Sniff Nasal Inspiratory Pressure in Patients with Moderate-to-Severe Chronic Obstructive Pulmonary Disease: Learning Effect and Short-Term Between-Session Repeatability

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Key Words

Chronic obstructive pulmonary disease · Learning effect · Maximal inspiratory pressure · Repeatability · Respiratory muscle strength · Sniff nasal inspiratory pressure · Volitional tests

Abstract

Background: Sniff nasal inspiratory pressure (SNIP) is a non-invasive measure of inspiratory muscle function often used as an outcome measure in clinical studies. An initial period of familiarisation with the test is recommended to minimise the learning effect. The repeatability of SNIP in patients with chronic obstructive pulmonary disease (COPD) is currently unknown. **Objectives:** The aim of this study was to assess the between-session repeatability of SNIP over a 3-week period in moderate-to-severe COPD patients and compare it with that of maximal inspiratory (PI_{max}) and expiratory pressure

(PE_{max}). **Methods:** Twenty-one patients (13 males) with a mean forced expiratory volume in 1 s (FEV_1) of 38% of predicted (SD: 15) and FEV_1 /forced vital capacity of 34.3% (SD: 10.4) performed SNIP and PI_{max} and PE_{max} manoeuvres on 3 different sessions (S1, S2 and S3) 3–7 days apart. SNIP was performed at functional residual capacity (FRC), and PI_{max} was performed at FRC and at residual volume (RV) to explore volume-dependent differences in the learning effect between sessions and PE_{max} from total lung capacity. **Results:** The intra-class correlation coefficient (ICC) for SNIP was the highest of the three measures: S1–S3 ICC (95% CI) SNIP: 0.96 (0.88–0.94); PI_{max} at FRC 0.82 (0.63–0.92); PI_{max} at RV: 0.89 (0.78–0.95), and PE_{max} : 0.96 (0.92–0.98), and had the lowest mean change between sessions [mean S2 – S1: 2.1 (p = 0.4) and S3 – S2: –0.3 (p = 0.9)]. **Conclusions:** SNIP is repeatable over a period of 3 weeks in medically stable, moderate-to-severe COPD patients. In our study, 2 sessions were adequate to learn how to perform the test.

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Introduction

Respiratory muscle function tests are often used in clinical practice to assess respiratory muscle weakness or to monitor changes in respiratory muscle strength over time. The most common tests are maximal inspiratory ($PI_{\max}$) and expiratory pressure ($PE_{\max}$), and sniff nasal inspiratory pressure (SNIP) [1]. These tests are relatively easy to perform and the development of portable devices has allowed their assessment in a variety of clinical settings. SNIP is a more natural manoeuvre than the $PI_{\max}$ or $PE_{\max}$ manoeuvres [2] and is used as an outcome measure in clinical studies, such as in patients with degenerative neuromuscular disease [3, 4] or chronic obstructive pulmonary disease (COPD) [5]. Due to its volitional nature, the SNIP, just like $PI_{\max}$ and $PE_{\max}$, requires a period of familiarisation before baseline measurements are accepted. In COPD, although values for SNIP have been reported [6], there is limited information about the repeatability of the measure.

The repeatability of SNIP has been studied in healthy subjects [4, 7]. In a study by Maillard et al. [7], SNIP values obtained after 1 day were maintained after a period of 1 month, and Terzi et al. [4] showed that SNIP had good reproducibility over 2 sessions a few days apart. The optimal number of sniffs per session has also been established in healthy subjects and a variety of patient groups [8] contributing to the standardisation of baseline assessments prior to clinical studies. However, there are currently no data on the between-session repeatability of SNIP in COPD patients.

The aim of this study was to explore the between-session repeatability of SNIP over a period of 3 weeks in COPD patients and compare it with that of $PI_{\max}$ and $PE_{\max}$. We also wished to establish how many practice sessions COPD patients need prior to entering an interventional study and to obtain information that would allow us to make sample size calculations for a longer repeatability study.

