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Sniff nasal inspiratory pressure (SNIP) in amyotrophic lateral sclerosis: Relevance of the methodology for respiratory function evaluation

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ABSTRACT

Objectives: We investigated two different methodological approaches for determining nasal inspiratory pressure during a sniff (SNIP) in patients with Amyotrophic Lateral Sclerosis (ALS).
Patients and Methods: We included 37 ALS patients and 11 controls. SNIP was measured in the sitting position, performed in each nostril with (SNIPocclud) and without (SNIPopen) closing the contralateral nostril. The best of 3 consistent results was considered for analyses. Patients were also assessed with MIP and the revised functional ALS rating scale (ALSFRS-R). Mann-Whitney U test, Wilcoxon test and Spearman's rank correlation coefficient with Bonferroni correction were applied. Coefficient of variation (CV) was calculated.
Results: SNIP was significantly lower in patients than controls, either for SNIPopen ($p = 0.011$) or SNIPocclud ($p = 0.002$). SNIPopen values were significantly lower both in ALS patients and controls than SNIPocclud ($p < 0.001$ and $p = 0.007$, respectively). SNIPopen CV was 8.14% and 8.51%, while SNIPocclud CV was 4.98% and 6.37%, respectively for controls and patients. SNIPopen and SNIPocclud were strongly correlated in both groups ($r = 0.761$ for controls; $r = 0.768$ for patients). In ALS, both methods were moderately correlated with MIP (respectively $r = 0.525$, $p = 0.006$ and $r = 0.685$, $p < 0.001$) and the respiratory subscore of ALSFRS-R (respectively $r = 0.525$, $p = 0.001$ and $r = 0.64$, $p < 0.001$). Although bulbar and spinal onset patients presented no differences for SNIPopen ($p = 0.157$), significant differences were found for SNIPocclud ($p = 0.018$).
Conclusion: SNIPocclud should be considered when evaluating ALS patients as its values present lower variability and favor longer follow-up.

1. Introduction

Nasal inspiratory pressure during a sniff (SNIP) is a respiratory test extensively promoted in Amyotrophic Lateral Sclerosis (ALS) for the assessment of the inspiratory muscle strength. In 1994, Héritier et al. [13] described this non-invasive technique, with results strongly correlated with the invasive sniff oesophageal pressure. In SNIP, the pressure generated at the contralateral nostril during maximal inspiration (from functional residual capacity) is measured by a cannula connected to a plug occluding one nostril. While maximal inspiratory pressure (MIP) assesses non-invasively the pressure generated at the mouth during an inspiratory effort and requires an effective lip closure around the mouthpiece [3,4], SNIP is more reliable in patients with facial weakness. Therefore it is frequently used as an alternative to MIP in ALS.

In healthy subjects, SNIP usually presents higher values than MIP [24], with similar reproducibility, and a low coefficient variation (CV), 6% [18]. It is sensitive to inspiratory muscle fatigue in different conditions [14], including neuromuscular disorders [23]. In ALS, SNIP is easier to perform than MIP, and its sensitivity might be higher in predicting ventilatory failure [17,11]. However, SNIP and MIP are not inter-changeable but complementary, as they mirror different ventilatory mechanics [23,20,21]. During SNIP, the generated effort is ballistic, while it is sustained during MIP. In addition, the diaphragmatic recruitment pattern is higher in SNIP [20,21], resulting in higher transdiaphragmatic pressures. When there is bulbar involvement, the correlation between SNIP and vital capacity (VC) is lower, probably due to difficulties in mouth closure, upper airway collapse and upper and

Abbreviations: ALS, amyotrophic lateral sclerosis; ALSFRS, ALS functional rating scale; ALSFRSb, bulbar subscore of ALSFRS-R; ALSFRSul, upper limb subscore of ALSFRSR; ALSFRSll, lower limb subscore of ALSFRSR; ALSFRS-R, revised ALSFRS; CV, coefficient of variation; FRC, functional residual capacity; FVC, forced vital capacity; MEP, maximal expiratory pressure; MIP, maximal Inspiratory pressure; MVV, maxiaml voluntary ventilation; RofALSFRS-R, respiratory subscore of ALSFRS-R; SNIP, nasal inspiratory pressure during a *sniff*; SVC, slow vital capacity; VC, vital capacity

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Table 1
Demographic characteristics of the subjects included, including differences between controls-ALS patients and bulbar-spinal onset patients.

