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Chemosensory function and food preferences among haemodialysis patients

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ABSTRACT

INTRODUCTION. Malnutrition and disturbed sense of smell and taste frequently occur in patients treated with chronic haemodialysis. The common denominator between chemosensation and nutrition may be food preferences. Our aim was to investigate smell and taste function as well as food preferences among haemodialysis patients and compare the results with those of age-matched controls.

METHODS. An observational case-control study was conducted on 29 patients on chronic haemodialysis and 39 age-matched healthy controls. Chemosensory function was evaluated using validated gustatory and olfactory tests. Food preferences were recorded using a questionnaire of 63 items including a five-point Likert scale of familiarity, liking and frequency.

RESULTS. Chemosensory function was significantly poorer among patients than among controls. Patients had significantly lower familiarity and frequency of consumptions of all food categories than controls and they also had significantly lower liking of vegetables, fruits and starches.

CONCLUSIONS. Implementation of the provided knowledge about haemodialysis patients' smell and taste function including their food preferences are suggested, such as enhancement of odorant intensity, use of taste amplification, cooking habits and exposure to more varied food items. Assessments of food preferences and chemosensory function prior to determination of individual dietary schedules are therefore recommended.

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Malnutrition frequently occurs in patients treated with chronic haemodialysis (HD) and may cause increased morbidity and mortality [1, 2]. The underlying mechanisms of malnutrition are multiple and include reduced food intake due to decreased appetite, reduced salivary flow and reduced taste perception. An inadequate dietary intake seems to be the most significant factor [3], and dietary adherence rates in HD patients are suboptimal [4, 5].

Disturbed sense of smell and taste is frequently reported among HD [6, 7]. Altered taste perception is associated with poorer nutritional status and increased mortality [8], and taste may play a role in dietary adherence in

patients with end-stage kidney disease [6, 9].

The aim of this study was to investigate chemosensory function and food preferences among patients treated with HD and to compare the results with those of age-matched healthy controls.

METHODS

In this observational study, food preferences and smell & taste function were examined in 29 patients with chronic renal failure treated with haemodialysis (HD) and the results were compared with those of 39 healthy age-matched controls. The study was conducted from February 2018 to August 2019. The patients underwent clinical examination and answered questionnaires before or during their haemodialysis. The controls underwent identical tests.

From a pool of 225 patients attending HD, 29 adults (17 males/12 females; median age 65 years) were enrolled in the study according to the following criteria: Age between 30 and 85 years, haemodialysis for a minimum of three months. A control group of 39 age-matched healthy controls (17 males; 22 females; median age 70 years) were recruited. They were included if they had no chronic illnesses and did not take any medication apart from blood pressure and cholesterol-lowering medications. The exclusion criteria in both groups were dementia, mental illnesses, less than one year after stroke, previous chemotherapy, head/neck radiation therapy or granulomatosis with polyangiitis.

Participants completed a questionnaire concerning subjective assessment of olfactory/gustatory function and medical treatment including intravenous iron therapy (a common treatment of patients in haemodialysis, which may result in a changed sense of taste). Furthermore, participants were screened for cognitive deficits by the Mini Mental State Examination (MMSE), for depression by the Major Depression Inventory (MDI) and for sinonasal diseases by the Sino-Nasal Outcome Test-22 (SNOT-22). A detailed, clinical ear-nose-throat-examination was performed including flexible rhinoscopy.

Smell was tested by the validated Sniffin' Sticks Threshold, Discrimination and Identification (TDI) test [10]. Taste was evaluated using the Taste Drop Test [11].

A modified food item questionnaire was used. Modifications were made from a validated questionnaire used in a similar study involving 100 teenagers in 2017 [12]. Minor modifications were introduced in order to adapt to the older generation's food habits. The resulting 63 food items were divided into six categories: vegetables, fruits, meat and fish, dairies, snacks and starches. The participant's liking, familiarity and frequency of the individual items were registered.

A re-test concerning food preferences was conducted 7-14 days after the primary test among 25 controls.

