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ORIGINAL ARTICLE

Validation of robust tools to measure sialorrhea in amyotrophic lateral sclerosis: A study in a large French cohort

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Abstract

There is an unmet need for validated tools to measure sialorrhea in amyotrophic lateral sclerosis, especially to evaluate treatments. We assessed the inter-/intra-rate reviewer reliability of two scales: the Oral Secretion Scale (OSS), specifically developed for ALS patients, and the Sialorrhea Scoring Scale (SSS), initially developed for Parkinson's disease patients. Sialorrhea was rated in 69 ALS consecutive patients by four evaluators: two neurologists, one nurse and one speech therapist. Inter-rater reliability was evaluated by the light kappa coefficient and intra-rater reliability by the weighted kappa coefficient. We also compared patients' and caregivers' answers. Results demonstrated that the two scales present a high inter-/intra-rater reliability: weighted kappas were 0.85 for both scales and light kappas 0.89 for the OSS and 0.88 for the SSS. Both scales also showed a good intra-profession reliability (OSS kappa = 0.84; SSS kappa = 0.79) and agreement between patients' and caregivers' answers. The SSS showed a higher responsiveness compared to OSS. In conclusion, both Oral Secretion Scale and Sialorrhea Scoring Scale are reliable tools to measure sialorrhea in ALS patients. Because of the wide range of salivation degrees, SSS may be more sensitive as a tool to evaluate treatments in patients with severe hypersialorrhea.

Key words: *Risk, ventilation, therapy*

Introduction

Sialorrhea is a frequent and disabling problem in patients with bulbar involvement related to amyotrophic lateral sclerosis (ALS). Sialorrhea can cause social embarrassment and worsen isolation in ALS. Excess of saliva may also increase the risk of aspiration. A retrospective pathological study on a large cohort of 100 ALS patients showed that bronchopneumonia and pneumonia were the main causes of death and were twice as frequent in bulbar compared to spinal ALS (1). Several strategies have been suggested to treat hypersialorrhea including speech therapy, aspiration devices, oral pharmacotherapy, botulinum toxin injections, radiotherapy and surgical

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interventions (2). However, evidence is weak, partly due to the lack of measuring tools specifically validated in ALS patients. In this study, we selected from the literature two scales, the Oral Secretion Scale (OSS) and the Sialorrhea Scoring Scale (SSS) that appear as particularly suitable for hypersialorrhea assessment in ALS. We evaluated their inter- and intra-rater reliability in a large cohort of French ALS patients followed in a specialized multidisciplinary care unit.

Methods

Patients

The questionnaires were prospectively administered to all patients admitted in the Paris ALS referral centre during April and May 2011 in the context of a one-day hospitalization for systematic respiratory and multisciplinary evaluation. Demented patients and patients who underwent tracheostomy were excluded. We included 69 patients whose mean age was 64 ± 13 ($31 - 86$) years; the gender ratio F/M was 35/34, 25% of the patients had a bulbar onset, the disease duration was 3.1 ± 3.4 ($0.5 - 22.0$), and 83% of patients had evidence of bulbar symptoms based upon the bulbar subscale at the beginning of this study. The local ethics committees approved the study and required only verbal consent, which was obtained in all the patients of our series.

Scales

Scores from the three scales tested were judged by bedside observation; the observer had to choose a single score the criteria for which most closely matched the patient's condition.

Oral Secretion Scale. The Oral Secretion Scale (OSS) is the only scale specifically designed for the evaluation of hypersialorrhea in ALS patients. It has been developed by Pamela A. Cazzolli, Benjamin Rix Brooks et al. (4) in Carolinas Neuromuscular/ALS-MDA Center (Charlotte, NC, USA). Saliva retention and swallowing are evaluated using five grades from very severe (scored 0) to normal (scored 4).

The scores correspond to the following features: constant drooling requiring constant lip-blotting, regular suctioning (score 0, very severe); difficult conscious secretion swallowing, frequent drooling in any position, lip-blotting $12 - 30$/h, intermittent suctioning (score 1, severe); conscious saliva swallow required, drooling upright leaning forward, lip-blotting $4 - 6$/h (score 2, moderate); automatic saliva swallow decreased, infrequent drooling (score 3, minimal); normal automatic saliva swallow, no drooling (score 4, normal).

Sialorrhea Scoring Scale. After an extensive literature review, we also selected the Sialorrhea Scoring Scale. This nine-grade scale has been successfully used in two clinical trials: Parkinson's disease patients and children with both developmental disabilities and excessive and bothersome sialorrhea (5,6), but there is no publication about its use in ALS patients. The SSS scale ranges from 1 (least severe) to 9 (most severe) (Table I).

