Side-selective, unobtrusive monitoring of nasal airflow and conductance

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Kohler, Malcolm, Robert Thurnheer, and Konrad E. Bloch. Side-selective, unobtrusive monitoring of nasal airflow and conductance. J Appl Physiol 101: 1760–1765, 2006.—Whether nasal obstruction disturbs sleep and nocturnal breathing is controversial because convenient techniques for measuring nasal resistance during sleep are lacking. Therefore, we developed a technique for unobtrusive, side-selective nasal conductance monitoring. The technique measures left and right nasal airflow and transnasal pressure using nasal cannulas, thin catheters inserted through the cannulas into the nasopharynx, and three pressure transducers. Their processed signals provide conductance as airflow-to-resistive pressure ratio for the left and right side and the sum, total nasal conductance. For validation, total nasal conductance was also determined by a flowmeter attached to a nasal mask and nasopharyngeal pressure that served as reference standard. Methods were compared in five normal subjects during pharmacological interventions and in 12 snorers during sleep. The novel technique accurately tracked total nasal conductance by the reference method at baseline, after nasal application of histamine and xylometazoline in normal subjects; mean difference (bias) was 1%, and limits of agreement (±2 SD of bias) were ±22% (75 comparisons). Corresponding values during overnight sleep studies in snorers were 0 ± 19% (192 comparisons); bias and limits of agreement of changes in nasal conductance were 1 ± 19% (180 comparisons). Conductance measured once at the beginning of sleep studies differed from subsequent measurements during the night by a mean ± SD of 26 ± 20%, P < 0.0001. The novel technique accurately measures side-selective conductance. It is suitable to investigate interactions among nasal obstruction, sleep and nocturnal breathing, and drug effects. One-time measurements at the beginning of sleep studies do not appropriately reflect the highly variable nasal conductance during an entire night.

flowmeter; physiological monitoring; nasal resistance; nasal cannula; sleep apnea; rhinitis

IMPAIRED NASAL BREATHING is uncomfortable, may disturb sleep, and predisposes to snoring and possibly to sleep-disordered breathing (12, 15, 16). Nasal obstruction may also interfere with successful continuous positive airway pressure therapy in patients with obstructive sleep apnea syndrome (9). The effect of treatment of rhinitis and of other causes of impaired nasal ventilation has been assessed by evaluating symptoms such as a blocked and runny nose (5) and corroborated by objective measures of nasal resistance by anterior or posterior rhinomanometry (2, 4) or by measuring the internal nasal dimensions by acoustic reflection (7). Due to the high variability of nasal resistance over time (3), one-time assessments in the evening or morning may not reflect the physiological conditions during an entire night’s sleep, but continuous conventional rhinomanometry for several hours during sleep is impractical and inconvenient because a nasal mask and other instrumentation have to be applied. Because investigation of the interaction of nasal resistance with sleep and nocturnal breathing disturbances is desirable, we developed a method for unobtrusive, continuous side-selective monitoring of nasal airflow and conductance suitable for application during sleep. The method combines side-selective monitoring of nasal airflow by nasal cannula connected to pressure transducers (8) and nasopharyngeal pressure monitoring using a special arrangement of small-bore catheters. The technique does not require application of a nasal mask and it measures left- and right-sided nasal conductance and airflow simultaneously and continuously during tidal breathing. The purpose of the study was to evaluate accuracy of the novel technique by comparison to standard measurements of nasal resistance by facemask pneumotachography and nasopharyngeal pressure recordings and in terms of tracking changes in nasal resistance induced by changes in body position, application of drugs that alter nasal resistance, and by observing spontaneous changes in nasal resistance during overnight sleep studies in patients with suspected sleep-disordered breathing.

METHODS

Volunteers and patients. Five healthy volunteers (age 30–41 yr, 1 woman) participated in the first part of the study. In the second part of the study, 12 habitual snorers (age 22–61 years, 3 women), four of them (1 woman) with obstructive sleep apnea syndrome (mean ± SD apnea hypopnea index 44 ± 15 events/h) were included. All participants gave informed consent and the protocol was approved by the hospital ethics committee.