The Ethical Committee of the Central Denmark Region approved the study, which was conducted in line with the Declaration of Helsinki Ethical Principles of Medical Research. Project number M-2018-188-18.

Statistics

Data are presented as means with 95% confidence intervals (CI) in case of normally distributed data. Binomial data are presented as frequencies and percentages.

The test-retest reliability of the food preference questionnaire was analysed in terms of the observed agreement rates and Cohen's kappa. The unpaired t-test was used to compare normally distributed data with equal variances. For data with unequal variance, an unequal t-test was used. Considering the small number of participants and the limitations of evaluating normality, Wilcoxon's rank sum test was subsequently performed

to validate statistical significance. A $p < 0.05$ was considered significant. The statistical analyses were conducted in STATA/IC 14.2 for Mac (StataCorp, Texas, USA).

Correlations were assessed using the Pearson's r correlation coefficient.

Trial registration: Danish Ethical Committee project number: M-2018-188-18.

RESULTS

Demographics are listed in **Table 1**. The controls were age matched but deviated from the patients by having a higher prevalence of females, fewer smokers, a higher educational level, more food allergies and chosen food restrictions. Patients had a higher BMI and a higher prevalence of sinonasal disease, depression and cognitive dysfunction.

TABLE 1 Demographics.

	Patients (N = 29)	Controls (N = 39)	p value
Gender, %	0.23		
Men	59	44	
Women	41	56	
Age, median (range), yrs	70 (34-82)	65 (45-78)	
Smoking			
Currently smoker, n	7	6	
Former smoker, n	9	3	
Mean smoking yrs, mean (95% CI)[a]	40.07 (19.71-60.44)	9.77 (3.60-15.96)	< 0.05
Food allergy, %	3	23	< 0.05
Chosen food restrictions, %[b]	0	18	< 0.05
Long education, %[c]	26	59	< 0.05
BMI, mean (95% CI), kg/m^2	25.92 (23.67-28.18)	24.38 (23.4-25.37)	0.16
SNOT-22-score, mean (95% CI)[d]	19.85 (12.09-28.61)	6.95 (4.63-9.27)	< 0.05
MDI score mean (95% CI)[e]	11.88 (7.75-16.02)	3.30 (2.17-4.44)	< 0.05
MMSE score, mean (95% CI)[f]	27.00 (25.86-28.14)	29.28 (28.98-29.57)	< 0.05

CI = confidence interval; MDI = Major Depression Inventory; MMSE = Mini-Mental State Examination; SNOT-22 = Sino-Nasal Outcome Test-22.
a) 1 smoking yr corresponds to 20 cigarettes daily for 1 yr.
b) Defined as vegetarian, vegan or flexitarian.
c) > 15 yrs in school.
d) Max score 110, high score: sino-nasal disease.
e) Max score 50, depression: ≥ 20.
f) Max score 30, dementia: ≤ 23.

Taste test results and smell test results are visually presented in **Figure 1**. Test score comparisons for patients versus controls are presented in **Table 2**. Overall, patients had a significantly poorer sense of smell and taste than controls. Patients' TDI scores were significantly lower than those of the controls, especially due to discrimination and threshold, whereas identification scores did not differ significantly between the groups.

FIGURE 1 Test results.