The OSS and the SSS are thus coded in a contrasting manner.

ALSFRS-R scale. The ALSFRS-R (3) is a validated rating instrument for monitoring the progression of disability in patients with ALS. It comprises 10 subscales and each of them is composed of five items ranging from 0 for the more severe patients to 4 for the normal functionality. ALSFRS bulbar subscale was defined as concurrent validity parameter.

Study plan

The two questionnaires OSS and SSS were translated using the standard translation/back-translation method (French version in supplementary materials).

To assess the intra-rater reliability, two evaluations of the patient were performed by the speech therapist one week apart. The second evaluation was conducted by phone among the patients, or caregivers when patients were unable to speak.

The inter-rater reliability was performed by four evaluators at the same day: two senior neurologists, one nurse and one speech therapist to assess the reliability inter-profession (for the four evaluators) and intra-profession (for the two neurologists).

Table I. Sialorrhea Scoring Scale (SSS) scale grades.

Score	Label
1	dry, never drools
2	mild, only the lips are wet, occasionally
3	mild, only the lips are wet, frequently
4	moderate, wet on the lips and chin, occasionally
5	moderate, wet on the lips and chin, frequently
6	severe, drools to the extent that clothing becomes damp, occasionally
7	severe, drools to the extent that clothing becomes damp, frequently
8	profuse, clothing, hands and objects become wet, occasionally
9	profuse, clothing, hands and objects become wet, frequently

Statistical analysis

In order to estimate the degree of intra-rater reliability and inter-rater reliability actually achieved above chance, we calculated the weighted kappa coefficient with Fleiss-Cohen weights (intra-rater reliability) and the light kappa coefficient based on weighted kappa (inter-rater reliability). For the intra-rater reliability, the kappa coefficient was first computed for all patients and, secondly, according to the patients' or caregiver's answers. For the inter-rater reliability, the kappa coefficient was computed between all professions and between neurologists only.

We calculated also for each analysis the percentage of complete agreement (the percentage of evaluations for which the reviewer (intra) or all the reviewers (inter) gave the same score) and the percentage of agreement within one point (the percentage of evaluations for which the difference between the highest and the lowest score given by the same reviewer (intra) or all the reviewers (inter) was one or zero).

Convergent validity was assessed as the correlation (Spearman correlation coefficient) between the two scales (OSS, SSS) and the ALSFRS (bulbar ALSFRS and the salivation items of the bulbar ALSFRS scale).

To calculate the confidence intervals of the kappa coefficient, we used a bootstrap procedure with 1000 replicates. Statistical analyses were performed with the R software (version 2.13.0 for Windows). We considered test results significant at the 0.05 level and reported two-tailed p-values.

Results

Intra-rater reliability

Intra-rater reliability was analysed in the 69 patients evaluated twice by the speech therapist. For the second evaluation, conducted by phone, the OSS and the SSS were scored among the patients ($n = 37$) or among the caregivers when patients were unable to speak ($n = 32$). The weighted kappa coefficients were over 0.85 for both the OSS and the SSS. The kappa coefficient was greater when the second evaluation was scored from the caregiver even if the differences were not statistically significant. In addition, OSS agreement was better but not statistically significant than the SSS agreement (Figure 1, Table II).

Inter-rater agreement

Inter-rater reliability was studied in 66 patients evaluated by at least two of the four reviewers (44 of the 66 patients were evaluated by four reviewers, 16 by three reviewers and eight by two). Light kappas were similar for both scales (Figure 2) (0.89 for the OSS, 0.88 for the SSS). However, only 47% of all four reviewers gave exactly the same scoring using the SSS, and 70% gave a score with less than one point of difference between them while they were 66% and 91%, respectively, for the OSS. Forty-five patients were evaluated by two neurologists (Table III). The reliability was slightly better, but not statistically different, for the OSS (0.84) than for the SSS (0.79) (Figure 2).

Concurrent validity between scales

For 53 patients, ALSFRS was measured in addition to the OSS and SSS. ALSFRS bulbar score correlated with both the OSS ($r = 0.803$, $p < 0.0001$) and the SSS ($r = -0.797$, $p < 0.0001$). The salivation items in bulbar ALSFRS were also correlated with both scales (OSS: $r = 0.931$, $p < 0.0001$; and SSS: $r = -0.909$, $p < 0.0001$). In addition, SSS and OSS were highly correlated ($r = -0.935$, $p < 0.0001$).

