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CLINICAL TRIAL

Efficacy and Safety of Thirst-Quenching Lozenges for Xerostomia in Patients Undergoing Hemodialysis: A Prospective, Single-Arm, Open-Label Study

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Abstract

Background: Xerostomia is a common symptom in patients with end-stage kidney disease (ESKD) undergoing hemodialysis and currently available treatments are of limited success.

Objectives: To evaluate the efficacy and safety of thirst-quenching lozenges (TQL) in patients with ESKD undergoing hemodialysis.

Design: A prospective, open-label, and single-arm study.

Participants: Adult (≥ 18 years) patients with ESKD undergoing hemodialysis thrice a week for ≥ 3 months were included and received TQL (1650 mg; thrice/day) for 2 weeks.

Measurements: The primary efficacy endpoints included change in xerostomia inventory (XI) and dialysis thirst inventory (DTI) scores from baseline to the end of the treatment. Secondary efficacy endpoints were proportion of patients satisfied in terms of thirst and dryness of mouth with lozenges and safety.

Results: Of 90 included patients, 83 were evaluable. Mean (standard deviation [SD]) age was 45.3 (13.7) years and the majority were men (69.0%). There was a significant improvement in mean (SD) of both XI and DTI scores from baseline to end of study (XI: 38.2 [10.8] vs. 25.4 [6.1]; $p < 0.001$ and DTI: 38.2 [10.8] vs. 16.1 [4.0]; $p < 0.001$). Mean (SD) fluid consumption also significantly reduced from baseline to end of study (718.9 [178.4]) vs. 568.1 [260.2] mL; $p < 0.001$). Most patients responded as satisfied versus unsatisfied with the study treatment (91.3% vs. 8.7%). No serious adverse events or deaths were reported; however, one patient discontinued the study due to diarrhea.

Conclusion: The TQLs were effective in reducing dryness of mouth and thirst without any safety concerns in patients with ESKD undergoing hemodialysis.

Keywords

End-stage kidney disease, Hemodialysis, Thirst-quenching lozenges, Xerostomia

Abbreviations

AE: Adverse Event; BMI: Body Mass Index; CI: Confidence Interval; DTI: Dialysis Thirst Inventory; EOS: End of Study; ESKD: End-stage Kidney Disease; IDWG: Interdialytic Weight Gain; QoL: Quality of Life; SD: Standard Deviation; TQL: Thirst Quenching Lozenge; XI: Xerostomia Inventory

Introduction

Xerostomia is a subjective complaint of dryness of oral cavity and is frequently reported (28% to 67%) in patients with end-stage kidney disease (ESKD); including those on chronic hemodialysis [1]. Xerostomia may be attributed to the reduced salivary flow as a result of atrophy and fibrosis of salivary glands as well as certain medications, which are commonly used in patients on hemodialysis [2-4]. Further, xerostomia and hyposalivation together augment the sensation of thirst in patients on hemodialysis. In these patients, xerostomia is associated with clinical consequences like, increased risk of oral infections and diseases, difficulty

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in chewing, swallowing, speaking, and may contribute to increased interdialytic weight gain (IDWG), which may reduce the overall quality of life (QoL) [1,5]. The oral diseases related to xerostomia include mucosal, gingival and tongue lesions, candidiasis, dental caries, periodontal disease, oral fungal and bacterial infections [6]. Furthermore, patients on chronic hemodialysis most often receive multiple drugs concomitantly and xerostomia is exacerbated by such polypharmacy [7]. Drugs causing xerostomia often are those with anticholinergic activity or those acting through mechanisms on brain centers to reduce fluid secretion [8].

Current treatment strategies for xerostomia generally target stimulation of the salivary glands either mechanically (e.g., sugar-free chewing gums, mouthwash, or acupressure) or pharmacologically (e.g., pilocarpine and cevimeline) [1]. Irrespective of mechanical and/or pharmacological actions, saliva substitutes are recommended for these patients with insufficient salivary secretion. These substitutes are available as different formulations containing either mucin, xanthan gum, carboxymethyl cellulose, hydroxyethyl cellulose or polyethylene glycol and have shown limited success [9-11]. Hence, novel strategies, which stimulate salivary secretions addressing xerostomia in patients with ESKD undergoing hemodialysis are warranted [1].

