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Klinik Araştırma

Nasal mucociliary clearance in chronic renal failure: Comparision of pre-dialysis and dialysis stages

Kronik böbrek yetmezliğinde nazal mukosiliyer klirens: Diyaliz öncesi ve diyaliz dönemlerinin karşılaştırılması

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ABSTRACT

Objective: Chronic renal failure (CRF) is an irreversible condition that has many otorhinolaryngological manifestations. In this study we aimed to investigate the effects of CRF and haemodialysis treatment on nasal mucociliary clearance (MCC) and to explain the possible pathophysiological mechanisms.
Methods: This study included 27 patients with end-stage CRF who were not undergoing haemodialysis (pre-dialysis group), 36 patients with CRF on haemodialysis (dialysis group), and 36 heathy individuals. Nasalmucociliary clearance was measured using the saccharin clearance test (SCT) and the results were statistically compared among the three groups.
Results: Mean SCT times in the control, pre-dialysis, and dialysis groups were 11.7±5.7, 30.16±11.66, and 27.33±9.4 min, respectively. The results for both the pre-dialysis and dialysis groups were significantly higher when compared with the control group (both $p<0.001$). There was no significant difference between the pre-dialysis and dialysis groups ($p=0.22$).
Conclusion: Both CRF and haemodialysis treatment cause severe prolongation of MCC time. Patients with CRF should be monitored closely for middle ear, sinonasal, and respiratory tract infections and informed about potential risks of infection.

Key words: Chronic renal failure, dialysis, infection, mucociliary clearance, saccharin

ÖZ

Amaç: Kronik böbrek yetmezliği (KBY), kulak burun boğaz açısından birçok klinik bulgu oluşturan ve geri dönüşü olmayan bir durumdur. Bu çalışmada, KBY'nin ve hemodiyaliz tedavisinin nazal mukosiliyer klirens üzerine etkisinin araştırılması ve olası patofizyolojik mekanizmaların açıklaması amaçlanmıştır.
Yöntemler: Bu çalışmaya, son dönem KBY olan ve diyaliz tedavisi almayan 27 hasta (pre-diyaliz grup), son dönem KBY olan ve diyaliz tedavisi almakta olan 36 hasta (diyaliz grubu) ve 36 sağlıklı birey (kontrol grubu) dahil edildi. Nazal mukosiliyer klirens ölçümü sakkarin klirens testi kullanılarak ölçüldü ve sonuçlar üç grup arasında istatistiksel olarak karşılaştırıldı.
Bulgular: Ortalama sakkarin klirens testi zamanı kontrol, pre-diyaliz ve diyaliz gruplarında sırasıyla 11,7±5,7, 30,16±11,66 ve 27,33±9,4 dk. olarak bulundu. Pre-diyaliz ve diyaliz gruplarında, her iki grup için elde edilen sonuç kontrol grubuna göre anlamlı ölçüde yüksekti (her iki $p<0,001$), pre-diyaliz ve diyaliz grupları arasında anlamlı fark saptanmadı ($p=0,22$).
Sonuç: Hem KBY hem de hemodiyaliz tedavisi nazal mukosiliyer klirens zamanında ciddi uzamaya neden olmaktadır. Bu nedenle KBY olan hastalar orta kulak, sinonazal veya solunum yolu enfeksiyonları açısından yakından takip edilmeli ve olası enfeksiyon risklerine karşın bilgilendirilmelidirler.

Anahtar kelimeler: Diyaliz, enfeksiyon, kronik böbrek yetmezliği, mukosiliyer klirens, sakkarin

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INTRODUCTION

Chronic renal failure (CRF) is defined as the inevitable damage and destruction of nephrons and a reduction in glomerular filtration rates resulting in chronic, progressive deterioration of the liquid-electrolyte balance [1,2]. CRF is an irreversible condition with multiple aetiologies that may lead to many physiological, haematological, metabolic, endocrine, cardiovascular, and respiratory system problems [3,4].