	Controls (n = 11)	ALS patients (n = 37)	*p*	Bulbar onset pts (n = 13)	Spinal onset pts (n = 24)	*p*
Gender (male)	5 (45.5%)	17 (45.9%)	0.977	5 (38.4%)	12 (50%)	0.501
Age at disease onset (years)	–	64.22 ± 10.5 (39–90)		69.1 ± 10.2 (55–90)	64.22 ± 10.5 (39–90)	0.054
Age at evaluation (years)	61.4 ± 16.1 (27–82)	–	0.912			
BMI	26.9 ± 4.4 (21–36)	24.22 ± 2.6 (19–30)	0.079	24.42 ± 2.6 (21–29)	24.12 ± 2.7 (19–30)	0.886
Disease duration at onset (mo)	–	22.33 ± 23.7 (1–117)	–	10.01 ± 6.82 (1–29)	29 ± 26.9 (4–117)	0.002*
Disease duration at evaluation (mo)	–	35.34 ± 40.2 (3–215)	–	16.13 ± 14.2 (3–57)	45.75 ± 45.8 (7–215)	< 0.001*
ALSFRS	–	30.9 ± 5.4 (17–38)	–	32.2 ± 5.4 (21–38)	30.2 ± 5.3 (17–38)	0.175
ALSFRSb	–	10.14 ± 2.2 (5–12)	–	8.15 ± 2.1 (5–11)	11.21 ± 1.5 (7–12)	< 0.001*
ALSFRSul	–	8.86 ± 3.2 (0–12)	–	10.4 ± 1.8 (8–12)	8.04 ± 3.53 (0–12)	0.042
ALSFRSll	–	8.11 ± 3 (1–12)	–	9.92 ± 2.9 (4–12)	7.13 ± 2.6 (1–11)	0.004*
RofALSFRS-R	–	11.41 ± 1.1 (8–12)	–	11.31 ± 0.95 (9–12)	11.46 ± 1.1 (8–12)	0.337
SNIPopen (cmH_2O)	75 ± 29.4 (38–136)	49.41 ± 25.2 (3–102)	0.011	42.08 ± 31.0 (3–100)	53.37 ± 21.0 (22–102)	0.157
SNIPocclud (cmH_2O)	94.73 ± 29.1 (52–149)	62.84 ± 26.8 (2–143)	0.002*	51.31 ± 37.9 (2–143)	67.38 ± 19.66 (38–107)	0.018
SVC (% predicted value)	89 ± 6.6 (83–101)	77.9 ± 19.0 (29–110)	0.209	68.38 ± 21.4 (29–88)	83.83 ± 15.2 (58–110)	0.051
FVC (% predicted value)	84.8 ± 3.1 (82–89)	75.8 ± 18.4 (26–109)	0.111	66.1 ± 20.3 (26–87)	81.81 ± 14.6 (55–109)	0.082
MIP (cmH_2O)	92.2 ± 11.7 (80–108)	52.85 ± 22.8 (3–85)	0.001*	42.4 ± 30.1 (3–81)	59.38 ± 14.25 (42–85)	0.215
MEP (cmH_2O)	129.4 ± 17.8 (104–151)	65.15 ± 29.9 (9–122)	0.001*	54.4 ± 35 (9–111)	71.88 ± 25.07 (33–122)	0.162
MVV (l/min)	99.42 ± 24.7 (74–145)	65.4 ± 25.6 (34–133)	0.009*	60.5 ± 38.7 (34-133)	67.38 ± 19.66 (38–107)	0.213

For abbreviations please see Abbreviation section.
* $p < 0.01$.

lower airway muscle dyspraxia. These factors also contribute to lower MIP values. It has been reported abnormal SNIP values in patients with normal VC [9]. SNIP is a predictor of survival [19,15] and of tracheostomy in ALS [6], but its decline rate could be lower than the decline rates of forced vital capacity (FVC) and the diaphragmatic amplitude of the phrenic nerve motor responses [22].