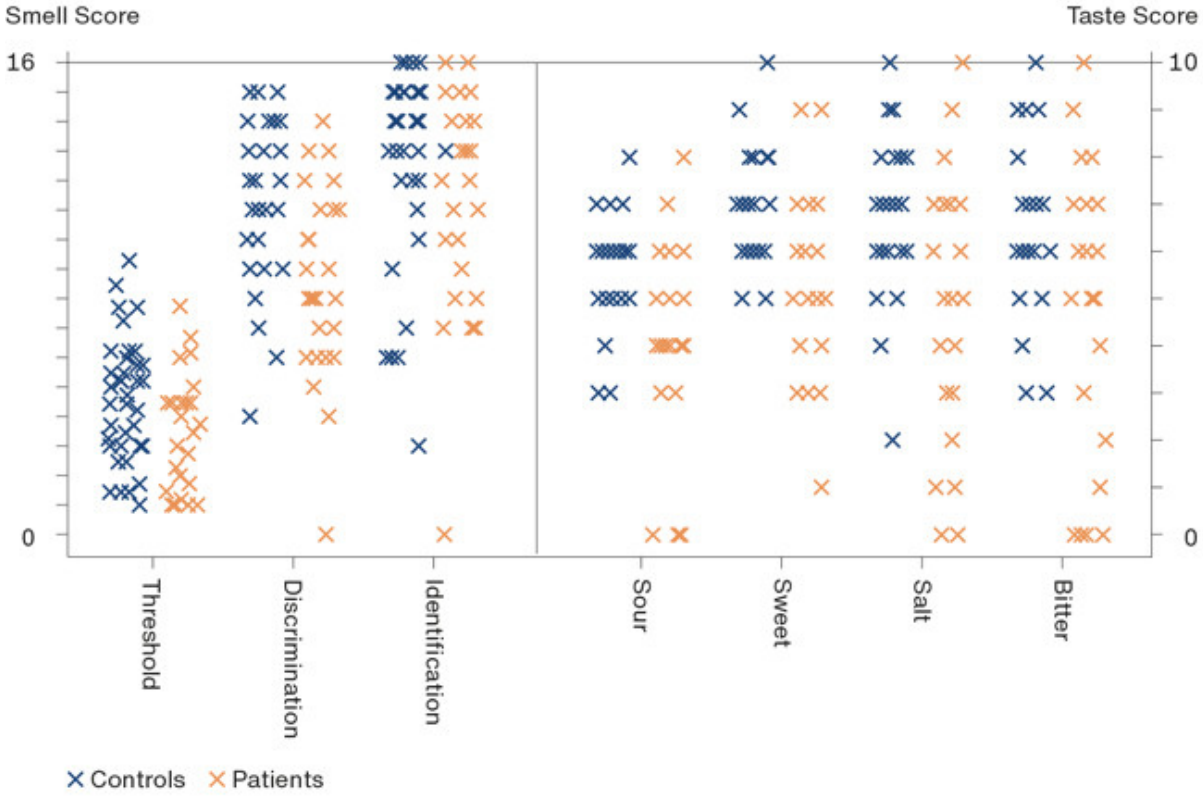

TABLE 2 Chemosensory function.

	Patients	Controls	p value[a]
Smell, mean (95% CI), score[b]			
Threshold	3.56 (2.78-4.33)	4.47 (3.79-5.15)	0.08
Discrimination	8.68 (7.5-9.89)	11.33 (10.42-12.25)	< 0.05
Identification	11.75 (10.37-13.14)	12.71 (11.58-13.85)	0.28
Total TDI test score	24.00 (21.19-26.82)	28.06 (25.85-30.27)	< 0.05
Taste, mean (95% CI), score[c]			
Sour	3.92 (3.1-4.75)	5.74 (5.4-6.08)	< 0.05
Sweet	5.17 (2.46-5.89)	6.77 (6.42-7.11)	< 0.05
Salty	5.10 (4.07-6.14)	6.87 (6.36-7.38)	< 0.05
Bitter	4.64 (3.43-5.86)	6.69 (6.17-7.2)	< 0.05
Total	18.82 (16.07-21.58)	26.08 (24.97-27.19)	< 0.05
Subjective, %			
$Smell_{Normal}$	80.7	47.4	< 0.05
$Smell_{Increased}$	0	42.1	< 0.05
$Smell_{Decreased}$	19.3	10.5	0.31
$Taste_{Normal}$	74	65.8	0.47
$Taste_{Increased}$	0	31.6	< 0.05
$Taste_{Decreased}$	26	2.6	< 0.05

TDI = Sniffin' Sticks Threshold, Discrimination and Identification.
a) By t-test and rank sum test.
b) Max score for each test = 16, max total score 48.
c) Max score for each test = 10, max total score 40, a score ≥ 22 is defined as normogeusia (normal taste), whereas a score < 22 represents hypogeusia (impaired taste).