Most patients on hemodialysis need to maintain a fluid-restricted diet to prevent a high IDWG [12]. The prevalence of xerostomia is higher in these patients than in controls thus necessitating an alternative treatment that can stimulate salivary secretions and keep the oral mucosa moist. To address this unmet need in patients with chronic kidney disease suffering from dry mouth and thirst, a sugar-free xylitol based thirst-quenching lozenge (TQL) with unique release profile, proprietary patented technology, has been developed by Dr. Reddy's Laboratories. Xylitol is a natural sweetener and was proven to be effective in relieving symptoms of drug-induced xerostomia [13]. This study evaluated the efficacy and safety of TQL in reducing dryness of mouth and thirst in patients with chronic kidney disease stage 5 undergoing hemodialysis. Moreover, patient satisfaction with the use of TQL in reducing thirst was determined.

Methods

Study design

This was a prospective, open-label, single-arm study to evaluate the efficacy and safety of TQL in patients with chronic kidney disease stage 5 who were on hemodialysis at two centers in India between 2018 and 2019.

Ethics statement

The study protocol and informed consent form were reviewed and approved by an Independent Ethics Committee at each study center. A written informed consent was obtained from all the patients prior to the study initiation after explaining to them the study protocol in the language that they understood. The study was conducted in accordance with the International Council for Harmonization good clinical practice guidelines and ethical principles of the Declaration of Helsinki.

Study population

Adult (aged ≥ 18 years) patients with ESKD undergoing hemodialysis thrice a week for at least 3 months with daily urine output of < 200 mL were included in the study. Key exclusion criteria were patients who were scheduled for kidney transplantation or immune suppressant therapy, those who exceeded average weekly IDWG of ~2.5 kg, those admitted for fluid overload in last 3 months prior to screening, or those who had heart failure (New York Heart Association class IV). Other exclusion criteria included patients with active systemic infections, autoimmune conditions causing dryness of mouth like Sjogren's syndrome, uncontrolled diabetes, hypertension, and drugs causing dry mouth. Patients receiving drugs (sympathomimetic, antihypertensive, cytotoxic, anti-HIV drugs, opioids, benzodiazepines, and anti-migraine agents) which cause xerostomia was excluded.

Study endpoints and assessments

Baseline demographics (age, sex and body mass index) and clinical characteristics (medical history and comorbidities) were recorded. The primary efficacy endpoints included pre and post changes in xerostomia inventory (XI) and dialysis thirst inventory (DTI) scores from baseline to the end of study (EOS; i.e. 2 weeks). The XI and DTI are the standard validated questionnaires for xerostomia and thirst, respectively, and were assessed at screening, baseline, and at the EOS (week 2). These included several questions to evaluate XI (Supplementary Table 1) and DTI (Supplementary Table 2) with the scale of 'never/almost never', 'occasionally', 'fairly often/very often'.

Secondary efficacy endpoint included the proportion of patients satisfied with TQL in reducing dry mouth and thirst. The thirst severity was recorded by patients on a visual analogue score scale of 0-10 thrice a day (morning, afternoon and night). Safety was evaluated by observing adverse events (AEs), recorded as per Common Terminology Criteria for AEs (CTCAE; version 4.0), physical examination, vital signs and clinical laboratory investigations. Both patient-reported and investigator-observed AEs were recorded at all visits. Clinical laboratory investigations included blood urea, serum creatinine, blood glucose, serum uric acid, hemoglobin, glycated hemoglobin, and serum albumin at baseline and at the EOS. Patients were provided with diaries to record their fluid intake throughout the day and data were collected during each visit.

Study treatment

The study consisted of a 1-day screening phase, 1-week stabilization phase, and a 2-week treatment phase with a 1-week follow-up. Overall, patients had 8 visits: screening (Visit 1: Day 0), baseline (Visit 2: Day 7 ± 1), treatment period (Visit 3: Day 9; Visit 4: Day 11; Visit 5: Day 14; Visit 6: Day 16; Visit 7: Day 18) and end of study (Visit 8: Day 21 ± 1). Patients were administered TQL weighing 1650 mg (manufactured by Dr. Reddy's Laboratories) thrice a day for 2 weeks. Each TQL contained xylitol, lactose monohydrate, isomalt, acacia, hydroxypropyl cellulose, sucralose and magnesium stearate. There was no relation of the drug dosage to the meals and patients were advised to continue with the permitted concomitant medications.

