to define the normal variation in nPEF, in women.

Materials & methods

This evaluation was carried out on data from our earlier study on nasal congestion during the menstrual cycle [3]. We enrolled 41 healthy, nonsmoking, nonmedicating women aged 15 to 45 years (mean age: 33 years) with a history of normal menstruation and without a history of allergy to airborne allergens. A total of 27 women were studied for 3 months and 14 women for 6 months. In their diaries, the women noted subjective levels of nasal obstruction (0 = none, 1 = slight, 2 = moderate, 3 = severe and 4 = total obstruction) every morning and evening. They also measured nPEF, standing up, three times on each occasion, using a mini-Wright peak-flow meter connected to an anesthetic mask covering the nose. Each woman was carefully instructed on how to use the equipment. All nPEF values were expressed in l/min and were rounded off to the nearest 10 l/min. For every occasion, the maximum value of the three registrations was used in later statistical analysis. Daily notes concerning respiratory tract infection, such as general malaise, nasal discharge, sore throat and raised temperature, were also registered.

For each subjective score, the mean values of nPEF were calculated for every woman, based on all registered days. For the calculations of total

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mean nPEF, as well as inter- and intra-individual variation of nPEF, the mean morning values of the day preceding menstruation for each woman were used in order to avoid the influence of variation due to the time of day and the menstrual cycle. Days with other signs of respiratory tract infections were then excluded.

All participants gave their informed consent. The study was approved by the Ethics Committee of Sahlgrenska University Hospital, Göteborg.

Results

Each woman contributed with 89 to 336 occasions (mean: 215). When mean morning values of the day preceding menstruation were used, each woman contributed with two to seven occasions (mean: 3.6). The mean value of nPEF was 277 l/min, with a standard deviation (SD) of 49 l/min. The intraindividual variation, expressed as SD, was 22 l/min. The mean nPEF values were related to the subjective congestion scores as shown in Figure 1. The differences in mean nPEF for every subjective score step (Δ nPEF) are shown in Figure 2.

Conclusion

In this methodologic evaluation, we found the mean value of nPEF in 41 women to be 277 l/min, with a SD of 49 l/min. The intraindividual variation was 22 l/min.

In another nPEF study of seven men and three women measured on 12 occasions, we found a mean value of 249 l/min with an interindividual variation of 95 l/min. The intraindividual variation was 19 l/min [4], which is comparable with the 22 l/min found in this study. Paulsson and

colleagues found a mean nPEF of 222 l/min (SD: 61 l/min) in their 2-month study of morning and evening registrations in 26 women, based on all occasions [5].

Figures from the present study provided the opportunity to perform power calculations – calculations for the power of the significance levels of different designs and clinical characteristics in the form of expected subjective scores. For example, with the estimated power of 90% (i.e., a 90% probability to detect a true difference) and a p-value of 0.05 (i.e., a 95% probability that the findings are not by chance), the required number of subjects in each group is given by either of the following formulae [6]:

$$Parallel = 2 \times \frac{10.5 \times (SD_{inter})^2}{D^2} + 2$$

$$Crossover = \frac{10.5 \times (SD_{intra})^2}{D^2} + 2$$

Where D = the interesting nPEF difference. In the case of two parallel groups, the interindividual SD is to be used, and in crossover studies, the intraindividual SD is used. The factor 10.5 gives an estimated power of 90% and a p-value of 0.05.

If the aim is to detect a difference in nPEF corresponding to 1 subjective score step out of 4 (the Δ nPEF, see Figure 2), different values have to be used for the power calculations, depending on what congestion scores are expected in the study population. If, for example, subjects have moderate nasal congestion (score 2), a parallel design would require 62 subjects in each group to detect an improvement of 1 subjective score step. Using the Δ nPEF of 29 l/min shown in Figure 2 and the interindividual SD of 49 l/min, that is;

$$2 \times \frac{10.5 \times 49^2}{29^2} + 2 = 62$$

With a crossover design only eight subjects would be needed, as the intraindividual SD is only 22 l/min, that is;

$$\frac{10.5 \times 22^2}{29^2} + 2 = 8$$

As shown in Figure 2, the Δ nPEF is smaller with lower subjective scores, which means that more subjects are required in studies on a population with less subjective congestion than on a population with more congestion.