While Héritier et al. [13] recommended 10 measurements, 5 per nostril, with 30-second intervals in between, others suggest the need for higher number of trials [16]. In ALS, fatigue is a concern when performing repeated evaluations. Variability of the measurements with different technical approaches has been poorly investigated, but it represents a major concern, particularly regarding standardization in clinical trials.

In the present study, we investigated two different SNIP technical approaches, either occluding the contralateral nostril (SNIPocclud) or keeping it open (SNIPopen) as originally reported [13] for the assessement of the respiratory function in ALS.

2. Patients and methods

2.1. Subjects

We included consecutive ALS patients followed in our Unit and referred to perform respiratory tests from January to February 2016. All patients had probable or definite ALS according to the revised El Escorial criteria [5], using the Awaji algorithm to define neurophysiological features [10]. Patients with dyspnea at rest or clinical evidence of dementia, diabetes or lung disorders were excluded.

During the same period, age-matched healthy controls were also investigated.

2.2. Investigations

2.2.1. ALS functional rating scale

In ALS patients, the ALS functional rating scale (ALSFRS-R) [7] was used to derive a total functional rating score (maximum score of 40). Bulbar (ALSFRSb), upper limb (ALSFRSul), lower limb (ALSFRSll) subscores and the respiratory (RofALSFRSR) subscores were also recorded [8].

2.2.2. Respiratory function tests

These tests were all performed in our Unit, by a single evaluator (SP), with the subjects in the sitting position.

2.2.2.1. Nasal inspiratory pressure during a sniff (SNIP). Nasal inspiratory pressure during a *sniff* (SNIP) was determined in all ALS patients and controls by using the MicroRPM® device (CareFusion®), with the probes provided by the same company. The probe size was chosen individually in order to completely occlude the subjects' nostrils. With one of the nostrils occluded by the probe, subjects were asked to breath out through the mouth to residual volume, to close the mouth and to perform a deep *sniff* through the nose while maintaining the mouth closed. Two different techniques were performed randomly during *sniff*, either having the contralateral nostril opened (SNIPopen) or closed (SNIPocclud) by the evaluator. For each nostril, several evaluations (more than 5) were made and testing was continued until 3 consistent results were recorded (< 20% variation). The maximal values were considered for analyses (cmH_2O).

2.2.2.2. Forced (FVC) and slow (SVC) vital capacities. Forced (FVC) and Slow (SVC) vital capacities were performed using the computer-based USB spirometer (microQuark®, Cosmed®) with the Omnia® Cosmed® software. The best of three satisfactory and consistent expiratory maneuvers, each obtained after a maximal inspiratory effort was used to determine the values of FVC and SVC. For FVC the subjects were asked to breath out forcefully while slowly for SVC. Absolute values were normalized to the GLI project values, accordingly to age, gender, height and weight. The percentage of the predicted values (%) was used for statistical analysis.

2.2.2.3. Maximal inspiratory (MIP) and expiratory (MEP) pressures. Maximal inspiratory (MIP) and expiratory (MEP) pressures were assessed as, respectively, the best result of three consistent inspiratory and expiratory measurements at the mouth, generated against an occluded airway. A MicroRPM® device (CareFusion®) was used for the evaluation, using the manufacturers' mouthpieces. The maximal values obtained (cmH_2O) were analyzed.

2.2.3. Statistical analysis

Demographic characteristics were compared between controls and ALS patients as well as between bulbar and spinal-onset ALS patients using the Mann-Whitney *U* test. Categorical tests were applied to compare gender frequency between the two groups. Wilcoxon test was used to compare SNIPocclud and SNIPopen within group subjects. The ratio standard deviation (SD): mean value was used to calculate the coefficient of variation (CV). Spearman's rank correlation coefficient with Bonferroni correction was used for multiple correlations. A *p* value