Original Article

Chewing gum and a saliva substitute alleviate thirst and xerostomia in patients on haemodialysis

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Abstract

Background. Most patients on haemodialysis (HD) have to maintain a fluid-restricted diet to prevent a high interdialytic weight gain (IWG). The prevalence of xerostomia (the feeling of a dry mouth) is higher in HD patients than in controls. Recently, we demonstrated that xerostomia and thirst were positively correlated with IWG in HD patients. Thus, this may play a role as a stimulus for fluid intake between dialysis sessions. The aim of the present study was to investigate the effect of chewing gum or a saliva substitute on xerostomia, thirst and IWG.
Methods. This study was a randomized two-treatment crossover design with repeated measures. After the use of chewing gum or saliva substitute for 2 weeks, a wash-out period of 2 weeks was introduced and hereafter the other regimen was carried out. Xerostomia and thirst were assessed by validated questionnaires as xerostomia inventory (XI) and dialysis thirst inventory (DTI), at baseline and after each treatment period, as were IWG and salivary flow rates.
Results. Sixty-five HD patients (42 men, 54.6 ± 14.1 years; 23 women, 54.7 ± 16.3 years) participated in this study. Chewing gum decreased XI from 29.9 ± 9.5 to 28.1 ± 9.1 ($P < 0.05$). Chewing gum as well as a saliva substitute reduced DTI significantly ($P < 0.05$), but no differences occurred for the average IWG or salivary flow rates.

Conclusions. The use of chewing gum and, to a lesser extent, a saliva substitute may alleviate thirst and xerostomia in some HD patients.

Keywords: chewing gum; haemodialysis; interdialytic weight gain; saliva substitute; thirst; xerostomia

Introduction

Most patients with end-stage renal disease (ESRD) on haemodialysis (HD) have to maintain a fluid-restricted diet in order to prevent fluid overload between dialysis sessions. High fluid intake through beverages and food results in high interdialytic weight gain (IWG) between dialysis sessions. Long-term non-compliance to the fluid-restricted diet can induce complications, such as hypertension, acute pulmonary oedema, congestive heart failure and cardiovascular comorbidity [1,2].

Several strategies have been advocated to reduce fluid intake and IWG in HD patients, such as the administration of an angiotensin-converting enzyme (ACE) inhibitor, dietary measures or, ultimately, increasing the frequency of HD sessions [3]. In 25 chronic HD patients with fluid overload, enalapril (an ACE inhibitor) modestly decreased IWG from 0.90 to $0.73\,\text{kg}$ per day. Dietary measures, such as the restriction of sodium intake or reducing high protein intake, have shown to be effective in reducing IWG in HD patients. However, compliance to the fluid restriction is also influenced by other factors, such as hormonal derangements, social and psychological

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changes, thirst and xerostomia. Xerostomia is a symptom, defined as the subjective feeling of a dry mouth [4]. Hyposalivation, on the other hand, is the objective measured reduction in salivary flow rate. The prevalence of both hyposalivation and xerostomia is higher in HD patients than in healthy controls [5,6]. Patients with xerostomia report increased water consumption to facilitate eating and speech.

Recently, we demonstrated that xerostomia in HD patients was positively associated with IWG and thirst, and, therefore, could play a role as a stimulus for fluid intake between dialysis sessions [4]. Besides an effect on fluid intake, oral dryness also has an impact on the oral health and on the quality of life of the xerostomic patients.

Xerostomia can potentially be improved by mechanical and gustatory stimulation of the salivary glands or by palliative care, such as saliva substitutes [7]. In a pilot study with seven non-compliant HD patients, the use of a saliva substitute reduced the number of dialysis sessions with a high IWG [8]. This suggests that saliva substitutes or stimulants could potentially be used to decrease xerostomia and, thus, the urge to drink in HD patients. This may increase compliance to the fluid-restricted diet and could, subsequently, result in a decreased IWG and an improved quality of life.

The aim of this clinical crossover trial was to investigate the potential effect of the use of sugar-free chewing gum and a saliva substitute on xerostomia, thirst and IWG in ESRD patients on HD.

Subjects and methods

Participants and crossover design

One hundred and thirty-seven ESRD patients, undergoing HD for ≥ 3 months, were approached in the participating dialysis centres. The inclusion criteria were ≥ 3 months on HD, ≥ 18 years of age and mentally and physically being able to participate and complete the study. This study was approved by the Medical Ethics Committee of the Vrije Universiteit Medical Centre, Amsterdam, The Netherlands.