All taste scores were significantly lower in patients than in controls. The differences between the two groups were most pronounced with regards to the thresholds for bitter and sour.

Smell was further evaluated by multiple regression analysis of patients on the TDI score, which included smoking status, age and gender. Kidney disease negatively affected the outcome of the TDI score by –3.9 points (95% CI: –7.3-–0.5). Age negatively affected the TDI score by –1.8 per ten years of age (95% CI: –3.4-–0.2) and smoking status seemed to negatively affect the outcome of the TDI score as well, but the effect was only borderline statistically significant with a mean TDI score drop of –4.3 (95% CI: –8.7-0.1).

The test-retest using the food questionnaire among the controls yielded an observed agreement of 75%. Adjusting for random answers yielded a Cohen's kappa of 0.46 (95% CI: 0.15-0.77), which corresponds to a moderate retest reliability.

Means of liking, familiarity and frequency pooled into six categories were significantly higher among controls except for liking of meat and fish, dairies and snacks. In general, patients had the lowest liking of most items, but this was most pronounced for vegetables, fruits, meat and fish, and starches. Patients had a slight tendency to prefer cucumber, meat (bacon, ham, liver and meatballs), dairy products (butter, cream and mayonnaise) and snacks (biscuits, chocolate biscuits and liquorice). Patients only liked winegum and white bread significantly better than controls.

Patients consumed most of the 63 items less frequently than did controls. No significant differences were found for potatoes, grapes, strawberries, ground beef, ham and liver, whereas patients ate winegum and white bread significantly more frequently than controls.

Comparisons between chemosensory function and food preferences revealed some statistical correlations: the higher smell scores were observed among both patients and controls, the more familiar were the respondents with vegetables ($r = 0.5558$, $p < 0.005$ and $r = 0.3727$, $p < 0.05$).

DISCUSSION

The key findings of the present study are summarised in **Table 3.** Both chemosensory functions and food preferences in patients treated with chronic haemodialysis deviated significantly from those of healthy age-matched controls. The patients were able to identify the odorants and tastants, but their thresholds and discrimination scores were reduced. They typically preferred healthy food items. However, such items were less consumed than among controls. Interestingly, many food items were less familiar in the patient group.

TABLE 3 Practical applications.

	Key finding	Practical application
Smell function	Significantly lower in patients	Patients should be served food with increased odour, e.g. heating and freshly preparing food can smell more intense
Taste function	Significantly lower in patients	Patients should have served food with increased taste, e.g. lemon is needed for fish, as they have difficulty tasting sour. Umami may be used as a taste amplifier in order to reduce the salt intake
Liking	Patients had a high liking[a] for more healthy items	E.g., offer patients potatoes, meatballs and rye bread cooked in a healthy way in different variations
Familiarity	Patients had a poorer familiarity with all items	Patients should be offered food courses to get to know different foods and to be inspired to make new foods
Frequency	Patients more frequently ingested white bread	It is important to offer patients freshly baked bread (increased smell), with different healthy toppings, contributing to a healthy, varied diet

a) Score > 4.5 out of 5.0.

Although multiple statistical tests were performed with no correction for multiple testing, many of the tests indicated a similar direction of differences between patients and controls, which supports the overall result that the chemosensory function of patients treated with chronic haemodialysis is impaired compared with that of controls.

Patients differed from controls as only age matching had been used for the feasibility of the study. The significantly higher SNOT-22, MDI and MMSE scores may reflect a large disease burden in the patient group in addition to the kidney disease itself. On the other hand, selection bias may explain some of the differences between patients and controls, as the control group may represent very healthy individuals with a great interest in participating in various studies to obtain results of their physical abilities. This is substantiated by the fact that almost two thirds of the controls were highly educated. However, chemosensory scores or food preferences

were not found to be associated with these demographic factors. Patients with granulomatosis with polyangiitis were excluded due to the suspicion that the neural and nasal symptoms of this disease in themselves reduce the sense of smell and taste.

