Eur Arch Otorhinolaryngol (2016) 273:1167–1171
DOI 10.1007/s00405-015-3712-8

RHINOLOGY

Evaluation of nasal mucociliary activity in patients with chronic renal failure

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Received: 8 February 2015 / Accepted: 2 July 2015 / Published online: 11 July 2015

Abstract The ability of respiratory mucosal surfaces to eliminate foreign particles and pathogens and to keep mucosal surfaces moist and fresh depends on mucociliary activity. Chronic renal failure (CRF) is an irreversible medical condition that may result in important extrarenal systemic consequences, such as cardiovascular, metabolic, and respiratory system abnormalities. Although there are studies describing nasal manifestations of CRF, data are lacking concerning the effects of the condition on nasal mucosa. The goal of the current study was to evaluate nasal mucociliary clearance (NMC) time in patients with CRF. This prospective cohort study conducted in a tertiary referral center included 32 non-diabetic end-stage CRF patients and 30 control individuals. The control group consisted of voluntary participants who had been referred to our clinic for symptoms other than rhinological diseases. The mean NMC times in CRF patients and control individuals were 12.51 ± 3.74 min (range 7–22 min) and 8.97 ± 1.83 min (range 6–13 min), respectively. The mean NMC time in patients with CRF was significantly longer than that in control individuals ($p < 0.001$). Clinicians must keep in mind that NMC time in CRF patients is prolonged and must follow-up these patients more closely for sinonasal and middle ear infections.

Keywords Chronic renal failure · Nasal mucociliary activity · Nasal mucociliary clearance time · Saccharine transit test

Introduction

The ability of respiratory mucosal surfaces to eliminate foreign particles and pathogens and to keep mucosal surfaces moist and fresh depends on effective ciliary activity and regular regeneration of airway fluids. These two functions comprise mucociliary activity, which is an important defensive mechanism of the nose [1]. The combined effect of mucous and the ciliary system can be evaluated by assessing nasal mucociliary clearance (NMC), which is measured as the elimination time of inhaled aerosols. NMC is a vital defense mechanism of respiratory system and it plays a crucial role in protecting the body against noxious inhaled materials. Any disturbance in mucociliary clearance system causes to stasis of secretions and secondary infections [1, 2].

Chronic renal failure (CRF) is an irreversible medical condition that may result in important extrarenal systemic consequences, such as cardiovascular, metabolic, and respiratory system abnormalities [3–5]. Several studies have demonstrated oropharyngeal, laryngeal, and cochleovestibular manifestations of CRF [6–9]. Although studies describing nasal manifestations of CRF exist [10, 11], data are lacking concerning the effects of CRF on nasal mucosa. The goal of the current study was to evaluate NMC rate in patients with CRF.

This study was submitted as an abstract for presentation at the 3th Congress of European ORL-HNS, June 7–11, 2015 in Prague, Czech Republic.

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Materials and methods

This cross-sectional study was conducted at the otolaryngology clinic of Dumlupinar University, Evliya Celebi Training and Research Hospital, Kutahya, Turkey. Kocatepe University Hospital Ethical Committee approved the study, and informed consent was obtained from the participants.

Participants

Patients with non-diabetic end-stage CRF undergoing hemodialysis who presented to the Nephrology outpatient clinic were enrolled in the study. The study group consisted of 32 CRF patients and 30 control individuals. The control group comprised voluntary participants who had been referred to our clinic for symptoms other than rhinological diseases. We excluded individuals with current upper respiratory tract infection, allergic rhinitis, major septal deviation, or a history of previous nasal surgery, smoking, or trauma.

Measurement of NMC

A particle of sodium saccharine measuring 1 mm across was placed on the surface of the inferior nasal concha, 1 cm behind its head to avoid the area of squamous epithelium. Clinical assessments were performed in a quiet room. Subjects were asked to avoid alcohol and coffee during the 6 h before their assessments. Owing to the circadian variation in mucociliary clearance, all assessments were performed between 14:00 and 17:00. Subjects who were able to taste saccharine deposited on their tongue were asked to report the first perception of a sweet taste. The saccharine transit test (STT) results were recorded in minutes. During the STT, subjects were asked to maintain normal ventilation and to swallow freely but to avoid deep breaths, talking, coughing, sneezing, sniffing, eating, and moving. The most patent nostril with the least resistance to physiological airflow was chosen.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (version 19.0, SPSS Inc., Chicago, IL, USA). As the distribution of the data was non-normal, nonparametric tests were used in the analyses. Comparison between groups was made using paired-samples *t* tests and unpaired *t* tests. Data are shown in the table as arithmetic mean ± standard deviation. The statistically significant level was accepted as a p value <0.05.

