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Interdialytic weight gain in patients on hemodialysis is associated with dry mouth and thirst

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Interdialytic weight gain in patients on hemodialysis is associated with dry mouth and thirst.

Background. Patients receiving hemodialysis (HD) have to maintain a fluid-restricted diet. Severe thirst can induce noncompliance to this diet, resulting in an increase of interdialytic weight gain (IWG = weight predialysis − postdialysis) associated with poor patient outcomes. Because oral dryness may contribute to experienced thirst, we investigated the possible relation between thirst, salivary flow rate, xerostomia, and IWG.

Methods. Unstimulated (UWS) and stimulated (CH-SWS) whole saliva were collected from 94 HD patients (64 men, 54.8 ± 15.5 years; 30 women, 59.5 ± 18.7 years). Secretion rates of saliva were determined gravimetrically. Xerostomia was assessed with a validated Xerostomia Inventory (XI), and thirst with a newly developed Dialysis Thirst Inventory (DTI).

Results. Before dialysis, 36.2% of the patients had hyposalivation (UWS ≤0.15 mL/min). The XI scores had a positive relation with IWG ($r = .250$, $P < 0.001$). Gender and age differences were observed for thirst, salivary flow rates, and xerostomia. The prevalence and severity of thirst and xerostomia were greater in younger subjects. Patients with urine output did not differ from those without urine output with respect to thirst, xerostomia, and IWG. Correlations were found between thirst (DTI) and both IWG and xerostomia (XI) ($r = .329$, $P < 0.001$, respectively; $r = .740$, $P < 0.001$). Other correlations were observed between xerostomia and both the salivary flow rate and total number of medications ($r = -.252$, $P < 0.05$, respectively; $r = .235$, $P < .05$).

Conclusion. In HD patients, xerostomia (XI) and thirst (DTI) are associated with a higher IWG. Our data provide evidence that, in HD patients, xerostomia is related to both salivary flow rate and thirst (DTI).

Key words: compliance, hyposalivation, interdialytic weight gain, saliva, flow rate, thirst, xerostomia.

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Patients with end-stage renal disease (ESRD) on hemodialysis (HD) have to maintain a fluid-restricted diet to prevent fluid overload [1]. During hemodialysis excess fluid is removed to normalize extracellular fluid volume and blood pressure. For many HD patients, however, it is difficult to adhere to this fluid restriction. Chronic fluid overload can result in hypertension, acute pulmonary edema, congestive heart failure, and premature death [2–6]. The interdialytic weight gain (IWG) is an indicator of compliance to the fluid-restricted diet, and is influenced by social and psychologic factors, but foremost by physical factors like excessive thirst [3, 4, 6–8].

Thirst or "the urge to drink" is affected by many different factors, including sodium intake, high plasma sodium, potassium depletion, angiotensin II, acute increases in plasma urea, low dry weight (postdialysis hypovolemia), and psychologic factors [7–10]. Besides thirst, a subjective feeling of a dry mouth (xerostomia) could also be a potential important stimulus for water intake [11–13]. Patients with xerostomia caused by radiation therapy, for example, report an increased water consumption in order to facilitate eating, articulation, and speech [14]. Xerostomia has also been reported in patients on HD [15]. In addition, other studies showed impaired saliva secretion in HD patients compared to healthy control patients [16–21]. Therefore, it is conceivable that xerostomia is one of the factors that contributes to the intake of fluid of HD patients and—consequently—to the IWG. The aim of the present study was to establish whether aspects of oral dryness, in particular, salivary flow rate and xerostomia, are related to thirst and IWG in HD patients.

METHODS

Participants

ESRD patients undergoing HD for at least three months were recruited from four different dialysis

Table 1. Clinical data ($N = 94$)

	Mean (SD)	Range
Mean age *years*	56.4 (16.7)	20–85
Mean time since first dialysis *months*	35.8 (31.0)	3–188
Mean IWG *kg*	2.2 (1.3)	0.0–5.6
Mean Kt/V	3.6 (1.1)	0.9–6.0
Mean SBP *mm Hg*	146 (22)	90–195
Mean DBP *mm Hg*	81 (13)	50–113
Mean number of systemic medication *N*	9.8 (3.7)	3–18
Mean number of xerogenic medication *N*	1.0 (1.0)	0–4

Abbreviations are: IWG, interdialytic weight gain; Kt/V, removal of urea by dialysis a week; V, volume of distribution of urea estimated as 55% of body weight; SBP, systolic blood pressure.

centers. Ninety-four patients on HD gave informed consent for this study, which was approved by the Medical Ethical Committee of the Vrije Universtiteit Medical Center, Amsterdam, The Netherlands.