Mucociliary clearance (MCC) is the primary defence mechanism in the respiratory system against noxious inhaled materials [5]. MCC occurs via the synchronised movement of cilia in the respiratory tract in a manner that propels mucus and other substances trapped within the mucus towards the pharynx to be swallowed [6]. In healthy individuals, MCC typically works effectively. However, a variety of systemic factors alter mucociliary activity, including diabetes mellitus [7], hypertension [7], and hypothyroidism [8].

Although CRF has a multifactorial systemic effect, its effect on MCC has received little attention. Therefore, we examined the effects of CRF and haemodialysis on MCC using the saccharin clearance test (SCT) and aimed to explain the possible pathophysiological mechanisms.

MATERIALS and METHODS

This study adhered to the guidelines of the Helsinki Declaration of the World Medical Association and was approved by the research ethics committee of a tertiary referral centre (no. 2015/38). Written informed consent was obtained from all participants before the study.

A total of 27 patients with end-stage CRF who were not undergoing haemodialysis comprised the pre-dialysis group; and 36 patients with CRF on haemodialysis comprised the dialysis group, and 36 heathy individuals were recruited as the control group. Patients with diabetes mellitus, cystic fibrosis, hypertension, hypothyroidism, nasal septum deviation, allergic rhinitis, and sinonasal infections, and smokers were excluded from the study .

The saccharin clearance test (SCT) was used to measure MCC. The SCT involves placing 5 mg (1/4 tablet) of saccharin behind the anterior edge of the inferior turbinate at the same location in all patients. The result was measured as the time (min) required for the patient to perceive the taste of saccharin. One researcher performed all of the SCTs.

The SCT times were compared statistically using SPSS for Windows software (ver. 20.0; SPSS, Chicago, IL, USA). Continuous variables were presented as means±standard deviation and categorical variables were presented as percentages. Qualitative values were compared using the chi-square test. The significance of different SCT times among the pre-dialysis, dialysis, and control groups was evaluated using analysis of variance (ANOVA). The Spearman correlation coefficient (r) was used to analyse the correlation of SCT time with disease duration in pre-dialysis and dialysis groups. A p-value of <0.05 was taken to indicate statistical significance.

RESULTS

The pre-dialysis group included 27 patients (15 females, 12 males) with a mean age of 41.17±12.32 years (range: 17-59 years). The dialysis group included 36 patients (21 females, 15 males) with a mean age of 38.55±10.74 years (range: 21-64 years). The control group included 36 healthy subjects (20 females, 16 males) with a mean age of 40±13.96 years (range: 18-55 years). The age and sex distributions of the patients did not differ significantly among the groups.

The mean duration of CRF was 5.18±2.33 years (range: 2.1-8.5 years) in the pre-dialysis group and 17.18±5.33 years (range: 3.8-31.3 years) in the dialysis group. The duration of CRF time was significantly greater in the dialysis group (p=0.013). The mean duration of haemodialysis was 10.52±5.3 years (range: 4-30 years).

The mean SCT time was significantly greater in the pre-dialysis and dialysis groups compared to the

controls (pre-dialysis: 30.16±11.66 vs. 11.7±5.7 min, respectively, p<0.001; dialysis: 27.33±9.4 vs. 11.7±5.7 min, p<0.001). Although the SCT time was higher in the pre-dialysis group, it was not significantly different from the dialysis group (30.16±11.66 vs. 27.33±9.4 min, respectively, p=0.22). Table 1 presents the SCT times. There was a negative correlation between the SCT time and disease duration between the pre-dialysis and dialysis groups (r=-0.712, p=0.016).

Table 1. SCT times.