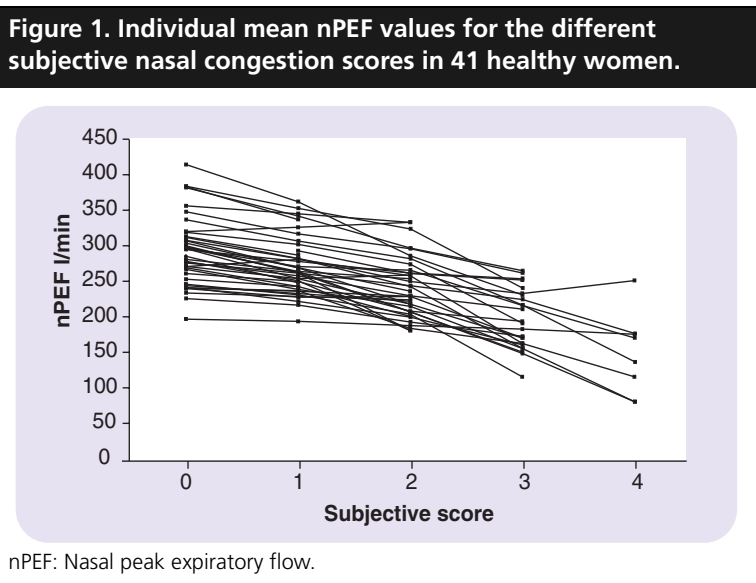
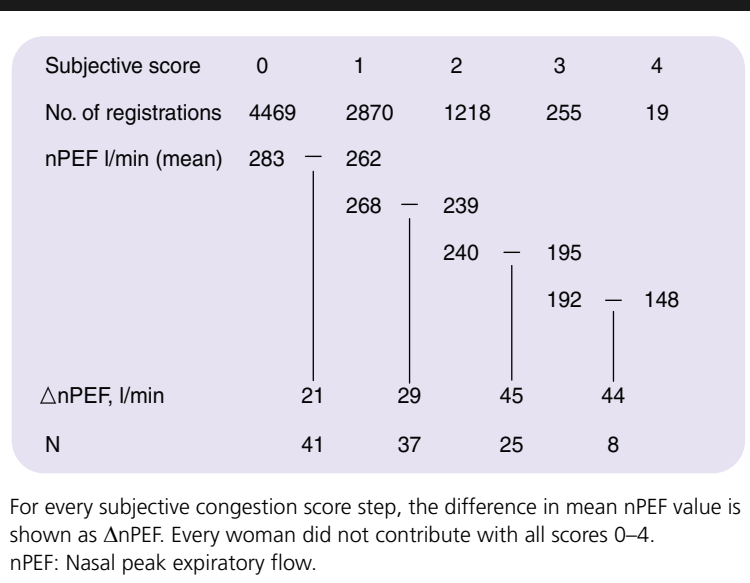


Figure 2. Subjective and objective measures of nasal congestion.



This variation in Δ nPEF reminds us that subjective scores are categorical data and that the steps cannot be considered equal in any objective sense. This is one reason for avoiding visual analog scales and the temptation to use their values as continuous data in calculations.

As there is a well-known influence of height on PEF, it also affects nPEF. However, as height is constant in adults, it does not influence intraindividual comparison, which is shown by the considerable difference between the inter- and intraindividual SDs in the present study. The use of the ‘Blockage Index’ [2] is one way to avoid this influence; however, it was not used in this study.

$$Blockage = \frac{PEF - nPEF}{PEF}$$

When using this index, the registrations of nPEF should precede those of PEF, in order to minimize the influence of the strain upon the nasal mucosa.