Age, gender, level of education, ethnic background, smoking habits, and use of alcohol were assessed with a questionnaire. Clinical data with regard to HD were retrieved from patient files in each participating center and are presented in Table 1. The pathology causing the chronic renal failure was classified according to the European Dialysis and Transplantation Association-European Renal Association [22]. The medication of the patients was categorized as potentially causing salivary hypofunction (putatively xerogenic) or not (nonxerogenic) [23, 24]. Patients were weighed before and after a dialysis session. IWG was defined as the amount of fluid (kg) removed during the session (weight predialysis minus weight postdialysis) with the assumption that all the weight gained in the previous interdialytic interval was lost during the dialysis session [5, 25].

Saliva collection

Unstimulated and chewing-stimulated saliva samples were collected before HD. All subjects were instructed to refrain from smoking, eating, drinking, and tooth brushing for one hour prior to the saliva collection.

Unstimulated whole saliva (UWS) was collected according to the spitting method [26], with some small modifications [27]. Several minutes before collection, the participants rinsed their mouth with tap water. The collection started with the instruction to void the mouth of saliva by swallowing. Subsequently, saliva was allowed to accumulate in the floor of the mouth, and the subjects were instructed to spit out into preweighed test tubes every 30 seconds. The saliva collection period was five minutes.

Chewing-stimulated whole saliva (CH-SWS) was collected for five minutes using a tasteless piece of parafilm (5×5 cm; 0.30 g; Parafilm "M," American National CAL, Chicago, IL, USA). During the saliva collection period, the subjects chewed at their natural pace. The mechanically stimulated saliva was also spit out into preweighed test tubes every 30 seconds for five minutes.

Saliva volumes were determined gravimetrically (assuming 1 g = 1 mL).

Salivary hypofunction was defined as $\leq$0.15 mL/min UWS [28].

Table 2. Items of the Dialysis Thirst Inventory (DTI) and the Xerostomia Inventory (XI), the proportion of patients' answers (%) for each item divided in three categories

Xerostomia Inventory	Never/ almost never	Occasionally	Fairly often/ very often
I sip liquid to aid in swallowing food	38.7	29.0	32.3
My mouth feels dry when eating a meal	57.0	21.5	21.5
I get up at night to drink	53.8	24.7	21.6
My mouth feels dry	25.8	44.1	30.1
I have difficulty in eating dry foods	47.8	20.7	31.6
I suck sweets or cough drops to relieve dry mouth	53.3	21.7	25.0
I have difficulties swallowing certain foods	67.0	22.0	10.0
The skin of my face feels dry	44.0	18.7	37.4
My eyes feel dry	65.6	19.4	15.0
My lips feel dry	30.1	34.4	35.5
The inside of my nose feels dry	62.6	20.9	16.5
Dialysis Thirst Inventory			
Thirst is a problem for me	30.4	30.4	39.1
I am thirsty during the day	14.1	38.0	47.8
I am thirsty during the night	43.5	27.2	29.3
My social life is influenced because of my thirst feelings	61.9	15.2	22.8
I am thirsty before dialysis	35.1	23.4	41.6
I am thirsty during dialysis	48.1	27.3	24.7
I am thirsty after dialysis	48.1	22.1	29.9

Assessment of xerostomia and thirst

During the dialysis session, all participants completed the Dutch translation of the validated Xerostomia Inventory (XI), which consists of 11 items, each with a five-point Likert-scale (never = 1, to very often = 5), see Table 2 [29, 30]. Examples of items from the XI are "My mouth feels dry . . ." "I have difficulty in eating dry foods . . ." and "I sip liquids to aid in swallowing food." The responses to the 11 items were summed, which resulted in an individual XI score for each patient that ranged from 11 (no dry mouth) to 55 (extremely dry mouth).

The Dialysis Thirst Inventory (DTI) is newly developed and is used to quantify the perceived thirst. The DTI is a questionnaire with seven items (see Table 2). Each items has a five-point Likert type scale (never = 1, to very often = 5). The scores are summed, and provide a DTI score ranging from seven (no thirst) to 35 (very thirsty). In order to determine whether the items of the DTI represented one construct, a factorial analysis was carried out. This revealed one factor with an Eigen value

Table 3. Mean flow rate ± SD of the unstimulated (UWS) and chewing-stimulated salivary flow rate (CH-SWS)

	UWS mL/ min (SD)	CH-SWS mL/ min (SD)	*N*
Gender			
Male	0.34 (0.23)[a]	1.19 (0.69)[a]	64
Female	0.21 (0.21)	0.75 (0.64)	30
Age group			
≤64 years	0.32 (0.25)	1.12 (0.73)	63
>65 years	0.25 (0.14)	0.92 (0.62)	31
Edentulous			
No	0.31 (0.24)	1.10 (0.74)	71
Yes	0.26 (0.13)	.89 (0.54)	22
Diabetic			
No	0.30 (0.22)	1.09 (0.71)	80
Yes	0.30 (0.26)	0.81 (0.61)	13
Urine output			
No	0.30 (0.23)	1.06 (0.77)	68
Yes	0.30 (0.21)	1.04 (0.52)	26
Xerogenic medication			
0	0.29 (0.19)	1.08 (0.68)	36
1	0.32 (0.26)	1.04 (0.76)	32
2	0.33 (0.26)	1.14 (0.69)	17
>3	0.25 (0.11)	0.90 (0.70)	8
Smoking status			
Non-smoker	0.28 (0.22)	1.00 (0.69)	73
Smoker	0.38 (0.24)	1.31 (0.77)	17
Alcohol consumption			
No	0.28 (0.23)	1.09 (0.79)	52
Yes	0.32 (0.22)	1.02 (0.60)	39
Time dialysis			
≤24 months	0.31 (0.20)	1.19 (0.58)	34
>24 months	0.29 (0.24)	0.98 (0.76)	59