Novel technique for monitoring nasal conductance. Nasal conductance (GN), the reciprocal value of nasal resistance, is derived from nasal airflow and nasopharyngeal pressure. Side-selective nasal airflow is measured using a cannula such as those used for oxygen therapy (Salter Labs, Irvine, CA) modified by blocking the connecting part between the two sides with a metal plug (Fig. 1; Ref. 8). Each side of the tubing is connected to a pressure transducer (Validyne; Northridge, CA). Airflow through the two nares, respectively, is derived from pressure swings recorded by the two transducers after linearization of the pressure-airflow relationship. This is achieved by a calibration procedure involving airflow recording by a flowmeter attached to a nasal mask during sequential unilateral nasal occlusion with tape over a few breaths (see APPENDIX; Ref. 8). Subsequently, the mask is removed and nasal pressure swings provide quantitative estimates of bilateral airflow without further need of a flowmeter or mask.

To measure nasopharyngeal pressure, the nasal cannulas are further modified by coaxially inserting small-bore, highly flexible catheters (outer diameter 1.3 mm, lateral holes at the distal end, sealed tip, Arrow International, Reading, PA) into each side of the nasal cannula tubing (Fig. 1). These two catheters provide symmetrical instrumen-
measurement of total nasal airflow, i.e., the sum of left plus right nasal airflow.

Protocol. In healthy volunteers, nasal conductance was monitored (by the novel technique) along with the signal of the flowmeter attached to a nasal mask during 5–10 min in each of the following conditions: 1) sitting, 2) supine position, 3) lateral position, 4) after application of one puff of histamine (0.5 ml, 32 mg/ml) into both nares, 5) after one puff of xylomethazoline (0.5 ml, 1 mg/ml) into both nares. Respiratory signals were digitally sampled at 50 Hz.

In patients, nasal conductance was monitored (by the novel technique) along with the signal of the flowmeter attached to a nasal mask while they slept in supine position over the course of a nocturnal polypgraphic sleep study lasting for ≥6 h. At the end of the study, patients rated their discomfort by the nasal mask and the catheters, respectively, on a three-level scale ranging from “not relevant,” “minor,” to “moderate to major.”

Data analysis. The relationship of left and right nasal cannula pressure vs. the corresponding airflow was obtained as previously described during initial calibration (Appendix: Ref. 8). Instantaneous total nasal conductance (GNL + NR) measured at 50 Hz by nasal cannula-pressure transducers was computed as: GNL + NR = (V’NL + V’NR)/ΔPN, where (V’NL + V’NR) is the sum of the instantaneous flow through the left plus right nose, and ΔPN (transnasal pressure) is the difference nasopharyngeal minus nasal mask pressure.

The reference for instantaneous total nasal conductance based on airflow measurement by the flowmeter (GFM) was computed as follows: GFM = V’/ΔPN.

Instantaneous GNL + NR and GFM, respectively, were averaged during three successive inspirations and expirations in normal subjects for each of the five experimental conditions (1 through 5) and at hourly intervals in patients during overnight sleep studies. Values of GNL + NR and GFM were expressed as milliliters per second per pascal (1 ml·s⁻¹·Pa⁻¹ = 1 ml·s⁻¹·0.01 cmH₂O⁻¹ = 0.11·s⁻¹·cmH₂O⁻¹).

The accuracy of GNL + NR was evaluated compared with corresponding GFM by calculating the mean difference (bias) and limits of agreement (±2 SD; Ref. 1) and by Pearson’s correlation coefficients. Paired measurements were evaluated by t-tests and analysis of variance with P < 0.05 considered as significant.

The individual variability of GNL + NR over the course of a night was assessed by calculating the mean absolute difference irrespective of the algebraic sign (i.e., the mean disagreement) of GNL + NR measured at the beginning of a sleep study with subsequent measurements over the course of the night.

RESULTS

Nasal conductance in five normal volunteers. The nasal cannula and nasopharyngeal catheters were well tolerated by all volunteers, and there was no need for topical anesthesia of the nasal mucosa. Mean values of total nasal conductance (GNL + NR) closely tracked corresponding estimates of GFM during all interventions (Fig. 2). GNL + NR in seated position was higher (mean ± SE 13.9 ± 1.5 ml·s⁻¹·Pa⁻¹) than in supine position (10.7 ± 0.7 ml·s⁻¹·Pa⁻¹), remained unchanged in lateral position (10.5 ± 1.0 ml·s⁻¹·Pa⁻¹), decreased more after application of histamine in supine position (6.7 ± 0.5 ml·s⁻¹·Pa⁻¹), and finally increased significantly (to 17.1 ± 1.8 ml·s⁻¹·Pa⁻¹) after application of xylomethazoline. All means of GNL + NR were statistically significantly different from each other (P < 0.05), with the exception of values in supine and lateral position, which were similar (Fig. 2). Interestingly, when subjects turned to the lateral position, an imbalance between the conductance of the two sides developed in favor of the nondependent side of the nose (mean GN of the