	Control Group (n=36)	Pre-dialysis group (n=27)	p*	Dialysis group (n=36)	p**
SCT (range)	6.3-16.6	9.5-48.8		9.3-60	
SCT (min)	11.7±5.7	30.16±11.66	<0.001[a]	27.33±9.4	<0.001[a]

SCT, saccharin clearance test; CRF, chronic renal failure.
[a]analysis of variances.
**analysis between control group and pre-dialysis group.*
***analysis between control group and dialysis group.*

DISCUSSION

Mucociliary clearance is a vital respiratory system defence mechanism. The ability of respiratory mucosal surfaces to eliminate foreign particles and pathogens and to keep mucosal surfaces moist and fresh depends on mucociliary activity. Effective MCC requires appropriate mucus production, coordinated ciliary activity, and the mucus-cilia interaction. Cilia line the nasopharynx, middle ear, paranasal sinuses, and tracheobronchial airways; therefore, any disturbance in MCC leads to the stagnation of secretions and recurrent middle ear, sinonasal, and lower respiratory tract infections [5,9-11]. There are two main causes of MCC impairment: impaired ciliary function or mucus structure and movement [12,13].

Chronic renal failure is a pathophysiological process that is associated with enhanced oxidative stress, hypoxia, and endothelial dysfunction [14]. Oxidative stress is the imbalance between the generation of reactive oxygen species (ROS) and anti-oxidative defence mechanisms. Renal toxicity, immunological disorders, ischemia and reperfusion result in the elevated production of ROS, which are active in the pathogenesis of endothelial dysfunction [15,16]. The primary pathological changes of endothelial dysfunction occur in small vessels or capillaries and result in capillary vasoconstriction, rarefaction, and limited oxygen diffusion, and decreased microcirculatory blood flow leads to chronic cellular hypoxia, which is associated with the pathogenesis of end-organ damage [17,18].

Our results do not fully explain the molecular mechanisms of the prolonged SCT times and MCC damage during CRF or haemodialysis treatment, but we speculate that ciliary movements are affected directly by the formation of free oxygen radicals or uremic toxins with resultant damage to dynein arms and microtubules. Endothelial dysfunction and vasoconstriction reduce blood flow and might also decrease periciliary blood flow and cause hypoxia in the cilia. Liquid-electrolyte imbalance or deterioration of glandular tissues by uremic toxins or oxidative stress can lead to an increase in mucus viscosity, rendering ciliary clearance ineffective. Furthermore, as supported by studies by Fahy and Dickey, an increase in mucus viscosity can cause the periciliary liquid layer to shrink, resulting in the cilias being squeezed underneath the mucus layer which also blocks their movement [19]. Previously, nasal biopsies of CRF patients revealed chronic inflammation and metaplasia of the epithelium with thin-walled vessels and extensive fibrosis [20].

To date, only one study evaluated MCC during haemodialysis treatment [21] using the SCT to compare a group of dialysis patients with healthy controls and found a significant difference in MCC (12.51±3.74 vs. 8.97±1.83 min). In that study, the mean disease duration was 6.38±6.74 years (range: 1-29 years). Our study also assessed pre-dialysis patients. The MCC was significantly higher in both the pre-dialysis and dialysis groups than in the controls. Although the duration of disease was much shorter in the pre-dialysis group than in the dialysis group, the MCC time was paradoxically higher. These findings suggest that haemodialysis reduces the effects of CRF on

mucociliary dysfunction. This phenomenon might be explained by haemodialysis which filters toxins and oxidants and shifts the liquid-electrolyte balance favourably.

In conclusion, CRF causes severe prolongation of the MCC time. The clinical significance of this effect is of concern in terms of middle ear, sinonasal, or respiratory tract infections. Patients with CRF or those undergoing haemodialysis should be monitored more closely and informed about the possible susceptibility to infections. This study suggests that haemodialysis might have shorten CRF-induced mucociliary clearance. Further studies will be necessary to elucidate the exact mechanism.

The strength of our study is the evaluation of both pre-dialysis and dialysis patients for the first time. However, the small sample size limits its interpretation and generalisability. The main limitation is the lack of clinical follow-up data on respiratory tract, middle ear, and sinonasal infections. Such information could determine the association between the possible side effects of CRF-related MCC impairment and relevant morbidities.

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