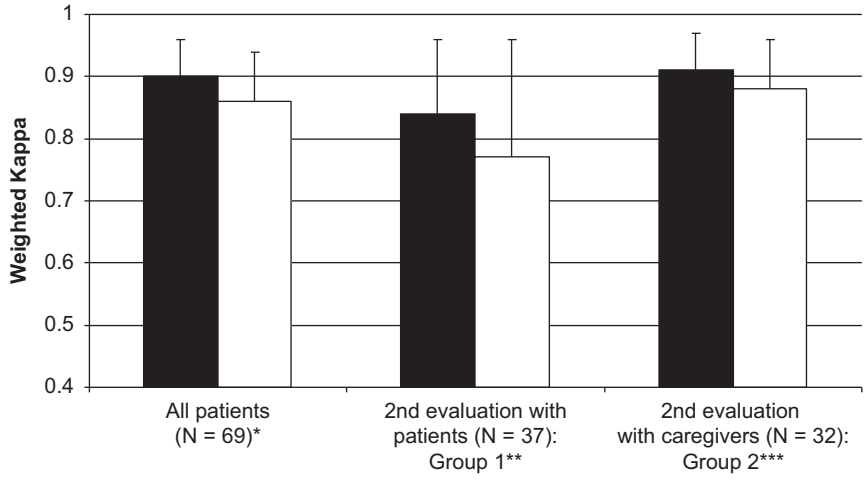

Figure 1. Intra-rater reliability indicators for Oral Secretions Scale (OSS) (black) and Sialorrhea Scoring Scale (SSS) (white) in three groups. *All patients. **When the second evaluation was according to the patient answers. ***When the second evaluation was according to the caregiver's answers.

Table II. Intra-rater reliability indicators for Oral Secretions Scale (OSS) and Sialorrhea Scoring Scale (SSS) in three groups: percentage of the complete agreement and the agreement within one point.

	All patients ($n = 69$)*		2nd evaluation with patients ($n = 37$) Group 1**		2nd evaluation with caregivers ($n = 32$) Group 2***	
	OSS	SSS	OSS	SSS	OSS	SSS
% agreement	81%	68%	81%	75%	81%	59%
% agreement within one point	94%	82%	95%	83%	94%	81%

*All patients.
**When the second evaluation was according to the patient answers.
***When the second evaluation was according to the caregiver's answers.

From the scatter plot, we noticed a floor effect for the OSS and the ALSFRS scales (Figure 3). The patients with SSS scores with severe salivation between 6 and 8 were badly discriminated by the ALSFRS scale or the OSS scale.

Discussion

Our results showed that the two scales SSS and OSS present a very good inter- and intra-rater reliability. Our population was representative of a standard ALS population since we prospectively included all the ALS patients attending a multidisciplinary evaluation during the study period.

These two scales therefore appear to be suitable tools for evaluation of sialorrhea in ALS patients. From a practical point of view, the two questionnaires are rapid to administer and do not exceed 5 min. SSS directly measures saliva leaking with a wide range of severity from mild (only the lips are wet, occasionally) to profuse (clothing, hands and objects become wet, frequently). Because the hypersialorrhea is a cause of discomfort and social embarrassment, this scale is clinically relevant and is likely to correlate with changes in quality of life due to hypersialorrhea.

Because of the wide range, SSS showed a higher responsiveness compared to OSS. This ability of SSS to detect relevant changes in patients with severe salivation is important for the assessment of the effect of different therapeutic agents, particularly botulinum toxin and radiotherapy. However, our study does not allow evaluating the sensitivity to change over time of the two scales.

Compared to the SSS, the OSS has the added advantage of measuring swallowing. Conscious swallowing of saliva may be associated with an increased risk of aspiration with ensuing pneumonia. Interestingly, a recent unpublished study suggests that abnormalities measured by OSS predict tolerance of non-invasive positive pressure ventilation (NPPV) and the need for end-of-life care or transition to tracheal positive pressure ventilation in ALS patients (4). In addition, in another unpublished study, the test/re-test of a Japanese version of the OSS was comparable to the present study with the French version of the OSS (7). The predictive value of SSS, and its comparison with OSS, remains to be studied. However, it should be noted that, in the opinion of the majority of the evaluators, the multiple gradations in each grade, while increasing the granularity of the scale, did not increase the sensitivity of the OSS compared to the SSS. A recent trial in Parkinson's disease showed that the SSS was able to detect changes due to treatment, but it is not possible to directly extrapolate to ALS, particularly because the severity of sialorrhea in Parkinson's disease patients is less important than in ALS patients (6).