Fig. 1. Catheter system for side-selective measurement of nasal airflow and conductance. A: nasal cannulas as used for oxygen therapy have been cut apart and reconnected with a metal plug that prevents pressure transmission between sides. Each side of the cannula tubing is connected to a separate pressure transducer. Small-bore, flexible catheters are coaxially inserted laterally into the nasal cannula tubing and advanced through the cannula so that their tip is positioned in the nasopharynx. These catheters are connected to a single transducer for recording nasopharyngeal pressure. B: catheter system is placed in the nose and secured with a tape on each side.
nondependent side 6.5 ± 0.6 vs. GN of the dependent side 4.1 ± 0.6, n = 15, P < 0.0003).

Individual paired estimates of GNL + NR and GFM were closely correlated (Pearson’s correlation coefficient r = 0.98, P < 0.0001) and the mean difference (bias) was close to zero [+0.1 ml·s⁻¹·Pa⁻¹, n = 75 comparisons, P = not significant (NS)], with limits of agreement (bias ± 2 SD) of ± 2.7 ml·s⁻¹·Pa⁻¹, which corresponds to ± 22%. Individual changes of nasal conductance as a result of the various interventions agreed closely among the two methods with a bias of changes in GNL + NR vs. GFM of 0% (n = 60, P = NS) and limits of agreement of ± 21%, and agreement among methods was not affected by changes in body position.

Nasal conductance in 12 patients during nocturnal sleep studies. Figure 3 illustrates recordings in a patient during a nocturnal sleep study. At the beginning of the night, the airflow through the left side of the nose exceeded that through the right side, indicating a higher conductance of the left side (Fig. 3, A1-A4). Three hours later, a nasal cycle had occurred, i.e., a shift from left-sided to right-sided predominance of airflow. At the same time, total nasal conductance (GNL + NR and GFM) had increased (Fig. 3, B1-B4). In another patient, the summary

Innovative Methodology

Fig. 2. In 5 volunteers, the sum of left and right nasal cannula-derived conductance (Gnr + nl) is similar to corresponding values of the reference method based on flowmeter and nasopharyngeal pressure measurements (GFM) during changes in body position and pharmacological interventions. GNL, left nasal conductance; Gnr, right nasal conductance. Data are means ± SE. P < 0.05 for all changes of Gnr + NL and GFM, respectively. All means of Gnr + NL were significantly different from each other, with exception of values in supine and lateral position. Xylometh, xylomethazoline.

Fig. 3. Raw data tracings obtained in a snorer during a sleep study at 2330 (A1-A4) and at 0230 (B1-B4). A1-A3 and B1-B3 show time series of nasal airflow with positive values reflecting inspiration obtained by nasal cannula on the left and right side (vnr, vnl; A1 and B1), the sum of the two (vnr + nl; A2 and B2), airflow by the flowmeter attached to a nasal mask (vfm; A2 and B2), and transnasal pressure from nasopharyngeal catheters (transnasal; A3 and B3). A4 and B4: side-selective nasal airflows and their sum are plotted vs. transnasal pressure. At 2330 (A1-A4), air was flowing predominantly through the left side (A1) and, accordingly, the left side exceeded the right-side nasal conductance as illustrated by the slopes of the flow/pressure plots in A4. Three hours later, at 0230 (B1-B4), a switch from left- to right-sided predominance of airflow. At the same time, total nasal conductance (GNL + NR and GFM) had increased (Fig. 3, B1-B4).
plot of $G_{NL} + G_{NR}$ and $GFM$ over the course of the night (Fig. 4) illustrates the agreement among the estimates of total nasal conductance by the novel and the reference technique despite varying contributions of the left and right nasal conductance to the total nasal conductance.