During the 6 week crossover trial, the patients randomly received either chewing gum or the saliva substitute regimen. After a wash-out period of 2 weeks, to control for any crossover effect between products, the other regimen (chewing gum or saliva substitute) was tested.

The low-tack, menthol-containing sugar-free chewing gum used was Freedent White™ (Wm Wrigley Jr Co., Chicago, IL, USA), sweetened with xylitol and sorbitol. To get optimal patient compliance, two flavours of this chewing gum were selected (Sweetmint® and Winterfresh®) and offered to the patients [9]. The participants were instructed to chew one or two pieces of gum gently, for ≥ 10 min, six times a day and as desired throughout the day when the mouth felt dry or when they were thirsty.

The saliva substitute used in this study was Xialine™ (Lommerse Pharma B.V., Oss, The Netherlands), which contains 0.92% xanthan gum and 2 p.p.m. sodium fluoride. Two bottles (each with 50 ml artificial saliva) were offered to the participants, who were instructed to use the spray at least six times a day and as desired throughout the day when the mouth felt dry or when they were thirsty.

Age, gender, ethnic background, denture wearing, smoking habits and use of alcohol were assessed with a questionnaire. The causes for the ESRD were classified according to the European Renal Association–European Dialysis and Transplantation Association. Clinical data at baseline, such as systolic (SBP) and diastolic blood pressures (DBP), normalized protein catabolic rate (nPCR) and weekly removal of urea by dialysis (Kt/V_{week}) were retrieved from patient files.

Xerostomia, thirst and KDQOL

At baseline and at the beginning and end of each experimental period, the main parameters xerostomia, thirst, IWG and salivary flow rates were determined. The Kidney Disease Quality of Life (KDQOL) was assessed at baseline of the trial to compare the study population with a reference population.

The xerostomia inventory (XI) was used to quantify the perceived xerostomia. The XI is a validated questionnaire with 11 items, each with a 5 point Likert-type scale (never = 1 to very often = 5). The scores are summed and provide an individual XI score ranging from 11 (no dry mouth) to 55 (extremely dry mouth) [4,10].

Thirst was assessed by using a shortened version of the dialysis thirst inventory (DTI), quantifying the occurrence of thirst before, during and after dialysis, and perceived thirst during day and night [4]. Each item has a 5 point Likert-type scale (never = 1 to very often = 5). The responses to the five items were summed, which results in a score ranging from 5 (never thirsty) to 25 (very often thirsty).

KDQOL was measured using the short version of the validated KDQOL–SF™ based on 36 items that focus on health-related concerns of individuals with kidney disease on HD [11]. These items are assigned to three kidney disease-related dimensions and to two generic dimensions: (a) symptom problem list; (b) effects of kidney disease; (c) burden of kidney disease; (d) SF-12 physical health; and (e) SF-12 mental health. The item scores were aggregated without weighting and transformed linearly to a 0–100 range, with higher scores indicating better states.

Interdialytic weight gain

Patients were weighed before and after each dialysis session. IWG was defined as the amount of fluid (kg) removed during the session (weight pre-dialysis minus weight post-dialysis) with the assumption that all the weight gained in the previous interdialytic interval had been lost during the dialysis session. The IWG was calculated and expressed as the mean IWG during a period of 2 weeks [4].

Saliva collection

Unstimulated whole saliva (UWS) and paraffin chewing-stimulated whole saliva (PC-SWS) were both collected before dialysis. All subjects were instructed to refrain from smoking, eating, drinking and tooth brushing for 1 h prior to saliva collection. UWS was collected according to the spitting method, with some small modifications [4]. Before collection,

the subjects rinsed their mouth with tap water. The collection started with the instruction to void the mouth of saliva by swallowing. Saliva was allowed to accumulate on the floor of the mouth and the subjects were instructed to spit into pre-weighted test tubes every 30 s. The saliva collection period was 5 min.

PC-SWS was collected for 5 min using a tasteless piece of parafilm (5 × 5 cm, 0.30 g; Parafilm 'M'; American National CAL, Chicago, IL, USA). The chewing-stimulated saliva was also spitted out into pre-weighed test tubes every 30 s for 5 min. During the saliva collection period, the subjects chewed at their natural pace. Saliva volumes were determined gravimetrically (assuming 1 g = 1 ml).