Results

A total of 62 patients completed the study. The CRF group consisted of 12 women and 20 men with a mean age of 61.44 ± 11.78 years (range 36–83 years); the control group consisted of 11 women and 19 men with a mean age of 63.57 ± 14.69 years (range 32–84 years). There were no significant differences between the patient and control groups in terms of age ($p = 0.52$) or sex ($p = 0.94$). Demographic data of the study and control patients are given in Table 1.

The STT was used to evaluate NMC in our study and it was carried out correctly in all subjects. Mean NMC times in the CRF and control groups were 12.51 ± 3.74 min (range 7–22 min) and 8.97 ± 1.83 min (range 6–13 min), respectively. The mean NMC time in patients with CRF was significantly longer than that in control individuals ($p < 0.001$; Fig. 1). Mean CRF disease duration was 6.38 ± 6.74 years (range 1–29 years). There was a positive correlation between CRF disease duration and NMC time; however, it was not statistically significant ($p < 0.062$; Fig. 2).

Discussion

Mucociliary clearance is the first line of the airway defense against noxious stimuli in the environment. Inhaled particles that may be harmful are retained by the mucus blanket and removed from the nasal cavity to the nasopharynx by the movements of cilia [12]. Measuring the rate of NMC is a reliable index of the clearance function of the upper and lower respiratory tract. There are three principal components that this mechanism depends on: the volume and composition of airway surface liquid (mucus and periciliary fluid), the ciliary structure and beating frequency, and the mucus–cilia interaction [13]. Therefore, alterations in either ciliary function or physical and chemical features of mucus can lead to ineffective mucociliary flow [14]. Prolonged transit times are considered to be indicative of impaired mucociliary clearance [2, 15]. Impaired nasal

Table 1 Characteristics of the study group vs. the control group

Characteristics	CRF group	Control group	p value*
Patients n (%)	32 (51.6 %)	30 (48.4 %)	0.44
M/F ratio	20/12	19/11	0.94
Mean age	61.44 ± 11.78	63.57 ± 14.69	0.52

CRF chronic renal failure, M/F male/female

* A p value <0.05 indicates significance

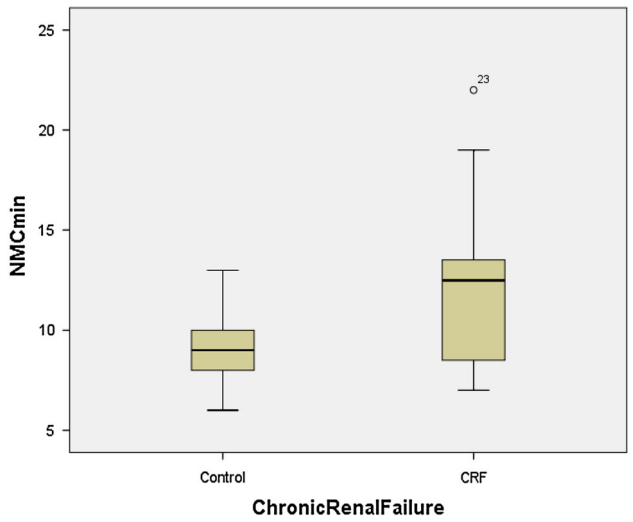

Fig. 1 The mean nasal mucociliary clearance time in patients with CRF was significantly higher than in the control group ($p < 0.001$). NMC min nasal mucociliary clearance minutes, CRF chronic renal failure

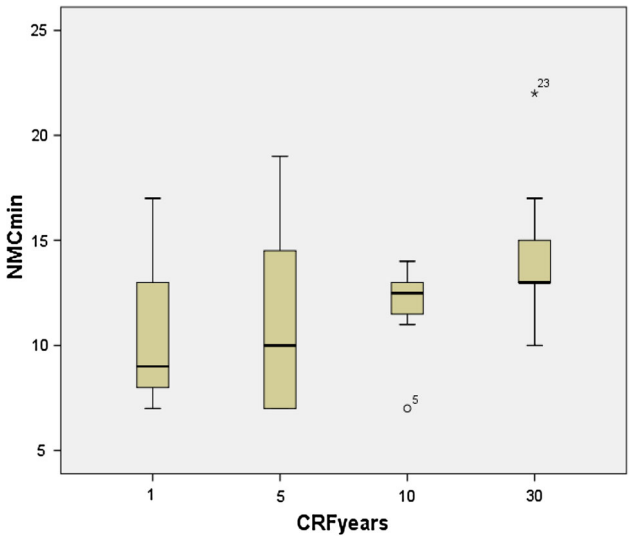

Fig. 2 There was a positive correlation between CRF disease duration and nasal mucociliary clearance time; however, it was not statistically significant ($p < 0.062$). NMC min nasal mucociliary clearance minutes, CRF chronic renal failure

mucociliary function may cause long-term respiratory tract diseases, and sinonasal and middle ear infections [16].