Nasal conductance measurements over at least 6 h were obtained in all 12 patients. The majority of patients, i.e., 11, rated the discomfort by the nasal catheters as “not relevant,” and one patient rated the discomfort as “minor.” In contrast, discomfort by the mask was rated as “not relevant” by only one patient, as “mild” by seven patients, and as “moderate to major” by four patients. The mean values of 96 paired estimates of $G_{NL} + G_{NR}$ and $GFM$ during inspiration were $15.3 \pm 10.4$ and $15.4 \pm 10.6 \text{ml} \cdot \text{s}^{-1} \cdot \text{Pa}^{-1}$, respectively ($P = NS$), and these values were lower than corresponding expiratory values of $G_{NL} + G_{NR}$ of $17.5 \pm 16.0 \text{ml} \cdot \text{s}^{-1} \cdot \text{Pa}^{-1}$ and of $GFM$ of $17.7 \pm 16.3 \text{ml} \cdot \text{s}^{-1} \cdot \text{Pa}^{-1}$ ($P < 0.005$ vs. the inspiratory value by the respective technique). Individual values of $G_{NL} + G_{NR}$ and $GFM$ were closely correlated (Pearson $r = 0.99$, $P < 0.0001$), and the bias and limits of agreement of $G_{NL} + G_{NR}$ vs. $GFM$ were $-0.1 \pm 3.3 \text{ml} \cdot \text{s}^{-1} \cdot \text{Pa}^{-1}$ for inspiration ($n = 96$) and $-0.2 \pm 3.4 \text{ml} \cdot \text{s}^{-1} \cdot \text{Pa}^{-1}$ for expiration ($n = 96$). When expressed in percent, bias and limits of agreement were $0 \pm 19\%$ for inspiration and expiration combined ($n = 192$). An identity plot and the corresponding Bland-Altman plot are displayed in Fig. 5.

Comparisons of 180 spontaneous changes of $G_{NL} + G_{NR}$ and $GFM$ during overnight sleep studies revealed a bias of $+1\%$ ($P = NS$) and limits of agreement of $\pm 19\%$.

The median disagreement (the median of absolute differences, irrespective of algebraic signs) between $G_{NL} + G_{NR}$ measured at the beginning of sleep studies and the subsequent measurements over the course of the night was 23\% (quartile range $8.7–36.9$, $n = 96$, $P < 0.0001$), with maximal disagreement of up to 112\%, indicating a high variability of nocturnal nasal conductance.

DISCUSSION

The novel technique described in this report allows for the first time the continuous measurement of simultaneous left and right nasal airflow and conductance over several hours using unobtrusive instrumentation of the nose. The technique proved to be accurate compared with a reference standard based on a flowmeter attached to a nasal mask, and it was appropriately sensitive to detect changes in nasal conductance related to changes in body position and induced by pharmacological interventions. In addition, the technique accurately tracked the spontaneous variation in total nasal conductance during overnight studies and allowed recording of the cyclic alterations in the side predominance of nasal ventilation (6) without the need for unilateral blocking of nasal airflow as required for conventional rhinomanometry. Because the novel technique is well tolerated without topical anesthesia even during sleep, it is suitable for investigating the nasal physiology and the effects of therapeutic interventions.

The novel technique comprises two principal components, the side-selective measurement of nasal airflow and the recording of transnasal pressure that drives nasal airflow. By moni-
toring airflow from cannulas inserted bilaterally into the nares (Fig. 1) and deriving left and right nasal airflow simultaneously from corresponding pressure swings according to a linearization table (8), our measurements did not require application of a nasal mask or alternating unilateral nasal occlusion, which would have interfered with normal physiology (11) and with the subject’s comfort during prolonged monitoring. The current data corroborate our previous study that demonstrated accurate side-selective nasal airflow monitoring by bilateral nasal cannula-pressure transducers compared with a standard flowmeter (8). It extends the validation to monitoring over several hours during nocturnal sleep studies. Nasal cannulas connected to a single pressure transducer are commonly used to monitor apnea/hypopnea during sleep studies but the pressure signal, even if square root transformed, does not provide quantitative estimates of nasal airflow over more than a few breaths (13). We suspect that independent variations of the left and right nasal airflow affect the pressure swings of a single transducer connected to conventional nasal cannulas in an unpredictable way that prevents accurate measurement of total nasal airflow over longer time periods by this method. Our novel technique overcomes these limitations by recording nasal pressure swings bilaterally and using individual calibration tables for linearizing the left and right pressure-airflow relationship instead of square root transformation (13). Our approach is not based on the assumption of a specific mathematical pressure-airflow relationship. Instead, the calibration tables reflect locally smoothed real observations. The calibration is therefore applicable even if the pressure-flow relationship cannot be appropriately modeled with a single mathematical function that describes the entire range of observed values (8).