Statistical methods

The data at baseline were stratified with regard to gender, age (≤ 64 and >64 years), residual urine output (yes/no) and full denture (yes/no) and analysed using analysis of variance (ANOVA). The period effect and the influence of the order in which the subjects received the therapy (treatment–period interaction) were investigated with two-sample *t*-tests. Since no treatment–period interaction was found, we compared the effect of each therapy (chewing gum and saliva substitute) with the main baseline variables using the general linear model of ANOVA (repeated measures design, followed by paired *t*-tests as post-hoc procedure). To explore the effect of gender, age, residual urine output and full denture, these variables were inputted separately in the model as between-subject factors. The data of the five dimensions of the KDQOL–SF^{TM} were compared with the reference population using paired *t*-tests. The statistical analysis was performed using the statistical software package SPSS (version 10.0; SPSS Inc., Chicago, IL, USA). All data are presented as means ± SD and levels of significance were set at $P < 0.05$.

Results

Patient demographics

One hundred and thirty-seven HD patients were approached to participate in this study. After explanation of the aim and design of the study, 89 patients gave informed consent for participation and entered the study. The main reasons for not participating in the study were no thirst ($n = 36$), not interested ($n = 6$) or illness ($n = 5$). Of the 89 HD patients who entered the study, 65 (73%) of the initial sample completed the 6 week crossover clinical trial: 42 men and 23 women (mean age: 54.6 ± 14.1 and 54.7 ± 16.3 years, respectively). Reasons for withdrawal during the trial were holidays ($n = 4$), language problems ($n = 3$), no xerostomia or thirst ($n = 2$), transplanted during study ($n = 2$), illness of the patient ($n = 1$) or other reasons not related to the intervention ($n = 12$). Causes for the chronic renal failure were renal vascular disease due to hypertension (15.4%), polycystic kidneys (12.3%), diabetes type 2 (6.2%), miscellaneous (26.1%) or unknown (40%). The clinical and socio-demographic data at baseline are presented in Table 1.

Table 1. Demographic and clinical data at baseline ($n = 65$)

Age (years)	54.6 (14.8)
Male gender	64.6% ($n = 42$)
Diabetes type 1 or 2	15.4% ($n = 10$)
Residual urine output	27.7% ($n = 18$)
Full denture	32.3% ($n = 21$)
Current smoker	26.2% ($n = 17$)
Alcohol use	38.5% ($n = 25$)
Educational level	
Primary school	21.5% ($n = 14$)
Secondary school	35.4% ($n = 23$)
High school or higher	43.1% ($n = 28$)
Ethnic background	
Dutch	60.0% ($n = 39$)
Indonesian	7.7% ($n = 5$)
Surinamese	6.2% ($n = 4$)
Moroccan	7.7% ($n = 5$)
Other	18.5% ($n = 12$)
Time on HD (months)	27.1 (24.0)
HD sessions per week	
2	6.1% ($n = 4$)
3	90.8% ($n = 59$)
>3	3.1% ($n = 2$)
IWG (kg)	2.1 (0.9)
IWG/day (kg/day)	0.94 (0.47)
SBP before dialysis (mmHg)	146.1 (18.9)
DBP before dialysis (mmHg)	80.5 (9.2)
SBP after dialysis (mmHg)	131.3 (19.0)
DBP after dialysis (mmHg)	74.4 (11.0)
Kt/V urea/week	4.2 (0.9)
nPCR (g/kg/day)	1.17 (0.31)
Albumin (g/l)	36.0 (4.4)

Mean values (SD) are given for continuous variables. IWG, SBP and DBP are mean values of the dialysis sessions that took place during the 2 weeks before the baseline measurements.

Baseline: XI, DTI, IWG and KDQOL

At baseline, differences were observed for the XI score, the DTI score and IWG for patients younger than 65 years and those without residual urine output (Table 2). The level of xerostomia, thirst and IWG were significantly higher in the younger age group compared with individuals >65 years. Patients with residual urine output had less xerostomia and thirst and a significantly lower IWG than those without residual urine output. The baseline values of the KDQOL–SF in our study population were comparable with those of a reference population of 428 HD patients in The Netherlands [12], thus, representing a normal Dutch HD population (Table 3).

