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Original article

The effect of non-diabetic chronic renal failure on olfactory function

S. Koseoglu [a], S. Derin [a,*], B. Huddam [b], M. Sahan [a]

[a] Department of Otolaryngology, Mugla Sıtkı Kocman University, School of Medicine, Mugla, Turkey
[b] Department of Nephrology, Mugla Sıtkı Kocman University, School of Medicine, Mugla, Turkey

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ABSTRACT

Objectives: In chronic renal failure (CRF), deterioration of glomerular filtration results in accumulation of metabolites in the body which affect all organs. This study was performed to investigate the olfactory functions, and determine if hemodialysis or peritoneal dialysis improves olfactory function in non-diabetic CRF patients.
Materials and methods: The olfactory functions were analyzed in CRF patients not on a dialysis program and had a creatinine level ≥ 2 mg/dL, in CRF patients on hemodialysis or peritoneal dialysis, and in healthy controls. Diabetic patients were excluded since diabetes alone is a cause of olfactory dysfunction. The study group consisted of a total of 107 individuals including 38 CRF patients on a hemodialysis program, 15 CRF patients on peritoneal dialysis, 30 patients with a creatinine level ≥ 2 mg/dL without any need for dialysis, and 24 healthy controls with normal renal functions. Olfactory functions were analyzed with "Sniffin' sticks" test, and the groups were compared for the test results.
Results: All test parameters were impaired in patients with CRF. The median TDI scores of the patients with CRF and the healthy subjects were 24.75 (13–36) and 32.5 (27.75–37.75), respectively, with a statistically significant difference in between ($P < 0.001$). The olfactory functions for the dialysis patients were better than those for the CRF patients not on a dialysis program ($P = 0.020$).
Conclusion: Non-diabetic CRF affects olfactory functions negatively. Dialysis improves olfactory functions in those patients.

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1. Introduction

Although olfactory dysfunction is frequent in the population and affects the quality of life negatively, neither physicians nor patients consider it important.

A number of conditions play a role in smell disorders. Olfactory dysfunction may be seen in nasal diseases such as chronic rhinosinusitis with or without nasal polyps. In addition, head trauma, neurodegenerative diseases, and some congenital syndromes may be accompanied by olfactory dysfunction.

Chronic renal failure (CRF) may be defined as a chronic and progressive deterioration of the metabolic and endocrine functions, resulting from impaired glomerular filtration and fluid-electrolyte imbalance. CRF is a frequently seen health problem. Its most frequent causes are chronic glomerulonephritis, diabetes, hypertension, polycystic kidney disease, obstructive uropathy, and interstitial nephritis. Various metabolites accumulate in the body due to impaired renal filtration, affecting all organs in the body.

CRF patients complain of olfactory impairment. Olfactory functions deteriorate in case of end-stage renal failure due to malnutrition and impaired fluid intake [1]. Impaired olfactory function has recently been shown in patients with CRF [2,3].

However, it has been shown that it is readily reversible by hemodialysis or kidney transplantation [3,4].

In this study, we aimed to investigate the olfactory functions in non-diabetic CRF patients, and determine whether hemodialysis or peritoneal dialysis improved olfactory function in this patient population.

2. Materials and methods

This study was conducted on 107 (51 females and 56 males) individuals aged between 18 and 75 years. The study group consisted of 38 CRF patients on hemodialysis program, 15 CRF patients on peritoneal dialysis, and 30 patients with a creatinine level ≥2 mg/dL and not needing dialysis. The control group included 24 healthy subjects with normal renal functions. The median age of the CRF group was 52 (19–73) years, and the median age of the control group was 44 (38–75) ($P = 0.411$). The distribution of the genders was similar in CRF and the control groups ($P = 0.235$) (Table 1).

* Corresponding author. Tel.: +90252 211 51 59.
E-mail address: serhanderin@yahoo.com.tr (S. Derin).

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Table 1
The data and comparison of the study and the control groups..

	Study group (mean ± std error)	Control (mean ± std error)		
	$n = 83$	$n = 24$	P	Statistical Method
Age (years)	52 (19–73)[a]	44 (38–75)[a]	0.411	Mann-Whitney U test
Gender (female/male)	37/46	14/10	0.235	Pearson's chi-squared test
Odor threshold score	4.81 ± 0.27	6.47 ± 0.33	0.001	Mann-Whitney U test
Odor discrimination score	9.79 ± 0.30	12.87 ± 0.29	<0.001	Mann-Whitney U test
Odor identification score	10.24 ± 0.27	12.95 ± 0.29	<0.001	Mann-Whitney U test
TDI score	24.75 (12–36)[a]	32.5(27.75–37.75)[a]	<0,001	Independent sample T test

TDI: Threshold, discrimination, identification.
[a] Median, minumum and maximum values of ages in control and study groups.