[a] $P < 0.01$.

of 3.98, which explained 56.9% of the variance of the items. The Chronbach's alpha for the DTI was 0.87.

When the subjects reported "occasionally" until "very often" on an item from either the XI or DTI, it was judged as 'present.' In all other cases, "never" and "almost never" were judged as 'absent.'

Statistical methods

Data are presented as mean ± SD. UWS and CH-SWS flow rates showed a skewed distribution, and were logarithmically transformed ($\log^{10}$) before statistical analyses. For readability, the original (untransformed) data are presented in Table 3. Normally distributed data (DTI and XI score) and the logarithmically transformed data were analyzed with independent Student *t* tests. Correlations between XI, DTI, IWG, and the logarithmically transformed UWS flow rates were subjected to Pearson's product-moment correlation analysis. To further explore relationships between IWG and both thirst (DTI score) and xerostomia (XI score), partial correlation coefficients were calculated after controlling for XI and DTI, respectively.

The main dependent variables (IWG, DTI score, XI score, salivary flow rates) were subjected to a univariate analysis of variance (ANOVA), with gender, age (≤64 years, >65 years), alcohol use, and smoking habits as factors. Potential interactions between these variables were explored using a full factorial model (two-way ANOVA). The statistical analysis was performed using the statistical software package SPSS (version 10.0, SPSS, Inc., Chicago, IL, USA). All levels of significance were set at $P < 0.05$.

RESULTS

Patient demographics

The total sample of this study comprised 94 HD patients, 64 men (mean age 54.8 ± 15.5 years) and 30 women (mean age 59.5 ± 18.7 years). The mean time of treatment with HD was 35.8 ± 31.0 months. The causes of chronic renal failure in the study group were renal vascular disease due to hypertension (16.0%), polycystic kidneys adult type (11.7%), glomerulonephritis (10.6%), miscellaneous (22.3%), and unknown (39.4%). In total, 13 patients suffered from diabetes mellitus (type 1 or 2), which was the cause of the chronic renal failure in five individuals.

The main categories of putatively xerogenic medication used by the HD patients were antihistamines (24.2%) and antihypertensives (21.1%). The IWG of the patients was 2.2 ± 1.3 kg. The average systolic and diastolic blood pressure were 146 ± 22 and 81 ± 13 mm Hg, respectively (Table 1). The mean normalized protein catabolic rate was 1.1 ± 0.2 g/kg/day and correlated significantly with IWG ($r = 0.291$, $P = 0.033$).

Saliva secretion

The mean salivary flow rates of UWS and CH-SWS were 0.30 ± 0.22 mL/min and 1.05 ± 0.70 mL/min, respectively. Normal values (0.25–0.50 mL/min) were reported in 34.2% of the patients, and hyposalivation (UWS <0.15 mL/min) was found in 36.2% of the cases [28].

Stratified data of the salivary flow rates are presented in Table 3. Male patients had significantly higher salivary flow rates than females, both for UWS and CH-SWS ($P < 0.001$). No diurnal differences in secretion rates were observed between patients who were treated in the morning versus the afternoon (data not shown). No significant differences in UWS and CH-SWS were observed with regard to age, dental status (dentate vs. edentulous), diabetics, urine output, alcohol consumption, smoking, or total time on dialysis. No significant association was observed between the number of putatively xerogenic medications used and the UWS flow rate ($r = -0.018$, $P = 0.914$).

Xerostomia (Xerostomia Inventory)

The mean XI score of the study population was 28.3 ± 9.1. Significant differences were observed with regard to gender, age, and alcohol consumption (Table 4). Women

Table 4. Mean XI score ± SD (Xerostomia Inventory) and DTI score ± SD (Dialysis Thirst Inventory).