Crossover study: effect on XI, DTI and IWG

A significant treatment effect was observed for xerostomia ($P = 0.024$) and thirst ($P = 0.015$) (Table 4). The use of chewing gum decreased the level of perceived xerostomia significantly from XI $= 29.9 \pm 9.5$ at baseline to XI $= 28.1 \pm 9.1$ after gum chewing ($P = 0.005$). Both chewing gum and the saliva substitute had a positive overall effect on the perceived thirst (DTI score) during the crossover clinical trial. Stratification of preference for the chewing gum (Sweetmint® or

Table 2. XI, DTI, IWG, UWS and PC-SWS at baseline ($n = 65$)

	XI (11–55)	DTI (5–25)	IWG (kg)	UWS (ml/min)	PC-SWS (ml/min)	n
Gender						
Male	28.7 (8.5)	16.8 (5.1)	2.2 (1.0)	0.32 (0.28)	0.95 (0.53)	42
Female	32.0 (10.9)	16.4 (5.3)	1.9 (0.8)	0.26 (0.16)	0.90 (0.74)	23
Age group						
<64 years	31.7 (9.3)[a]	17.7 (4.4)[a]	2.3 (0.9)[a]	0.32 (0.27)	0.96 (0.62)	46
>65 years	25.5 (8.7)	14.0 (5.9)	1.6 (0.7)	0.24 (0.16)	0.88 (0.61)	19
Residual urine output						
Yes	24.7 (7.9)	13.9 (5.4)	1.4 (0.8)	0.32 (0.18)	0.96 (0.48)	18
No	31.9 (9.4)[a]	17.7 (4.7)[a]	2.4 (0.8)[b]	0.28 (0.27)	0.93 (0.66)	47
Full denture						
Yes	30.5 (11.3)	15.5 (6.6)	1.8 (1.0)	0.33 (0.37)	1.00 (0.59)	21
No	29.8 (8.5)	17.4 (4.1)	2.2 (0.8)	0.28 (0.17)	0.90 (0.63)	44

Data were analysed by ANOVA. [a]$P < 0.05$; [b]$P < 0.01$.

Table 3. Overview of the five dimensions of the KDQOL at baseline compared to a reference population [12]

Dimension	Study ($n = 65$)	NECOSAD ($n = 428$)
Symptom problem	77.6 (13.7)	74.8 (15.6)
Effect of kidney disease	73.0 (17.2)	69.3 (19.4)
Burden of kidney disease	48.8 (24.0)	45.9 (25.5)
SF-12 physical	37.1 (11.4)	36.1 (9.8)
SF-12 mental	47.0 (9.6)	45.8 (10.3)

Data were analysed with Student's *t*-tests. No significant differences were observed.
NECOSAD = Netherlands Cooperative Study on Adequacy of Dialysis.

Winterfresh®) showed no different treatment effect. The IWG during treatment with chewing gum or the saliva substitute did not differ from the average IWG measured at baseline (Table 4). Also the SBP and DBP were not affected by saliva substitute or chewing gum (data not shown).

Gender, age and wearing a full denture had no effect on the response to the different treatment modalities. However, a significant interaction was observed for residual urine output with the XI scores. In patients without residual urine output the XI scores decreased significantly from 31.9 ± 9.4 at baseline to 29.3 ± 9.1 after gum chewing ($P = 0.003$) and to 30.6 ± 9.5 after saliva substitute ($P = 0.038$) (Table 5).

In HD patients with thirst, an overall treatment effect of chewing gum and saliva substitute on thirst (DTI) and xerostomia (XI) was found (Table 5). Chewing gum reduced both the XI and the DTI scores. In patients with thirst, the saliva substitute had no effect on the level of xerostomia. Patients with thirst had significantly higher IWG values than those without thirst. However, neither gum nor spray affected the IWG in the 'thirst group'. No significant difference was found for the number of patients with diuresis between the 'thirst' group and the 'no thirst' group.

In patients with hyposalivation (UWS ≤ 0.16 ml/min), an overall treatment effect was found on the XI scores. Gum chewing reduced the XI scores significantly from 33.2 ± 9.1 to 29.7 ± 8.4 ($P < 0.05$; Table 5). During both treatment modalities, the DTI levels were comparable between both groups (Table 5) and no overall treatment effect was found. Patients with hyposalivation and those with normal salivary flow rates did not differ with respect to the IWG. Also, the treatment did not have an effect on the IWG.

In a subgroup of HD patients ($n = 12$) without residual urine output, suffering from thirst (DTI = 16–25) and hyposalivation (UWS ≤ 0.16 ml/min), the highest mean XI-values were observed. A significant reduction of the XI score was observed after the use of chewing gum for 2 weeks (from 37.8 ± 7.2 to 32.6 ± 6.6). The use of a saliva substitute, however, did not affect the XI score. In this subgroup, no treatment effects were found for the level of thirst (DTI) and IWG (data not shown).