The etiological factor for CRF was hypertension in 33 (39.75%), polycystic kidney disease in 12 (14.45%), glomerulonephritis in 10 (12.04%), obstructive uropathy in 6 (7.22%), idiopathic in 10 (12.04%), and other factors (gout, eclampsia, pyelonephritis, nephrectomy, etc.) in 12 (14.45%) patients.

None of the patients had an obstructive nasal pathology on otorhinolaryngological examination. Nasopharynx, oropharynx and laryngeal examinations were normal.

Diabetic patients were excluded since diabetes alone is a cause of olfactory dysfunction. Hemoglobin (Hb) and C-reactive protein (CRP) levels of all participants were determined. The exclusion criteria were acute upper or lower respiratory tract inflammation, chronic rhinosinusitis with or without nasal polyps, tumors of nasal cavity, nasopharynx, oropharynx, larynx, brain disorders and neurodegenerative diseases. The patients with post-traumatic olfactory dysfunction and major depressive disorders were also excluded from the study.

The study protocol was approved by the Clinical Research Ethics Committee of Muğla Sıtkı Koçman University. All participants provided their written informed consents.

2.1. Smell test

"Sniffin' sticks" test (Burghart GmbH, Wedel, Germany) was used to measure olfactory function, and Threshold, Discrimination, Identification (TDI) score was used to present the results. The same otorhinolaryngologist did smell tests and otorhinolaryngological examination of the patients. The smell test was performed within the first hour of hemodialysis.

The smell test sequence was odor threshold test, odor discrimination test, and finally odor identification test, with 3-minute breaks between tests.

For odor presentation, the researcher removed the pen cap for 3–4 s, and the tip of the pen was placed 1–2 cm in front of the participant's nostrils. The test consisted of one threshold and two suprathreshold sub-tests. Odor threshold (OT) was assessed using n-butanol as a single odorant. The smell threshold was determined in a so called "staircase procedure". The odor thresholds were determined as the mean of the last 4 from a total of 7 staircase reversals. Odor discrimination (OD) between two different odorants was assessed. The subject was presented with three pens; two contained the same odorant and one contained a different one. The subject's task was to indicate which one smelled different. This comparison was performed for 16 triplets. Odor identification was performed for 16 common odors. Identification of individual odors was performed from a card which included 4 alternatives. OI score was the sum score of the correctly identified odors. Lastly OT, OD, and OI scores were summed up to determine TDI score. Subjects with a TDI score > 30 were considered to have a normal olfactory function (normosmia); subjects with a TDI score of 15–30 were considered to have decreased olfactory function (hyposmia); and subjects with a TDI score < 15 were considered to have loss of olfactory function (anosmia) [5].

The patient and the study groups were compared for OT, OD, OI and TDI scores. In addition, the CRF group was divided into 3 subgroups as hemodialysis, peritoneal dialysis, and no-dialysis groups, and compared for the results of the olfactory tests.

2.2. Statistical analysis

SPSS (Statistical Package for Social Sciences) for Windows, version 22.0 program was used to analyze data. Normality of data distribution was tested with Kolmogorov-Simirnov test. The differences between the means of the variables were tested with Oneway Anova test, and the differences were tested with Tukey HDS test or 2 independent Samples T test, if the distribution of the variables were normal. Mann-Whitney U or Kruskal-Wallis tests were used if the distribution of the variables were not normal. The significance level was set at $P < 0.05$.

3. Results

We determined functional anosmia in 7 (8.43%), hyposmia in 55 (74.69%), and normosmia in 14 (16.86%) of 83 patients with CRF. OT, OD, OI, and TDI scores of the CRF group were significantly lower compared to the control group ($P = 0.001$, $P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively). When CRF patients were grouped for the etiological factors (hypertension, polycystic kidney disease, glomerulonephritis, obstructive uropathy, idiopathic, and other factors), it was seen that the TDI scores did not show any difference among the groups ($P = 0.514$).

The CRF group was divided into 3 subgroups as hemodialysis group, peritoneal dialysis group, and no-dialysis group. There were no statistically significant differences among those three groups for age or gender ($P = 0.097$ and 0.074, respectively). Comparison of three subgroups for Hb and CRP levels did not reveal any statistically significant results ($P = 0{,}347$ and $P = 0{,}392$, respectively). The TDI score was 25.5 (13–35.25) in hemodialysis group, 27.5 (14.5–36) in peritoneal dialysis group, and 22.5 (12–33.75) in no-dialysis group. The TDI scores of the hemodialysis and peritoneal dialysis groups were significantly better when compared to no-dialysis group ($P = 0.020$). In addition, OT scores were significantly better in dialysis groups when compared to no-dialysis group ($P = 0.029$). Three CRF subgroups did not show any differences for OD or OI scores ($P = 0.381$ and $P = 0.081$, respectively) (Table 2). When the patients who did not need dialysis were analyzed separately, no negative correlation was seen between the creatinine levels and the TDI scores. (TDI score was independent from creatinine levels).

4. Discussion

The results of this study indicated that olfactory functions, as reflected by odor threshold, odor discrimination, odor identification, and TDI scores, were significantly impaired in patients with

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