	XI score (SD) (range 11–55)	DTI score (SD) (range 7–35)	*N*
Gender			
Male	26.7 (8.5)[a]	19.3 (6.6)	60
Female	31.6 (9.7)	22.2 (8.4)	28
Age group			
≤64 years	31.4 (9.1)[b]	22.2 (6.5)[b]	49
>65 years	23.1 (7.7)	16.7 (7.7)	23
Edentulous			
No	29.1 (8.7)	21.0 (6.7)	65
Yes	25.7 (10.1)	18.1 (9.0)	22
Diabetic			
No	27.7 (8.6)	20.8 (7.7)	76
Yes	31.5 (12.0)	20.2 (7.3)	12
Urine output			
No	28.8 (9.1)	20.5 (7.3)	64
Yes	26.8 (9.3)	19.8 (7.7)	24
Xerogenic medication			
0	28.2 (8.5)	19.9 (7.2)	32
1	28.5 (9.5)	21.3 (7.3)	32
2	26.9 (9.5)	20.0 (8.5)	16
>3	28.6 (13.3)	18.7 (7.4)	7
Smoking status			
Nonsmoker	28.4 (8.8)	20.3 (7.2)	71
Smoker	27.3 (10.8)	20.7 (8.5)	16
Alcohol consumption			
No	30.0 (10.0)[a]	21.4 (7.8)	49
Yes	25.9 (7.4)	18.8 (6.7)	38
Time dialysis			
≤24 months	26.1 (8.3)	18.0 (7.4)	34
>24 months	29.6 (9.4)	21.6 (7.1)[a]	54

[a] $P < 0.05$; [b] $P < 0.01$.

had higher XI scores (31.6 ± 9.7) than men (26.7 ± 8.5; $P = 0.019$). Participants older than 65 years reported significant lower XI scores (23.1 ± 7.7) than subjects below the age of 65 years (31.4 ± 9.1; $P < 0.0005$). In 74.2% of the patients a subjective dry mouth was present. A small majority of the study population (52.3%) reported to have problems with eating dry food, and 61.3% of the patients sipped liquids to aid in swallowing food.

The total number of all medications used was positively correlated with the XI score ($r = 0.257$, $P = 0.016$). However, no significant association was found between the number of putatively xerogenic medications used and the XI score ($r = 0.039$, $P = 0.717$). A large difference was observed between female patients who smoked (DTI score: 32.0 ± 4.2) and nonsmoking patients (21.3 ± 8.0). In contrast, no difference was observed between male smokers and nonsmokers.

Thirst (Dialysis Thirst Inventory)

The mean DTI score of the patients was 20.3 ± 7.3. Patients over the age of 65 years had significantly lower DTI scores than subjects younger than 65 years (16.7 ± 7.7 and 22.2 ± 6.5, respectively; $P < 0.0005$) (see Table 4). Patients >24 months on dialysis reported more thirst (DTI score: 21.6 ± 7.1) than patients ≤24 months on dialysis (DTI score: 18.0 ± 7.4). Table 2 gives an overview of the scores for each item of the DTI. Of the patients, 39.1% reported thirst as a problem (fairly to very often). During daytime, 47.8% of the patients reported to have thirst. During the night, the proportion of patients with thirst decreased to 29.3%. In 38.1% of the study group, social life is influenced by thirst. Before a dialysis session, the perceived thirst is much higher (41.6% 'fairly often' or 'very often') than during dialysis (24.7%) or afterwards (29.9%).

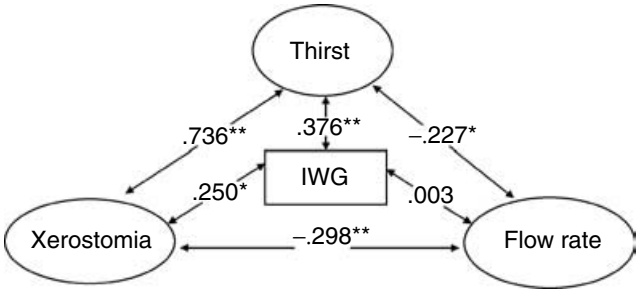

Fig. 1. Pearson correlations between xerostomia (XI score), thirst (DTI score), and flow rate (UWS) and interdialytic weight gain (IWG). $^{*}P < 0.05$, $^{**}P < 0.01$.

A nearly significant association was observed between the DTI score and the number of medications used ($r = 0.212$, $P = 0.065$). Significant two-way interactions for the DTI score were observed between gender and smoking [$F(1, 65) = 4.63$, $P < 0.05$] and between age and alcohol [$F(1, 65) = 5.91$, $P < 0.05$]. A large difference was found between female patients who smoked (DTI score: 32.0 ± 4.2) and nonsmoking patients (DTI score: 21.3 ± 8.0). In contrast, no difference was observed between male smokers and nonsmokers.

Relationships between IWG, thirst, xerostomia, and saliva secretion

A strong positive correlation between thirst and xerostomia was found ($r = 0.736$, $P < 0.0005$; Fig. 1). Thirst and xerostomia are associated with IWG, as shown by the significant correlations of both the XI score and DTI score with IWG ($r = 0.376$, $P = 0.001$ and $r = 0.250$, $P = 0.020$ respectively; Figs. 2 and 3). Thirst was inversely and significantly correlated with the UWS flow rate ($r = -0.227$, $P = 0.049$). No significant correlation was observed between UWS flow rate and the IWG.