Saliva secretion: at baseline and therapy effect

UWS and PC-SWS flow rates showed a skewed distribution and were square-root transformed before statistical analyses. For clarity, the untransformed data are presented. At baseline, the mean UWS was 0.26 ± 0.15 ml/min (median: 0.24 ml/min; range: 0.01–1.80 ml/min). The mean PC-SWS was 0.89 ± 0.44 ml/min (median: 0.82 ml/min; range: 0.18–3.78 ml/min). Treatment with chewing gum or the saliva substitute did not influence UWS and PC-SWS (Table 4).

Discussion

Thirst and xerostomia are major problems for patients on HD [4,6,13,14]. Oropharyngeal factors, such as a dry mouth, have been associated with thirst [4].

Table 4. The effect of the two treatment modalities (chewing gum and saliva substitute for 2 weeks) on the main outcome variables in 65 HD patients

	XI (11–55)	DTI (5–25)	IWG (kg)	UWS (ml/min)	PC-SWS (ml/min)
Baseline	29.9 (9.5)	16.6 (5.1)	2.09 (0.9)	0.26 (0.2)	0.89 (0.5)
Chewing gum	28.1 (9.1)[a]	15.4 (4.8)[a]	2.07 (0.9)	0.28 (0.2)	0.81 (0.4)
Saliva substitute	29.0 (9.6)	15.5 (5.0)[a]	2.08 (1.0)	0.30 (0.2)	0.89 (0.5)
Treatment (*P*-value)	0.024	0.015	NS	NS	NS

The columns provide data for the main outcome variables.
P-values are for the effect of the sequence and the overall treatment (repeated measures MANOVA). The two treatment modalities (chewing gum and saliva substitute) are compared with baseline and tested with a GLM-ANOVA, followed by paired *t*-tests as post-hoc procedures. [a]$P < 0.05$; NS, not significant.

Table 5. The effect of the two treatment modalities (chewing gum and saliva substitute) on the XI, DTI and IWG with regard to residual urine output, hyposalivation and thirst

	Residual urine output ($n=18$)			No residual urine output ($n=47$)		
	XI (11–55)	DTI (5–25)	IWG (kg)	XI (11–55)	DTI (5–25)	IWG (kg)
Baseline	24.7 (7.9)	13.9 (5.4)	1.4 (0.8)	31.9 (9.4)[a]	17.6 (4.7)[a]	2.4 (0.8)[a]
Chewing gum	24.7 (8.7)	12.8 (4.9)	1.3 (0.8)	29.3 (9.1)[b]	16.4 (4.3)[a]	2.4 (0.7)[a]
Saliva substitute	24.8 (8.6)	12.2 (5.5)	1.3 (0.8)	30.6 (9.5)[a,c]	16.7 (4.3)[a]	2.4 (0.9)[a]
Treatment (*P*-value)	NS	NS	NS	<0.05	NS	NS
	No thirst (DTI 5–15) ($n=26$)			Thirst (DTI 16–25) ($n=39$)		
	XI (11–55)	DTI (5–25)	IWG (kg)	XI (11–55)	DTI (5–25)	IWG (kg)
Baseline	22.8 (6.0)	11.4 (3.5)	1.8 (0.9)	34.5 (8.6)[d]	20.1 (2.3)[d]	2.3 (0.9)[d]
Chewing gum	22.5 (7.3)	12.2 (4.5)	1.7 (0.9)	31.6 (8.6)[b,d]	17.6 (3.6)[b,d]	2.3 (0.8)[d]
Saliva substitute	21.2 (5.5)	11.7 (3.9)	1.8 (1.2)	33.8 (8.6)[d]	18.0 (4.1)[b,d]	2.2 (0.8)
Treatment (*P*-value)	NS	NS	NS	<0.05	< 0.001	NS
	No hyposalivation (>0.16 ml/min) ($n=46$)			Hyposalivation (≤0.16 ml/min) ($n=19$)		
	XI (11–55)	DTI (5–25)	IWG (kg)	XI (11–55)	DTI (5–25)	IWG (kg)
Baseline	28.5 (9.4)	15.9 (5.5)	2.1 (1.0)	33.2 (9.1)[e]	18.4 (3.7)	2.1 (0.7)
Chewing gum	27.4 (9.5)	14.8 (4.7)	2.1 (1.0)	29.7 (8.4)[b]	17.2 (4.6)	2.0 (0.7)
Saliva substitute	27.3 (9.4)	14.8 (5.3)	2.1 (1.0)	33.0 (9.1)[e]	17.2 (3.9)	2.1 (1.0)
Treatment (*P*-value)	NS	NS	NS	<0.05	NS	NS