The lack of association between some of the patient characteristics and test results was surprising. For instance, a negative correlation between chemosensory function and smoking was expected, but this was only the case when data from both patients and controls were pooled, indicating that the size of the groups was too small for identification of significant correlations.

Current smoking among patients was not associated with lower TDI scores. Although there is some controversy in regard to the effect of smoking on olfactory function, our findings are in line with those of a recent larger study on the association between smoking and TDI score [13].

In contrast to the psychometric tests of smell and taste, the majority of patients rated their own sense of smell and taste as normal. The reason for this discrepancy may be that a slowly deteriorating sense of smell and taste may not be recognised by the patients, or their focus may be on other serious comorbidities. Other studies have also concluded that ratings of olfactory function are unreliable in healthy, untrained subjects, and olfactory testing using reliable and validated tests therefore appears indispensable.

Overall, the liking-familiarity-frequency scores obtained by the food questionnaire in our study were lower in the patient group than in the control group. Fruits, vegetables and dairy products are often restricted in patients with end-stage kidney disease due to their potassium or phosphate content [4]. This restriction may be reflected in our results as patients ate vegetables, fruits and dairies less often than the controls did. Our results are in line with those of Dobell et al. who also reported a preference for vegetables, fish and chicken among patients treated with haemodialysis [14]. Dobell et al found that the patients “disliked” sweets and red meat; we only found a tendency towards this, probably due to the relatively low number of patients in our study. The results obtained by Dobell et al. in conjunction with our findings contrast with Ipema et al. [3]. Ipema's patient population included both in-centre haemodialysis patients, nocturnal home haemodialysis patients and home haemodialysis patients, whereas our patients were treated in-centre.

We observed several associations between liking, familiarity and frequency and bitter taste threshold. This is in line with previous reports [12, 15, 16]. The relatively low level of food familiarity among our patients may relate to the lower level of education and to the reduced sense of taste.

In patients with chronic kidney disease, high blood pressure is generally salt sensitive and may be difficult to treat [17]. Whereas sodium restriction may improve the gustatory threshold for salty taste [18], it is relevant to bear in mind that this improvement does not occur instantaneously but requires patience and adherence to dietary intervention. Compliance may prove difficult as salt generally improves the palatability of food; not only can salt improve flavour intensity, it also enhances sweetness and masks metallic taste [19].

Based on the individual patient’s preferences and chemosensory function, it will be possible to tailor an appropriate diet in collaboration with a dietician taking into account food items that are needed or should be avoided. Some general advice is listed in Table 3. In case of reduced sense of smell, the smell of food should be increased by adding, e.g., spices. Likewise, the dietician should consider adding more salt (only if blood pressure allows), sour, sweet or bitter flavour depending on what taste modalities are impaired. Furthermore, umami may be used as an alternative taste amplifier reducing the salt consumption. Cooking habits and exposure to more varied food items should also be involved. Finally, an example: A patient, who scores chicken and avocado high on the liking scale and has a low taste test score for sour may be offered a healthy salad with avocado and lemon together with spiced lemon balm chicken.

CONCLUSIONS

Dietary assessment is of paramount importance in providing optimal care to dialysis patients [2, 4]. Knowledge of haemodialysis patients' food preferences as well as taste and smell function is expected to contribute to improving patients' food intake. It is of outmost importance that patients adhere to their diet plans, including restrictions on sodium, potassium and phosphate. The aim of this study was therefore not to change diet plans. Instead, we aimed to shed some light on factors that may improve the clinicians' ability to construct a more individualised diet. Therefore, it is recommended to assess both food preferences and chemosensory function among patients treated with haemodialysis. Future studies are needed to confirm that assessments and recommendations as indicated in Table 3 will increase adherence to dietary requirements and improve the nutritional status of the patients.

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