Patients and Methods

Patients

The study was conducted as part of a larger rehabilitation study and participants were the first 21 patients (13 males and 8 females) who were recruited in that study. Patients had moderate-to-severe COPD [forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) <70% and FEV_1 <60% of predicted] and were recruited from outpatient clinics at the King's College Hospital, London, and from South London British Lung Foundation Breathe Easy groups. Data were collected from March 2000 to March 2002 in the

context of a larger rehabilitation study that was ongoing and registered in January 2004 (ISRCTN: 19258620), before the 13th September 2005 deadline set by the International Committee of Medical Journal Editors for clinical trial registration.

The inclusion criteria for the study were: positive smoking history, absence of exacerbations of COPD for at least 4 weeks prior to the initial session and no change in medication for the same period. The exclusion criteria were: coexisting severe heart disease, hypertension or cor pulmonale and long-term oral corticosteroid treatment due to its effect on inspiratory muscle function that could potentially influence our measurements [9]. The protocol was accepted by the local ethics committee and patients gave their informed consent.

Study Design and Measurements

Our COPD patients attended 3 laboratory-based sessions (S1, S2 and S3) 3–7 days apart. During each session, patients performed SNIP, $PI_{\max}$ and $PE_{\max}$ manoeuvres. Pressures were measured using Validyne MP45 differential pressure transducers (Validyne, Northridge, Calif., USA). The pressure signal from the pressure transducer was amplified by a carrier amplifier (Validyne) and acquired on a Macintosh PowerMac computer running Labview 4.1 software (National Instruments, Austin, Tex., USA). The same investigator performed the measurements during all sessions. In each session, the highest value for each measure was accepted for analysis as long as it was within 5% of the previous two highest values.

Participants were naive to the investigations and performed the following tests.

Lung Function

Lung function testing was performed during the 1st session only by senior clinical physiologists in the Lung Function Department of the King's College Hospital. Measurements of FEV_1 and FVC were obtained using a dry bellows spirometer (S Model; Vitalograph, Maids Moreton, UK) while total lung capacity (TLC) and residual volume (RV) were measured by constant whole body plethysmography (Auto-link; Morgan Medical, Gillingham, UK). Blood gases were measured from arterialed ear lobe capillary samples (Rapidlab 248; Chiron, Norwood, Mass., USA).

Sniff Nasal Pressure

SNIP manoeuvres were performed from functional residual capacity (FRC) with patients in the sitting position. Each patient had custom-made nasal plugs made from dental putty and hand-fitted around the tip of an 80-cm catheter connected to a pressure transducer (Validyne MP45). Each nasal plug was kept in a named envelope for use in subsequent sessions. Patients were asked to perform a strong, sharp, maximal sniff. Pressure tracings were accepted for analysis if they had a smooth downstroke, a sharp peak and took a maximum of 400 ms from baseline to peak. A minimum of 10 efforts were made with rest intervals of 30 s and the peak value was recorded. Visual feedback and strong verbal encouragement was given throughout.

Maximum Inspiratory Pressure

$PI_{\max}$ was assessed from two lung volumes, FRC and RV, using a flanged mouthpiece (PK Morgan, Rainham, UK) connected to a metal tube. A valve in the tube allowed normal breathing before maximal efforts were made and a separate hole in the tube ensured maintenance of an open glottis. The metal tube was connected to

Fig. 1. Repeated measures per test in COPD patients. Each data point represents the maximal value for each patient during the sessions. The horizontal lines represent the mean value of the group per session.

a differential pressure transducer (Validyne MP45) and $PI_{\max}$ tracings were recorded in real time. All patients were seated upright and encouraged to make maximal inspiratory efforts sustained for 1 s. Nose clips were worn at all times and patients performed a minimum of 10 efforts with rest intervals of 30–60 s between efforts. The peak value was recorded. Visual feedback and strong verbal encouragement was given throughout.