The columns provide data for the main outcome variables.
P-values are for the effect of the overall treatment (repeated measures MANOVA). The two treatment modalities (chewing gum and saliva substitute) are compared with baseline and tested with a GLM-ANOVA, followed by paired *t*-tests as post-hoc procedure. NS, not significant; [b]$P < 0.001$; [c]$P < 0.05$.
[a,d,e]Values in the right column ('no residual urine output', 'thirst' and 'hyposalivation') are significantly different from the corresponding value in the left column (one-way ANOVA).

Therefore, it is feasible that mechanical stimulation of saliva secretion by chewing gum potentially could reduce thirst.

This study is the first large-scale clinical crossover study to investigate the effect of chewing gum and a saliva substitute on xerostomia (XI), thirst (DTI) and IWG in patients on HD. Overall, the use of chewing gum for 2 weeks among HD patients significantly reduced both thirst and xerostomia. This is in agreement with other studies that investigated the effect of chewing gum on xerostomia in other patient populations, such as rheumatic patients [15] or in patients with a malignant disease [16]. Besides the role of oral dryness, other elements, such as sodium intake, high plasma sodium, potassium depletion, angiotensin-II levels, rapid increases in plasma urea and psychological factors, are involved in the multicomplexity of thirst and fluid intake among HD patients [4,13,17,18].

In this study the use of a saliva substitute by HD patients reduced perceived thirst but had no effect on xerostomia. In the literature, conflicting data about the efficacy of saliva substitutes have been presented. In 30 patients with radiation-induced xerostomia,

feelings of a dry mouth decreased after the use of a saliva substitute. However, other studies failed to show a substantial effect of saliva substitutes after radiation therapy or in patients with Sjögren's syndrome [7,19].

Although the effect of the therapy on the XI and DTI scores was modest, the majority of patients (72.3%) rated chewing gum as a beneficial therapy. Chewing gum was also rated best with respect to effectiveness, ease of use and taste compared with the saliva substitute (data not shown). Therefore, chewing gum seems preferable in the reduction of oral dryness and thirst among HD patients.

The mean salivary flow rates were normal and comparable, both to reference values for healthy individuals and to other studies in HD patients [14]. In general, patients with severe hyposalivation respond best on saliva substitutes [7]. This is in contrast to our study, in which gum chewing reduced xerostomia best in the subgroup with hyposalivation (UWS ≤ 0.16 ml/min). The most plausible reason is that xerostomia and hyposalivation in other investigations is of different origin [7,19,20]. Since it is likely that salivary glands are not affected by the HD treatment [4], mechanical or gustatory activation by chewing is still possible, in contrast to patients suffering from severe Sjögren's syndrome.

Previously, we have shown that thirst is significantly related to IWG [4]. Compliance to the fluid-restricted diet (500 ml/day) was measured by IWG. Although gum chewing and spraying with saliva substitute significantly reduced thirst, the IWG in HD patients was not affected. Several patients indicated that chewing and spraying had a distracting effect and resulted in postponing fluid intake; however, the net fluid intake remained the same in the study period. This might be explained by the patients knowing how much weight they are allowed to gain between dialysis sessions and, thus, how much they can drink, although no thirst is present. It might also be possible that a 2 week period is too short to affect the fluid intake and, thus, the IWG. The contribution of fluid intake due to the use of artificial saliva was negligible, since the average volume of artificial saliva used did not exceed 7 ml/day.

A potential limitation of this study is the lack of blinding. However, this is unavoidable in this crossover design in which the participant received two potential active agents (chewing gum and saliva substitute).

In conclusion, this crossover clinical trial shows that a saliva-stimulating agent (chewing gum) and a saliva substitute both induced a modest reduction in the level of thirst (DTI) in HD patients. The level of xerostomia (XI) was reduced after the use of chewing gum. However, no evidence of reduced fluid intake or weight gain could be obtained. HD patients younger than 65 years without residual urine output have to deal most with thirst and xerostomia, and could therefore benefit from chewing gum or artificial saliva. We conclude that the use of chewing gum, and to a lesser extent a saliva substitute, may alleviate thirst and xerostomia in some HD patients on a fluid-restricted diet and, thus, should be considered as a clinical tool to assist HD patients in adhering to the fluid-restricted diet.

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