Partial correlation coefficients between thirst and IWG remained significant after controlling for the XI score ($r = 0.253$, $P = 0.031$). After controlling for DTI score, the correlation between xerostomia and IWG was no longer significant ($r = 0.038$, $P > 0.05$). The correlation between DTI score and XI score remained high after controlling for IWG ($r = 0.700$, $P < 0.01$). No significant interactions of gender and age with smoking status and alcohol consumption were observed for IWG, thirst, xerostomia, or salivary flow rate.

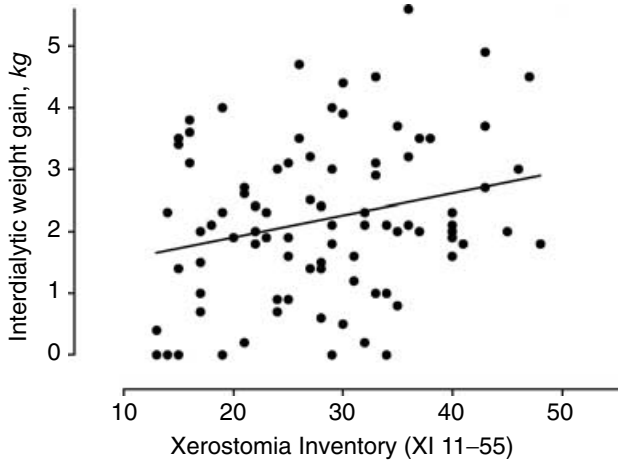

Fig. 2. Relationship between interdialytic weight gain (IWG) and Xerostomia Inventory (XI). Pearson correlation ($r = 0.250$, $P < 0.05$).

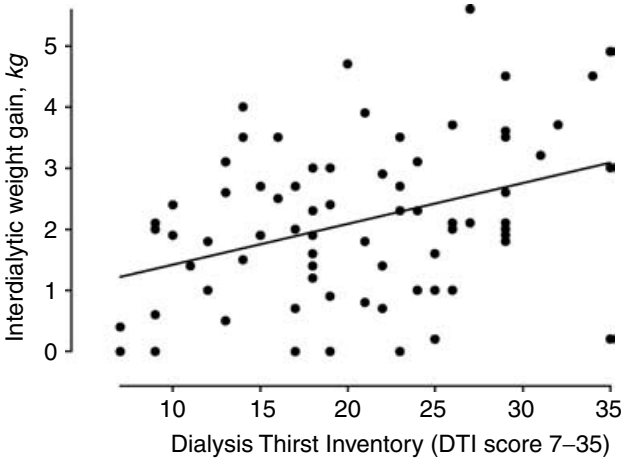

Fig. 3. Relationship between interdialytic weight gain (IWG) and Dialysis Thirst Inventory (DTI). Pearson correlation ($r = 0.376$, $P < 0.005$).

DISCUSSION

The present study is the first large scale, multicenter study to investigate whether aspects of oral dryness, especially salivary flow rate and xerostomia, were related to thirst and IWG. We indeed found significant relationships between a dry mouth (both xerostomia and reduced salivary flow rates) and thirst, and xerostomia and IWG. This suggests a possible role of oral dryness to explain higher fluid intake between HD sessions, and opens future interventions to manipulate dry mouth and/or flow rates to decrease thirst and IWG in HD patients.

A subjective feeling of a dry mouth (xerostomia) in HD patients was assessed using a validated xerostomia questionnaire (XI), with high scores indicating severe complains of oral dryness. We found that the subjective dry mouth feelings of HD patients (XI = 28.3 ± 9.1) were similar to patients receiving radiotherapy for head- and-neck cancer two months after the initial radiotherapy (XI = 31.4 ± 7.3) [29]. A relatively large proportion of the HD patients in our study reported having a dry mouth (76.4%). This is in agreement with previous studies on HD patients, in which the percentage of patients reporting a dry mouth ranged between 32.9% [17] and 66.7% [18]. Remarkably, no significant association was observed between the number of putatively xerogenic medications used and the XI score. The absence of this association may be either the result of the relatively broad classification of putatively xerogenic medication or the interaction between multiple medications used by HD patients [31].

In our study, the mean XI score of HD patients over the age of 65 years (XI = 23.1 ± 7.7) is similar to reports of oral dryness in healthy subjects over 65 years (XI = 20.0 ± 7.0) [31]. However, HD patients under the age of 65 years have much higher XI scores (31.4 ± 7.7), which might be explained by a gradual habituation to a dry mouth over the years. It has been suggested that younger subjects may also be more likely to experience symptoms of oral dryness when salivary flow is low, while in older persons symptoms of dry mouth could be related to a more complex constellation of factors where salivary flow is only one component [32]. A large-scale epidemiologic survey among an adult population, however, found a strong positive correlation between age and reports of a dry mouth [33]. Similarly, in our study, age and gender differences for the level of xerostomia (XI) and salivary flow rates (UWS and CH-SWS) in HD patients were observed. This is consistent with previous studies that men have higher salivary flow rates than women, and women report more xerostomia [31, 32, 34, 35].