We have earlier reported the intraindividual variation (CV) in triplicate nPEF to be only 6.4% in this female population [3]. When we examined the registrations of the first 14 days, we could find no indication of a need for a run-in period. The use of a nose mask is preferred, as there is a risk of leakage through the mouth in a mask also covering the mouth, and it is natural to register the maximum of the three blows, as in PEF. It is not a good idea to make more than three nPEFs in a

row as the nasal mucosa is influenced by the strain. The reasons for the diurnal variation are physiologic, as the nose is more congested in the morning. There are other reasons for variation over time, such as the menstrual cycle. This has nothing to do with the method in itself, and it has to be kept in mind whatever method is used when measuring nasal congestion.

It is important to study nasal reactions with objective methods, as we know that the subjective sensation of nasal congestion varies greatly between subjects and can be influenced by factors which do not have anything to do with mucosal swelling. The feeling of congestion may be distorted by prolonged use of local decongestants, as the decongested status is then considered by the patient to be ‘normal’ [7]. The administration of menthol may induce a false sensation of decongestion, supposedly by an influence on the cold receptors [8].

However, different methods measure different variables. For example, the rhinostereometer registers the swelling of the mucosa of a very small area, whereas the cross-sectional areas and even more, volumes of acoustic rhinometry, contain information from much larger parts of the nose. This may explain why there was only a weak correlation between registrations with these sensitive methods in a histamine provocation study of 30 patients with vasomotor rhinitis [9]. In a similar study of 13 healthy subjects, a significant correlation ($R = 0.63$) between mucosal swelling and subjective scores was found only after a high dose of histamine, when the turbinate was close to the septum [10]. Thus the subjects did not detect the mucosal changes until the nose was almost totally obstructed. The individual variation in correlation was considerable ($R = 0.05\text{--}0.85$) [11]. Nasal inspiratory and PEF methods were more sensitive than acoustic rhinometry and anterior rhinomanometry for detecting the reactions to 0.1 mg/ml of histamine in a study of seven women and 34 men [12]. Rhinomanometry is, however, considered to be more accurate for detecting changes after allergen provocations [13].

Therefore, the results of the studies of objective measurements need to be seen not only in terms of statistical significance, but also in terms of clinical significance – which is what the patients are able to feel. Thus the relationship between objective and subjective measurements is important, and should be included in the power calculations as suggested above.

Clinical studies often include men only. In a study carried out by the Ethics Committee, one motivation given by the applicants was ‘the lack of knowledge of women’s physiology’ [14]. The present study is a step towards improving such knowledge. It should be followed by a corresponding study in men, as normal values should to be established for each gender separately.

Highlights

- There are currently several subjective and objective methods of measuring nasal congestion in practice.
- Nasal peak expiratory flow (nPEF) is an inexpensive objective method, easy for the subject to handle in various settings, making repeated measurements possible for prolonged periods of time. However, no normal data on women have been available.
- We studied 41 healthy women, who registered subjective nasal congestion scores of 0–4 and nPEF morning and evening for 3 to 6 months.
- The difference in mean nPEF between the subjective score steps was 21, 29, 45 and 44 l/min, respectively.
- Normal data for women were established, which make adequate power calculations possible for studies in female populations with different expected levels of nasal congestion.

nPEF is an inexpensive, simple method of measuring nasal congestion, and is suited for repeated measurements at home or at work. The figures for normal women reported in this study make adequate power calculations possible for further studies.

Outlook

The normal values of nasal congestion need to be established for women separately, in order to evaluate how they react to medications and to other agents. Even though nPEF has been widely used, normal values and the relation to subjective scores were not precisely known. Other methods of evaluating nasal congestion also need to be studied in the same manner.

Hopefully, our figures will stimulate and help others to plan further studies of women’s noses. It is possible that in the near future we will know more concerning how women react to the overuse of nasal decongestants, and how effective nasal steroids are in the treatment of different diseases.

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