Maximum Expiratory Pressure

$PE_{\max}$ was assessed from TLC using the same equipment as for the $PI_{\max}$ measurements. Patients wore nose clips, had visual feedback and were given strong verbal encouragement throughout. A minimum of 10 manoeuvres were performed and the peak pressure was recorded in each session.

Statistical Analysis

Data were analysed under the null hypothesis that there were no differences in SNIP, $PI_{\max}$ and $PE_{\max}$ between the 3 sessions. Differences between sessions (S2-S1, S3-S2 and S3-S1) were analysed using a paired t test and the intra-class correlation coefficient (ICC) was calculated for all 3 sessions. The significance level was set at 5%. Data were analysed using SPSS (17.0) and graphs were created in GraphPad Prism (version 3.03).

Results

All patients tolerated the tests well. There were no complaints of pain or discomfort during the tests. The baseline characteristics of the study participants are presented in table 1.

SNIP values were repeatable between sessions. SNIP showed greater repeatability than $PI_{\max}$, especially following the 2nd session (S2). The mean SNIP value was consistently higher than $PI_{\max}$ in each session, regardless of

Table 1. Anthropometric and spirometric characteristics of the study participants

Males/females	13/8
Age, years	71.9 (10)
MRC scale	3 (0.8)
Body mass index	26.4 (2.3)
Pack years	69 (51)
FEV ₁ , litres	0.9 (0.3)
FEV ₁ , % of predicted	38 (15)
FEV ₁ /FVC, %	34.3 (10.4)
TLC, litres	6.5 (1.3)
RV, litres	4.1 (1.2)
TLC, % of predicted	117.2 (13.2)
RV, % of predicted	180.5 (40.5)

Data are presented as means (SD). MRC = Medical Research Council.

the lung volume the $PI_{\max}$ measurements were assessed from (fig. 1). When the best value of all 3 sessions was considered, SNIP was [mean (SD)] 72.21 (18.14) cm H₂O while $PI_{\max}$ at FRC was 64.60 (12.75) cm H₂O and $PI_{\max}$ at RV was 64.92 (13.88) cm H₂O. Therefore, the SNIP value was 11.8% higher than $PI_{\max}$ at FRC and 11.2% higher than $PI_{\max}$ at RV.

$PI_{\max}$ at RV was more repeatable than $PI_{\max}$ at FRC and tended to plateau after the 2nd session (ICC 0.89 and 0.82, respectively). ICC for S1–S3 for $PE_{\max}$ were 0.96 and 0.94, respectively.

A summary of the results is shown in table 2.

Table 2. Between-session repeatability of SNIP, $PI_{\max}$ and $PE_{\max}$ (in cm H₂O)

Tests	Mean (SD)			Mean differences (p value)			ICC (95% CI)
	S1	S2	S3	S2 – S1	S3 – S2	S3 – S1	S1 – S3
SNIP	65.69 (15.65)	67.78 (18.06)	67.49 (20.25)	2.1 (0.4)	–0.3 (0.9)	1.8 (0.6)	0.94 (0.88 – 0.98)
$PI_{\max}$ at FRC	58.60 (12.83)	55.04 (13.18)	56.24 (15.62)	–3.6 (0.2)	1.2 (0.7)	–2.4 (0.4)	0.82 (0.63 – 0.92)
$PI_{\max}$ at RV	57.60 (11.72)	60.04 (16.13)	58.95 (13.50)	2.4 (0.4)	–1.1 (0.6)	1.4 (0.5)	0.89 (0.78 – 0.95)
$PE_{\max}$	90.41 (28.47)	91.73 (28.81)	92.96 (31.30)	1.3 (0.7)	1.2 (0.7)	2.6 (0.3)	0.96 (0.92 – 0.98)

p < 0.05 was considered statistically significant. Differences between sessions were analysed using a paired t test.