There are many factors affecting NMC time, such as temperature, moisture, partial oxygen pressure, pH, smoking and various inhaled agents' anatomic barriers (such as septum deviation and adenoid hypertrophy), and systemic diseases such as viral infections, chronic sinusitis, chronic and allergic rhinitis, cystic fibrosis, hypothyroidism, and diabetes mellitus [17–19]. Therefore, we excluded patients with major septal deviation, active infections, chronic pulmonary infections, and diabetes mellitus, and patients with a history of allergic rhinitis, septal surgery, and trauma.

Many in vivo and in vitro techniques have been used for the measurement of NMC. In vitro techniques such as stroboscopy, photon–electron techniques and phase contrast microscopy determine the ciliary beat frequency. However, they are too expensive and not suitable for routine use. In vivo techniques such as the STT and rhinoscintigraphy can be performed easily and are not expensive [20]. Although rhinoscintigraphy is a reliable and simply reproducible method, it has potential side effects. Therefore, we used the STT to evaluate NMC in the current study. The STT is the primary research tool for determining the effects of environmental, microbiological, or pharmacologic variables on NMC rate [21].

Chronic renal failure is a pathophysiological process with multiple etiologies, resulting in the inevitable destruction of nephron numbers and function. It is an irreversible medical condition that impairs kidney function [22]. When CRF reaches an advanced stage, dangerous levels of fluid, electrolytes, and wastes can accumulate in the body [22, 23]. Through direct or indirect effects on biological events, CRF may result in many extrarenal signs and symptoms. In the ear, nose, and throat, hearing loss accompanied by cochleovestibular symptoms such as tinnitus and dizziness is the most commonly encountered symptom of CRF. Hearing loss observed in CRF is a mild to moderate bilateral sensorineural hearing loss [8, 24]. In the larynx, the most common symptom is a hoarse voice, with a decrease in the thickness of the vocal folds [7]. In the oral cavity, a broad variety of manifestations have been reported in CRF patients including gingivitis, xerostomia, mucosal pallor and lesions, tooth mobility, and malocclusion [25].

A few studies have suggested that CRF also leads to nasal manifestations [9–11]. In a study conducted to define the changes in nasal mucosa due to CRF, Adler and Ritz [10] evaluated the nasal septum of 104 CRF patients (74 on maintenance hemodialysis; 30 after cadaveric renal transplantation). They observed spontaneous perforation of the nasal septum in eight of the patients. All patients showed a round or oval defect of the non-osseous septum, which was accompanied by marked atrophic rhinitis. They postulated that various factors may play a role in the pathogenesis of this lesion, including local trauma from postoperative nasal catheters, impaired mucosa cell proliferation, disturbed innervation of the vessels in the nasal septum due to polyneuropathy of the autonomic nervous system, and ischemia secondary to arteriolar narrowing. In a study by Mitschke [11], the examination of nasal biopsies of 113 patients with CRF yielded histological findings invariably showing wide, thin-walled vessels in the subepithelium and

the stroma, with chronic inflammation and metaplasia of the epithelium.

To the best of our knowledge, this study is the first to evaluate the effect of CRF on NMC as measured by the STT. We found a significant increment in NMC time in this patient population. CRF is known to accelerate the progression of atherosclerosis and microvascular disease involving smaller vessels [3, 23]; these processes may play a role in explaining our findings. Moreover, salivary flow may decrease in patients with CRF [26, 27], reaching levels even below the limit of hyposalivation [28], and the underlying mechanism might be related to direct glandular damage [29]. The possible mucus gland damage may be the other factor that leads to deteriorating NMC.

Infectious complications are the main cause of morbidity and the second cause of mortality after cardiovascular disease in patients with CRF undergoing hemodialysis [30]. Understanding the reasons for infectious diseases and the underlying pathologies in this patient population may provide the opportunity for prophylaxis. Preventive measures such as health education could inform patients of the risks of infectious diseases and provide cautionary advice.

The strength of our study is the assessment of NMC in CRF patients for the first time. However, the results presented are preliminary and the sample size was limited. Another important limitation was the absence of pathophysiological evaluation of nasal mucosa of the participants. Further studies are needed to determine the exact mechanisms of the disturbing effect of CRF on sinonasal mucosa in a larger cohort.

Other limitations of the present study relate to disadvantages of the STT, which depends on the sensation of taste and, therefore, individual differences in taste sensation could affect the results. In addition, unlike rhinoscintigraphy, the STT could not supply objective and detailed information for quantitative analyses [12]. Furthermore, rhinoscintigraphy provides more accurate test results than the STT [31, 32]. Although rhinoscintigraphy is a reliable and easily reproducible method, low-dose radiation exposure is a disadvantage of the technique [33]. The STT is considered a safer and easier method to evaluate NMC in patients with CRF.

Conclusion

Clinicians must keep in mind that NMC time in CRF patients is prolonged and should follow-up these patients more closely for respiratory tract diseases, and sinonasal and middle ear infections. Awareness should be created among patients and health-care providers, and proper intervention strategies should be put in place.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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