The mean salivary flow rates of both unstimulated (UWS) and stimulated saliva (CH-SWS) in HD patients were normal and comparable to reference values for healthy subjects [36]. However, it should be mentioned that the original flow rate date was skewed to the right and had a large standard deviation. Many HD patients have low salivary flow rates. The calculated mean rates were normal due to a few HD patients with high flow rates. The mean UWS in our study was also consistent with the study of Galvada et al [16], who found an average UWS flow rate of 0.26 ± 0.28 mL/min in HD patients compared to control patients (UWS = 0.28 ± 0.16 mL/min). Kho et al [17] investigated 22 patients undergoing HD and found an average UWS flow rate of 0.30 ± 0.18 mL/min.

Our observation that the mean CH-SWS of HD patients was comparable to reference values for healthy subjects [36] differs from previous studies reporting that the stimulated salivary flow rates were significantly reduced in HD patients compared to control groups [15, 17, 20, 21]. This could be explained by the fact that in our study a tasteless piece of parafilm was used to stimulate salivary flow, while previous studies used other mechanical or chemical stimuli like 2% citric acid. The altered taste perception of HD patients may also partially contribute to these different findings [37].

The salivary flow rate (UWS) and the perception of a dry mouth (XI) correlated significantly ($r = -0.298$, $P < 0.05$), which is in agreement with previous studies reporting a correlation between objective measures of a dry mouth (salivary flow rate) and subjective reports of a dry mouth (xerostomia) in patients with rheumatoid arthritis [38, 39]. Responses to questions related to eating (such as 'my mouth feels dry during eating a meal,' 'sipping liquids to aid swallowing,' and 'difficulties in swallowing dry food') were highly indicative of salivary performance [40]. However, a subjective dry mouth is not always necessarily related to a reduced salivary flow rate [39–41], and other factors including anxiety, depression, and stress might play a role in the perception of a dry mouth [35, 42]. It has been demonstrated that anxiety, depression, and stress also play a role in the compliance of HD patients to fluid restriction, measured by the IWG [4].

For this study a new Dialysis Thirst Inventory (DTI) was developed, focusing on perceived thirst. Significantly lower thirst scores were observed in the age group over 65 years, which is comparable to reduced complaints of oral dryness (XI) in the older aged HD patients. Our findings are also in agreement with diminished feelings of thirst and reduced fluid intake in healthy elderly persons [43, 44]. Older subjects may have a higher osmotic operating point for thirst sensation, a diminished response by baroreceptors to volume changes, or adaptation to the fluid restriction [44].

Several investigators have suggested that the salivary glands are directly damaged by either uremic involvement or the fluid-restricted diet [15–18, 21]. In the present study, the salivary flow rates are not influenced by the duration of HD treatment. This is in agreement with the study of Bayraktar et al [21], in which no differences in salivary flow rate were observed between patients on HD for more or less than 24 months. Also, the large difference between the unstimulated and stimulated flow rate in our study indicates that the salivary glands have maintained their secretory capacity. This all indicates that the salivary glands are probably not damaged by chronic HD treatment.

Because our study clearly demonstrates that thirst (DTI) and xerostomia (XI) are associated with greater IWG, management of thirst and xerostomia is potentially clinical important in the treatment of HD patients. Patients on daily HD were less thirsty and also showed less fluctuation in body fluid volume [45]. In addition, xerostomia can be reduced by either stimulation of the saliva secretion (mechanical, gustatory, or pharmacologic) or palliative care using mouthwashes or saliva substitutes [46–49]. In healthy subjects, gum chewing increases flow rate to 187% during the first minute of chewing [50] and gum chewing can—especially in those with low salivary function—increase unstimulated flow rates, and might contribute to reduced levels of xerostomia [51]. Regular use of gum for two weeks resulted even in a long-term persistent increase in unstimulated salivary secretion rate and showed to be effective in reducing xerostomia [52]. Also, in patients with advanced cancer, daily use of chewing gum or a saliva substitute showed to be effective in reducing xerostomia [48]. Use of saliva substitutes reduced dry mouth feelings in patients with irradiation-induced xerostomia [53]. In a small pilot study, use of a saliva substitute in HD patients resulted in a reduction of fluid overload [54].

CONCLUSION

The mean unstimulated and stimulated salivary flow rates of HD patients in this study are relatively normal. However, a large proportion of the patients have reduced unstimulated flow rates. Thirst, IWG, and xerostomia are associated in HD patients, indicating a possible role of oral dryness to explain higher fluid intake between HD sessions. In other studies, the use of saliva stimuli or saliva substitutes showed to be effective in reducing feelings of a dry mouth. This might also diminish the urge to drink in HD patients, enhancing compliance to the fluid-restricted diet and leading to a decreased IWG and fewer systemic complications. The potential clinical effect of saliva stimuli and saliva substitutes will be investigated in future studies.