Discussion

Volitional measures of respiratory muscle function are often used in clinical rehabilitation studies for sequential assessment of changes in muscle strength. The main advantage over their non-volitional equivalent is that they are easier to perform in a variety of clinical settings, such as in community studies, and avoid the need for insertion of balloon catheters [1] and possible patient discomfort. However, they are influenced by motivation and patients may learn how to do the test better on each session. The exploration of the between-session repeatability of these measures allows us to estimate how much of the change observed after a clinical study is due to the intervention under investigation or due to the learning effect.

The between-session reproducibility of SNIP has been studied in healthy subjects [4, 7]. Terzi et al. [4] found the measure repeatable over a period of 2 weeks and more reproducible than $PI_{\max}$. Similarly, Maillard et al. [7] studied the SNIP over a period of 1 month and showed that it had good repeatability in healthy subjects. The number of sniffs required to eliminate the learning effect in the same session has also been investigated by Lofaso et al. [8] who studied SNIP in patients with a variety of neuromuscular and respiratory diseases. The authors showed that more than 10 sniffs were required per session to achieve accurate SNIP measurements. To the best of our knowledge, the between-session repeatability of SNIP has not yet been investigated in COPD patients. This patient group is often reported to have functional inspiratory muscle weakness, and the outcome of rehabilitation interventions that may affect the degree of dynamic hyperinflation, or respiratory muscle function, can be evaluated by the non-invasive SNIP.

Our study showed that the SNIP was a repeatable measure in COPD patients who were free of exacerbations

over a 3-week period. The test had better repeatability than $PI_{\max}$, regardless of the lung volume at which $PI_{\max}$ was measured, and generated a higher group mean value (fig. 1).

The better repeatability of SNIP could be attributed to the fact that the sniff is a more natural manoeuvre than the static $PI_{\max}$ manoeuvre and is therefore rarely underperformed [2]. In COPD patients, SNIP has a disadvantage as a measure in that it underestimates slightly the more invasive sniff oesophageal pressure [6], but its non-invasive nature makes it an ideal test in non-laboratory-based clinical studies. In addition, SNIP improves diagnostic precision when used in tandem with $PI_{\max}$ [10] or diaphragm twitch mouth pressure [11] and it is therefore important for the non-invasive assessment of respiratory muscle function. In our study, SNIP group values were consistently higher than the $PI_{\max}$ values in each session. A similar result was observed when we identified the best value from all 3 sessions. In particular, SNIP values were 12% greater than $PI_{\max}$ at FRC and 11% greater than $PI_{\max}$ at RV. The consistency in higher values of SNIP in our group suggests that this test is a valuable outcome measure for repeated measures in COPD patients who are participating in interventional studies or rehabilitation programmes.

Our COPD patients performed a minimum of 10 SNIP manoeuvres per session and we recorded the maximum value from each session. Our results showed that the maximum value plateaued after the 2nd session. This suggests that 2 sessions, 3–7 days apart, are adequate to minimise the learning effect from SNIP in COPD patients as long as more than 10 sniffs are performed per session.

In contrast to previous studies, we did not observe a significant learning effect associated with $PI_{\max}$ and $PE_{\max}$. $PI_{\max}$ measurements have been reported to be sen-

sitive to the learning effect due to the nature of the manoeuvre. In COPD patients, the learning effect of $PI_{\max}$ and $PE_{\max}$ has been evaluated in a study by Larson et al. [12] over a period of 4 weeks. The authors suggested that a substantial amount of practice was required to learn to do the test, but the number of manoeuvres per session was not specified. In addition, two researchers participated in the data collection although instructions were standardised. In our study, one experienced investigator performed the measurements in all 3 sessions. It is possible that $PI_{\max}$ measurements show greater repeatability between sessions if the same investigator is involved throughout the sessions. Future studies need to investigate the variation in results when experienced and novel researchers take the measurements.

