Hydration alters viscosity of nasal secretions in postnasal drip

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Dear Editor:

In our recent study, increased viscosity, delayed mucociliary clearance as well as hyposensitivity/dysesthesia of the nasopharynx seemed to play a relevant role in the pathophysiology of postnasal drip (PND) [1]. Earlier concepts of PND, regarding an increased volume of secretions and atopy, do not seem to hold true since our latest analyses showed no significant difference between cases and controls [1]. However, to this day its therapy is debated and the evidence for an effective treatment of PND is lacking so far. The fundamental rheological properties of nasal mucus constitute of the viscosity and elasticity [2-4]. The viscosity of nasal secretions results from factors including the degree of hydration, pH, the electrolyte concentration, the quantity and types of mucins present, the presence of extracellular material, alterations in electrostatic interactions among mucins, as well as polymer length and degree of cross-linking [5]. Therefore, we aimed to elucidate whether systemic hydration with 1 litre of water has an influence on the viscosity of nasal secretions and PND symptoms in our subject group. Accordingly, after approval by the local ethics committee, 13 patients with typical symptoms of PND at the Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital of Zurich were enrolled in a prospective data collection evaluating the effect of systemic hydration with 1 litre of water on the viscosity of nasal secretions and PND symptoms. All patients were required to report the sensation of fluid dripping down into the throat. In addition, at least two other typical PND symptoms such as foreign body sensation in the throat, nasal discharge, chronic cough or frequent throat clearing had to be mentioned. Only chronic PND patients (duration of symptoms >3 months) were recruited. All patients withheld oral corticosteroids for at least two weeks and intranasal cortisone as well as antihistamines for 24 hours. Comorbidities of all patients were recorded and specifically assessed for diseases influencing nasal secretions. Our subject group was fasting for eight hours until we collected nasal secretions for the first time in the same manner as described in our previous study [1]. Afterwards, 1 litre of water had to be orally consumed within two hours until the analysis of nasal secretions was repeated in the same way. After hydration, patients were asked for a change in PND symptoms on a 3-point scale ("improved", "same" or "worsened"). Rheological analyses of viscosity of nasal secretions at 1 1/s ($p = 0.0433$) as well as 100 1/s ($p = 0.0239$) showed significant differences in fasting compared to hydrated PND subjects (Figure 1). The mean viscosity in fasting PND patients was 8.51 ± 10.20 Pas at 1 1/s or 0.13 ± 0.13 Pas at 100 1/s and in hydrated ones 2.24 ± 2.00 Pas at 1 1/s or 0.04 ± 0.04 Pas at 100 1/s, respectively. Eleven out of thirteen patients (84.62%) reported a subjective reduction in PND symptoms after hydration. Two out of the thirteen patients (15.38%) reported no change, and none reported worsening of symptoms after hydration.

Conclusions

Our research provides two important new findings concerning the therapy of PND. First, systemic hydration has significant effect on the viscosity of nasal secretions in PND patients. Second, subjective PND symptoms were reduced after hydration. This has – to the best of our knowledge – not been demonstrated so far. In the study at hand, we could demonstrate that increased viscosity seems to have a major impact in the pathophysiology of PND and correlates with extended symptom-free intervals [1]. Our new findings are in line with this hypothesis. Based on these results, we therefore suggest including hydration of patients in PND treatment algorithms.

List of abbreviations

PND: Postnasal Drip.