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REFERENCES

1. Mallick NP, Gokal R: Haemodialysis. *Lancet* 353:737–742, 1999
2. Kimmel PL, Varela MP, Peterson RA, *et al*: Interdialytic weight gain and survival in hemodialysis patients: Effects of duration of ESRD and diabetes mellitus. *Kidney Int* 57:1141–1151, 2000
3. Oldenburg B, MacDonald GJ, Perkins RJ: Factors influencing excessive thirst and fluid intake in dialysis patients. *Dial Transplant* 17:21–23, 1988
4. Everett KD, Brantley PJ, Sletten C, *et al*: The relation of stress and depression to interdialytic weight gain in hemodialysis patients. *Behav Med* 21:25–30, 1995
5. Leggat JE, Orzol SM, Hulbert-Shearon TE, *et al*: Noncompliance in hemodialysis: Predictors and survival analysis. *Am J Kidney Dis* 32:139–145, 1998
6. Moran PJ, Christensen AJ, Lawton WJ: Social support and conscientiousness in hemodialysis adherence. *Ann Behav Med* 19:333–338, 1997

7. Van Stone JC: Controlling thirst in dialysis patients. *Semin Dial* 9:47–50, 1996
8. Fitzsimons JT: The physiological basis of thirst. *Kidney Int* 10:3–11, 1976
9. Fitzsimons JT: Physiology and pathology of thirst and sodium appetite, in *The Kidney: Physiology and Pathophysiology*, edited by Seldin DW, Giebisch G, New York, Raven Press, 1985, pp 885–901
10. Rolls BJ, Wood RJ, Rolls ET, *et al*: Thirst following water deprivation in humans. *Am J Physiol* 239:476–482, 1980
11. Wirth JB, Folstein MF: Thirst and weight gain during maintenance hemodialysis. *Psychosomatics* 23:1125–1134, 1982
12. Brunstrom JM: Effects of mouth dryness on drinking behavior and beverage acceptability. *Physiol Behav* 76:423–429, 2002
13. Figaro MK, Mack GW: Regulation of fluid intake in dehydrated humans: Role of oropharyngeal stimulation. *Am J Physiol* 272:R1740–R1746, 1997
14. Wijers OB, Levendag PC, Braaksma MMJ, *et al*: Patients with head and neck cancer cured by radiation therapy: A survey of the dry mouth syndrome in long-term survivors. *Head Neck* 24:737–747, 2002
15. Epstein SR, Mandel I, Scopp IW: Salivary composition and calculus formation in patients undergoing hemodialysis. *J Periodontol* 51:336–338, 1980
16. Gavalda C, Bagan J, Scully C, *et al*: Renal hemodialysis patients: Oral, salivary, dental and periodontal findings in 105 adult cases. *Oral Dis* 5:299–302, 1999
17. Kho HS, Lee SW, Chung SC, Kim YK: Oral manifestations and salivary flow rate, pH, and buffer capacity in patients with end-stage renal disease undergoing hemodialysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 88:316–319, 1999
18. Kao CH, Hsieh JF, Tsai SC, *et al*: Decreased salivary function in patients with end-stage renal disease requiring hemodialysis. *Am J Kidney Dis* 36:1110–1114, 2000
19. Kaya M, Cermik TF, Ustun F, *et al*: Salivary function in patients with chronic renal failure undergoing hemodialysis. *Ann Nucl Med* 16:117–120, 2002
20. Postorino M, Catalano C, Martorano C, *et al*: Salivary and lacrimal secretion is reduced in patients with ESRD. *Am J Kidney Dis* 42:722–728, 2003
21. Bayraktar G, Kazancioglu R, Bozfakioglu S, *et al*: Stimulated salivary flow rate in chronic hemodialysis patients. *Nephron* 91:210–214, 2002
22. EDTA-ERA and WHO diagnostic codes. *Nephrol Dial Transplant* 6:524–525, 1993
23. Vissink A, Nieuw Amerongen AV, Wesseling H, *et al*: Dry mouth: Possible cause—pharmaceuticals. *Ned Tijdschr Tandheelkd* 99:103–112, 1992
24. Sreebny LM, Schwartz SS: A reference guide to drugs and dry mouth—Second edition. *Gerodontology* 14:33–37, 1997
25. Saran R, Bragg-Gresham JL, Rayner HC, *et al*: Nonadherence in hemodialysis: Associations with mortality, hospitalization, and practice patterns in the DOPPS. *Kidney Int* 64:254–262, 2003
26. Navazesh M: Methods for collecting saliva. *Ann N Y Acad Sci* 694:72–77, 1993
27. Bosch JA, Brand HS, Ligtenberg TJ, *et al*: Psychological stress as a determinant of protein levels and salivary-induced aggregation of *Streptococcus gordonii* in human whole saliva. *Psychosom Med* 58:374–382, 1996
28. Navazesh M, Christensen C, Brightman V: Clinical criteria for the diagnosis of salivary gland hypofunction. *J Dent Res* 71:1363–1369, 1992