The second component of the technique for monitoring nasal conductance consists in recording the nasopharyngeal pressure by the small-bore flexible catheters inserted in a special way coaxially through the nasal cannula (Fig. 1). This particular montage assured secure fixation of the catheters by the nasal cannula to prevent displacement during prolonged measurements. Depending on the individual anatomy, the catheters can be advanced as required to appropriately position the distal lumen in the nasopharynx for recording the common transnasal pressure difference relevant for computation of the left and right nasal conductance.

The recorded bilateral flow and transnasal pressure were graphically displayed as time series (Fig. 3, A1-A3 and B1-B3), and as flow vs. pressure plots (Fig. 3, A4 and B4) that are similar to those obtained by anterior or posterior active rhinomanometry. In contrast to guidelines for conventional rhinomanometry (2), however, we have quantified the mean flow-to-pressure ratio (i.e., the conductance) measured multiple times over the inspiratory and expiratory breathing cycles rather than by the inspiratory nasal airflow at a single fixed transnasal pressure of 150 Pa. This was because the standard pressure difference of 150 Pa was rarely reached if at all in our subjects and patients during quiet breathing with both sides of the nose open, which differentiates our technique from conventional rhinomanometry that requires sequential unilateral nasal occlusion. Furthermore, we considered the mean value of conductance computed for the entire breathing cycle to be more meaningful than a single value at a fixed pressure given the nonlinear nasal flow-pressure relationship (Fig. 3, A4 and B4), and the hysteresis that may result in different flows at a given inspiratory transnasal pressure (2). If desired, our technique allows computation of flow or resistance at any given transnasal pressure observed during the breathing cycle.

The higher nasal conductance in seated vs. supine position (Fig. 2) is consistent with previous studies using conventional rhinomanometry and acoustic reflection (14). Together with the changes in nasal conductance observed after application of histamine and xylometazoline, the findings illustrate that our technique is suitable to monitor position-related and pharmacologically induced effects on nasal conductance.

Although a pathophysiological link between impaired nasal breathing and sleep apnea has long been suspected, the studies involving rhinomanometry and polysomnography found only loose or no correlation among one-time measurements of nasal resistance before or after sleep and polysomnographic measures of snoring and sleep-disordered breathing (14, 15). This may relate in part to the fact that nasal resistance varies largely during a night (Figs. 3 and 4; Ref. 10) as demonstrated in the current study by a mean disagreement of 26% between the nasal conductance measured at the beginning and during the subsequent course of a sleep study. Therefore, a single assessment of nasal resistance in the evening before a sleep study does not appropriately reflect the pathophysiology during the entire night.

Because our novel technique unobtrusively records apnea/hypopnea as well as side-selective nasal resistance, it is particularly suited to further investigate the interactions of nasal breathing and sleep apnea, including the assessment of the effects of unilateral obstructions and of the nasal cycle.

In conclusion, the proposed technique accurately tracks simultaneous left and right nasal airflow and conductance during physiological changes occurring with positional changes, during overnight sleep studies, and during pharmacological interventions. Because the technique does not require wearing a nasal mask or sequential unilateral nasal occlusion to assess side-selective conductance and because it can be applied during natural breathing, it is particularly suited for physiological monitoring over prolonged time and during sleep.

APPENDIX

Linearization of Left and Right Nasal Cannula-Derived Pressure-Airflow Relationship

To measure left and right nasal airflow by the nasal cannula-pressure transducer system, the nasal cannula-derived pressure-airflow relationship is determined separately for the left and right side during a calibration procedure over a few breaths as described in detail previously (8). Briefly, calibration is sequentially performed for the left and right nose while the contralateral external meatus nasi is occluded with tape. A nasal mask with a flowmeter attached is strapped over the nose, taking care that the mask is sitting airtight and does not touch and deform the nose. Unilateral nasal cannula-derived pressure and airflow by the flowmeter are then recorded over a few breaths, first for one, and then for the other side. The resulting pairs of side-selective nasal pressure and corresponding airflow values are stored to serve as calibration look-up tables. The calibration is then completed, and the nasal mask and the tape are removed. Left and right nasal airflow can subsequently be monitored without further requirement of a mask or flowmeter by translating the left and right nasal cannula-derived pressure into a side-selective flow according to the stored calibration table for the corresponding side.
GRANTS

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