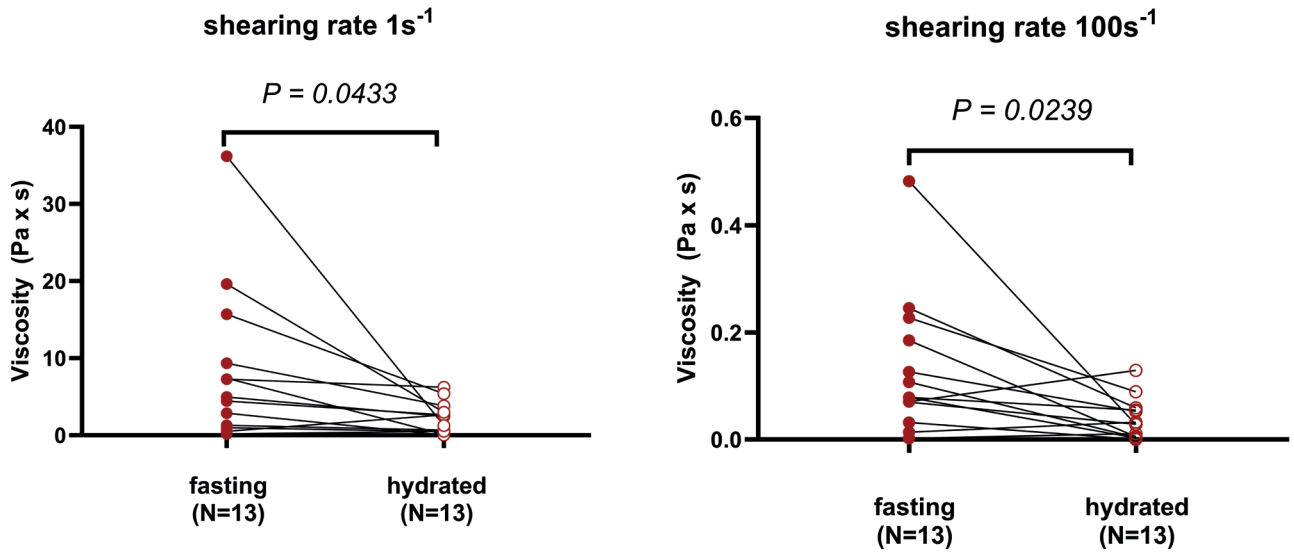

Figure 1. Rheological analysis of viscosity of nasal secretions shows significant differences at 1 1/s (p = 0.0433) and 100 1/s (p = 0.0239) between fasting and hydrated PND subjects.

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None.

Authorship contribution

SB has planned and structured the study, recruited the patients, collected samples, has performed some laboratory analysis, has written the manuscript and performed result analyses; TMLF recruited the patients, collected samples and has performed some laboratory analysis; YS has done the statistical testing and reviewed the manuscript; MBS has planned and supervised the study and drafted the manuscript.

Conflict of interest

The authors declare no conflict of interest concerning the contents of this study.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Materials and methods

Ethics

After approval from the Swiss Ethics Committee on research involving humans (ID: KEK 2018-00603) Informed Consent was obtained from every patient. It was conducted in compliance with formalities of the independent ethical commission, the current Helsinki-Declaration as well as the Swiss law.

Study design and population

This monocentric prospective cohort study of patients with PND was conducted at the Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital of Zurich. The study population consisted of 13 patients with typical symptoms of PND. All these patients were required to report the sensation of fluid dripping down into the throat. In addition, at least two other typical PND symptoms such as foreign body sensation in the throat, nasal discharge, chronic cough or frequent throat clearing had to be mentioned. These symptoms were the trigger for seeking medical help. Only chronic PND patients (duration of symptoms >3 months) were recruited from outpatient clinics at the University Hospital Zurich and examined by the same trained examiners (SB and TMLF). To be included in the study, participants were required to be aged between 18 and 70 years and able to give written consent. Exclusion criteria for all participants were current nasal medication, neoplasia of the naso-, oro- and hypopharynx or larynx as well as acute states of PND. All patients were asked about their medication and its potential influence on nasal secretions was evaluated. Therefore, all patients withheld oral corticosteroids for at least two weeks and intranasal cortisone as well as antihistamines for 24 hours. Comorbidities of all patients were recorded and specifically assessed for diseases influencing nasal secretions such as cystic fibrosis or primary ciliary dysfunction. Since all our patients were adults, chloride sweat tests were not regularly performed. Our subject group was fasting for eight hours until we collected nasal secretions for the first time as described below. After the first collection of nasal secretions, 1 litre of water had to be orally consumed within two hours until the collection was repeated in the same way.

Data collection

Collection and viscoelasticity of mucus

The nasal mucus was collected by using one 24 x 9 mm thin Merocel sponge (Medtronic Xomed, Jacksonville, Fl. USA) for each nostril. The Merocels were placed in the anterior part of nasal cavity for 20 minutes. Afterwards, they were centrifuged twice on 4500 rotations per minute at 25°C for 15 minutes. Analyses of viscosity of nasal mucus were conducted by a rotational rheometer (Modular Compact Rheometer MCR 501, Anton Paar, Graz, Austria) with a cone-plate geometry (CP25-1) at 37°C. The samples of the patient nasal mucus were placed on the lower plate of the measuring geometry to allow equilibration for 30 seconds at 37°C, ensuring nearly in vivo conditions. Flow curves with shear rates from 1 and 1000 1/s (25 measuring points) were used to obtain the shear viscosity as a function of shear rate. Shear viscosity values at shear rates of 1 and 100 1/s were used for further analysis. All measurements were directly conducted after mucus collection to minimize alterations in rheological characteristics.

Change in PND symptoms

After hydration, patients were asked for a change in PND symptoms on a 3-point scale. PND symptoms were registered as either "improved", "same" or "worsened".

Statistical analyses

Statistical analysis was performed using GraphPad Prism Version 10.2.0 for (GraphPad Software, Boston, MA, USA, www.graphpad.com). Paired t-tests were conducted and results with a P value <0.05 were considered statistically significant. Data are presented as mean ± SD.