The SSS is a nine-grade scale while the OSS is a five-grade scale. It has been shown that the larger the number of scale categories, the greater the potential for disagreement, with the result that unweighted

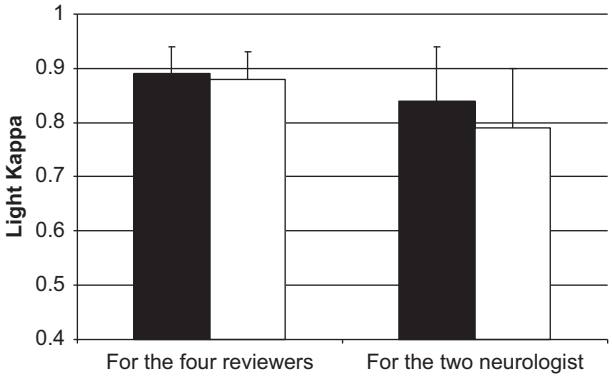

Figure 2. Inter-rater agreement indicators for Oral Secretions Scale (OSS) (black) and Sialorrhea Scoring Scale (SSS) (white) scales.

Table III. Inter-rater agreement indicators for Oral Secretions Scale (OSS) and Sialorrhea Scoring Scale (SSS): percentage of the complete agreement and the agreement within one point.

	OSS	SSS
For the four reviewers		
% agreement	66%	47%
% agreement within one point	91%	70%
For the two neurologists		
% agreement	73%	55%
% agreement within one point	93%	75%

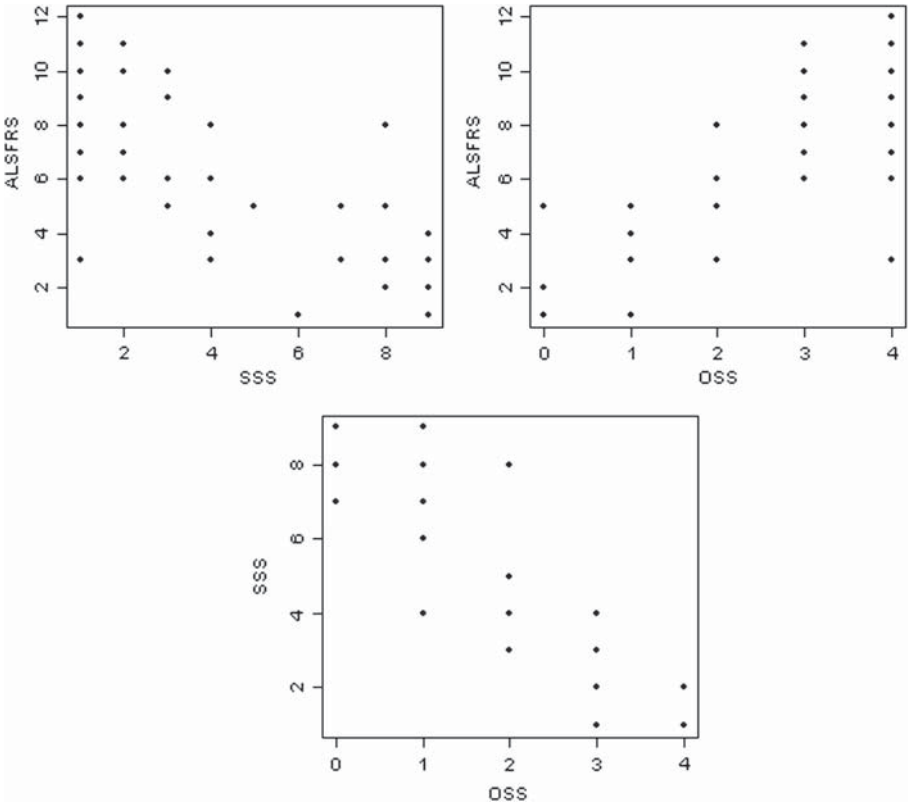

Figure 3. Scatter plot of ALSFRS, Oral Secretions Scale (OSS) and Sialorrhea Scoring Scale (SSS) scales correlations.

kappa will be lower with many categories than with few. The weighted kappa coefficient with Fleiss-Cohen weights that was used in the study is a solution to address this point (8).

Given the very good agreement between patients' and caregivers' answers in the intra-rater test, we can practically assess saliva retention by telephone interview using either one of the two scales OSS or SSS, thus enabling remote monitoring of therapeutic effect in a trial setting.

In conclusion, we validated two scales OSS and SSS as tools to measure sialorrhea in ALS patients. We suggest that these scales are useful tools to monitor hypersialorrhea in clinical practice and are suitable endpoints in clinical trials aiming to treat hyper salivation in ALS.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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