29. Thomson WM, Williams SM: Further testing of the xerostomia inventory. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 89:46–50, 2000
30. Thomson WM, Chalmers JM, Spencer AJ, Williams SM: The Xerostomia Inventory: A multi-item approach to measuring dry mouth. *Community Dent Health* 16:12–17, 1999
31. Thomson WM, Chalmers JM, Spencer AJ, Slade GD: Medication and dry mouth: Findings from a cohort study of older people. *J Public Health Dent* 60:12–20, 2000
32. Billings RJ, Proskin HM, Moss ME: Xerostomia and associated factors in a community-dwelling adult population. *Community Dent Oral Epidemiol* 24:312–316, 1996
33. Nederfors T, Isaksson R, Mornstad H, Dahlof C: Prevalence of perceived symptoms of dry mouth in an adult Swedish population—Relation to age, sex and pharmacotherapy. *Community Dent Oral Epidemiol* 25:211–216, 1997
34. Bergdahl M: Salivary flow and oral complaints in adult dental patients. *Community Dent Oral Epidemiol* 28:59–66, 2000
35. Bergdahl M, Bergdahl J: Low unstimulated salivary flow and subjective oral dryness: Association with medication, anxiety, depression, and stress. *J Dent Res* 79:1652–1658, 2000
36. Dawes C. Factors influencing salivary flow rate and composition, in *Saliva and Oral Health*, edited by Edgar WM, O'Mullane DM, London, British Dental Journal, 1996, pp 27–41
37. Astbäck J, Fernström A, Hylander B, *et al*: Taste buds and neuronal markers in patients with chronic renal failure. *Perit Dial Int* 19:S315–S323, 1999
38. Nederfors T, Holmstrom G, Paulsson G, Sahlberg D: The relation between xerostomia and hyposalivation in subjects with rheumatoid arthritis or fibromyalgia. *Swed Dent J* 26:1–7, 2002
39. Bardow A, Nyvad B, Nauntofte B: Relationships between medication intake, complaints of dry mouth, salivary flow rate and composition, and the rate of tooth demineralization in situ. *Arch Oral Biol* 46:413–423, 2001
40. Fox PC, Busch KA, Baum BJ: Subjective reports of xerostomia and objective measures of salivary gland performance. *J Am Dent Assoc* 115:581–584, 1987
41. Spielman A, Ben Aryeh H, Gutman D, *et al*: Xerostomia—Diagnosis and treatment. *Oral Surg Oral Med Oral Pathol* 51:144–147, 1981
42. Anttila SS, Knuuttila ML, Sakki TK: Depressive symptoms as an underlying factor of the sensation of dry mouth. *Psychosom Med* 60:215–218, 1998
43. Rolls BJ, Phillips PA: Aging and disturbances of thirst and fluid balance. *Nutr Rev* 48:137–144, 1990
44. Kenney WL, Chiu P: Influence of age on thirst and fluid intake. *Med Sci Sports Exerc* 33:1524–1532, 2001
45. Kooistra MP, Vos J, Koomans HA, Vos PF: Daily home haemodialysis in The Netherlands: Effects on metabolic control, haemodynamics, and quality of life. *Nephrol Dial Transplant* 13:2853–2860, 1998
46. Nieuw Amerongen AV, Veerman EC: Current therapies for xerostomia and salivary gland hypofunction associated with cancer therapies. *Support Care Cancer* 11:226–231, 2003
47. Brennan MT, Shariff G, Lockhart PB, Fox PC: Treatment of xerostomia: A systematic review of therapeutic trials. *Dent Clin North Am* 46:847–856, 2002
48. Davies AN: A comparison of artificial saliva and chewing gum in the management of xerostomia in patients with advanced cancer. *Palliat Med* 14:197–203, 2000
49. Odusola F: Chewing gum as aid in treatment of hyposalivation. *N Y State Dent J* 57:28–31, 1991
50. Bots CP, Brand HS, Veerman ECI, *et al*: Preferences and saliva stimulation of eight different chewing gums. *Int Dent J* 54:143–148, 2004
51. Jenkins GN, Edgar WM: The effect of daily gum-chewing on salivary flow rates in man. *J Dent Res* 68:786–790, 1989
52. Aagaard A, Godiksen S, Teglers PT, *et al*: Comparison between new saliva stimulants in patients with dry mouth: A placebo-controlled double-blind crossover study. *J Oral Pathol Med* 21:376–380, 1992
53. Regelink G, Vissink A, Reintsema H, Nauta JM: Efficacy of a synthetic polymer saliva substitute in reducing oral complaints of patients suffering from irradiation-induced xerostomia. *Quintessence Int* 29:383–388, 1998
54. De Nour AK, Czaczkes JW: A saliva substitute as a tool in decreasing overdrinking in dialysis patients. *Isr J Med Sci* 16:43–44, 1980