Results

In total 13 patients with typical PND symptoms were assessed. The male:female ratio of the study population (n=13) was 8:5 and the average age was 55.53 ± 17.94 years. No patients with chronic or acute rhinosinusitis were included. Allergic rhinitis was seasonal and, apart from potentially associated PND symptoms, not active during examination in all patients assessed. Neither primary ciliary dyskinesia nor cystic fibrosis were recorded in our study population. Further demographic information is presented in Table S1. There were no missing values concerning parameters of interest. Analyses of viscosity of nasal secretions at 1 1/s ($p = 0.0433$) as well as 100 1/s ($p = 0.0239$) showed significant differences in fasting compared to hydrated PND subjects (Figure 1). The mean viscosity in fasting PND patients was 8.51 ± 10.20 Pas at 1 1/s or 0.13 ± 0.13 Pas at 100 1/s and in hydrated ones 2.24 ± 2.00 Pas at 1 1/s or 0.04 ± 0.04 Pas at 100 1/s, respectively. Except for two specimens at 1 1/s and three at 100 1/s, all the other fasting PND patients clearly showed higher viscosity compared to hydrated PND patients (Figure S1 and S2). Eleven out of thirteen patients (84.62%) reported a subjective reduction in PND symptoms after hydration (Figure S3). Two out of the thirteen patients (15.38%) reported the same PND symptoms after hydration (Figure S3). One of these patients showed increased viscosity at 1 1/sec as

well as at 100 1/sec. The other patient reported no subjective change in symptoms although the viscosity showed a decrease of 50% at 1 1/sec and 30% at 100 1/sec, respectively. None of the PND patients reported worsening of symptoms after hydration (Figure S3).

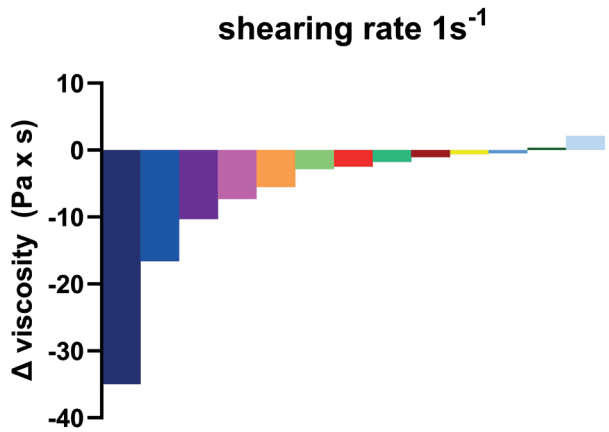

Figure S1. Change in viscosity after hydration. 11 out of 13 patients showed a decreased viscosity after hydration at 1 1/s. Each patient is labelled with the same color in this Figure and in Figure S2.

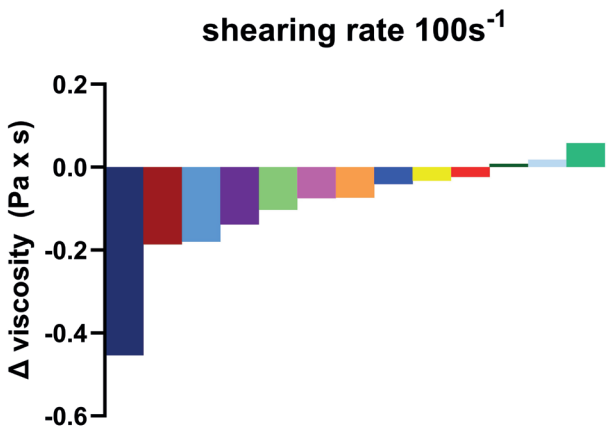

Figure S2. Change in viscosity after hydration. 10 out of 13 patients showed a decreased viscosity after hydration at 100 1/s. Each patient is labelled with the same color in this Figure and in Figure S1.

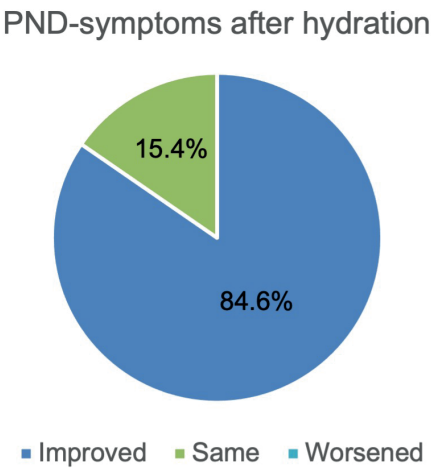

Figure S3. Reduction of subjective PND symptoms after hydration in 84.6%.

Table S1. Demographic information of study population.

Characteristics	Postnasal drip patients
Male / female (n = 13)	8 / 5 (61.54%/38.46%)
Mean age (years)	55.5 39.27 ± 17.94
CRS / no CRS	0 / 13 (0%/100%)
RARS / no RARS	0 / 13 (0%/100%)
Smoker / non-smoker	0 / 13 (0%/100%)
Mean number of medications	2.54 ± 2.76
Comorbidities	1.54 ± 1.45

Abbreviations: CRS = Chronic Rhinosinusitis, RARS = Recurrent Acute Rhinosinusitis