Equally, repeatability of the measure is influenced by the lung volume at which it is measured. $PI_{\max}$ is conventionally measured at RV [1] as measurements are expected to be more repeatable from this minimal volume. Pressures generated at RV are more negative than those measured at FRC as the pressure reflects the contribution of the elastic recoil of the respiratory system as well as the optimal length and configuration of the inspiratory muscles [1]. Our results confirmed that the $PI_{\max}$ value at RV was more negative than the pressure from FRC in most sessions, but we found that both were repeatable, especially after the 2nd session. When the best value of all 3 visits was considered, $PI_{\max}$ at FRC was close to the $PI_{\max}$ value at RV. This result could be attributed in part to the large number of practice manoeuvres each patient had to perform throughout the 3 sessions and the fact that only one investigator was performing the test.

$PE_{\max}$ was also a repeatable measure in our study. The $PE_{\max}$ manoeuvre requires recruitment of the abdominal muscles that are usually activated by coughing. Therefore, this manoeuvre is perhaps more natural than the $PI_{\max}$ manoeuvre. It is also well standardised as it is always performed from TLC [1]. Some studies, however, have shown less good repeatability, as in a study in bronchiectasis patients without cystic fibrosis [13]. Moran et al. [13] found that $PE_{\max}$ increased significantly in their 2nd session, which was 10–14 days after the 1st one. In healthy subjects [14] and COPD patients [12], the repeatability and reproducibility of $PE_{\max}$ has been more consistent between sessions. The results of our study are in agreement with these studies and suggest that $PE_{\max}$ is highly repeatable in COPD patients over a period of 3 weeks and that 2 practice sessions are adequate for baseline measurements prior to clinical studies.

Limitations of the Study

This study examined the repeatability of SNIP over a period of 3 weeks aiming to determine the minimum number of practice sessions needed to minimise the learning effect prior to clinical studies. Clinical studies or rehabilitation programmes often take longer to complete, usually 7–8 weeks. Therefore, results of this study may not be generalisable to longer periods of time. In addition, the sample size could not be determined in advance in our study, as there was limited information about the between-session standard deviation for SNIP in COPD patients. However, based on the largest standard deviation of SNIP between sessions in our cohort ($S_3 - S_1$, $SD = 17.14$), we estimated that a future study would need 21 patients to explore the repeatability of SNIP over a longer period, with a 5% significance level and 80% power.

Furthermore, the results of our study provide information about the repeatability but not the reproducibility of SNIP. In our study, the same investigator performed all assessments as we aimed to exclude between-investigator bias. However, clinical studies are often conducted at different sites and more than one investigator takes measurements of respiratory muscle function. Therefore, future studies need to establish the reproducibility of these measures over repeat sessions using more than one investigator and more than one setting.

Finally, this study examined the repeatability of SNIP in patients with moderate-to-severe disease who were optimally managed and stable. The results may not apply to COPD patients in, for example, the early period of recovery after an exacerbation.

Conclusion

Sniff nasal pressure is a highly repeatable test over a period of 3 weeks in patients with moderate-to-severe COPD. Two repeat practice sessions are adequate to minimise the learning effect associated with SNIP prior to interventional studies, as long as more than 10 attempts are performed in each session. In contrast to previous studies, we did not observe a significant learning effect for $PI_{\max}$ and $PE_{\max}$.

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Erratum

The authors of the article entitled 'Leukotriene receptor blockade as a life-saving treatment in severe bronchopulmonary dysplasia' [*Respiration* 2014;88:285–290, DOI:10.1159/000365488] wish to publish the following two corrections.
On page 288, table 2, the correct p value is 0.02, see below:

Table 2. Survival according to treatment

	Nonsurvivors	Survivors
Patients	1	10
Controls	7	4

All but one of the infants in the treatment group (patients) survived, whereas 7 of the 11 infants in the control group died. $p = 0.02$, Fisher's exact test.

On page 290, left column, the text should read:

This study was partly funded by an unrestricted grant from the Oberfrankenstiftung and the Orchesterakademie, Bayreuth, Germany, which had no influence on the design, collection, analysis, or interpretation of data or publication.