Statistical analysis

The effect of treatment was compared with the baseline variables using the general linear model of Chi-square tests. The XI scale, DTI scale and the patient satisfaction scales were recorded on a 5 and 7 points Likert scale, respectively. The responses were cumulatively grouped as the worst response together and the best responses together and then the analysis was carried out using Chi-square for the frequency outcome comparison of before and after the intervention for the overall population.

Results

Patients

A total of 90 patients were enrolled and received TQL, of which 89 patients completed the study and one patient withdrew consent. At the discretion of the principal investigator, 6 patients were excluded from the study due to non-compliance and final data set evaluation was done for 83 participants. The mean age of the patients was 45.3 years and the majority were men (69.0%). Half of the patients had normal body weight (Table 1).

Efficacy

Patients displayed favourable outcomes to the TQL with a reduction in the mean (SD) XI (Baseline: 38.2 [10.8] vs. EOS: 25.4 [6.1]; $p < 0.001$; Table 2) and DTI scores (Baseline: 38.2 [10.8] vs. EOS: 16.1 [4.0]); $p < 0.001$; Table 2) from baseline, indicating improvements, when compared with those at the EOS. In context with XI questionnaires, percentage patients opted for 'fairly often' as a response for following questions (baseline vs. EOS): required sip of liquid to swallow food (39.3% vs. 6.0%), dry mouth while eating food (41.7% vs. 10.8%), got up in the night to drink (27.4% vs. 3.6%), difficulties in eating dry fruits (34.5% vs. 16.9%), dry face skin (36.9% vs. 10.8%), and dry eyes (17.9% vs. 2.4%). Percentage patients opted for 'fairly often' as a response for following DTI questions (baseline vs. EOS): thirst is a problem for me (31.0% vs. 3.6%), thirsty during day (40.5% vs. 8.4%), thirsty during night (25.0% vs. 8.4%), social life is influenced by thirst (15.5% vs. 1.2%), thirsty before dialytic session (50.0% vs. 8.4%), thirsty during dialytic session (27.4% vs. 8.4%), thirsty after dialytic session (45.2% vs. 7.2%). Detailed responses on XI and DTI questions are described in Table 3.

Most patients responded as satisfied versus unsatisfied with the study treatment (91.3% vs. 8.7%; Table 4). Patients' response on overall treatment satisfaction questionnaires showed that a greater number of patients were satisfied in terms of relief in condition, relief in symptoms, side effects, timing of medication, and overall confidence on medication and

Table 1: Demographic and baseline characteristics.

Characteristics	Total patients (N = 84)
Age, mean (SD), years	45.3 (13.7)
Sex, n (%)	
Men	58 (69.0)
Body mass index score (Kg/m^2), n (%)	
Underweight (< 18.5)	4 (4.8)
Healthy or normal weight (18.5-24.99)	50 (59.5)
Overweight (25-29.99)	27 (32.1)
Obese (≥ 30)	3 (3.6)
Presence of comorbid conditions, n (%)	
One systemic illness	58 (69.0)
More than one form of illness	23 (27.4)
Not mentioned	3 (3.6)
Pulse rate, mean (SD)	78.9 (3.9)
Respiratory rate, mean (SD)	18.4 (7.2)

Note: SD: Standard deviation.

Table 2: Primary efficacy parameters in patients treated with thirst-quenching lozenges.

Parameters	N	Mean (SD)	Mean difference	p-value
Xerostomia inventory score				
Baseline	84	38.2 (10.8)	12.8	< 0.001
End of the study	83	25.4 (6.1)		
Dialysis thirst inventory score				
Baseline	84	38.2 (10.8)	22.1	< 0.001
End of the study	83	16.1 (4.0)		

Note: SD: Standard deviation.

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Table 3: Patients' response to xerostomia inventory and dialysis thirst inventory questionnaires at baseline and end of the study treatment.

	Never, n (%)		Almost never, n (%)		Occasionally, n (%)		Fairly often, n (%)		Very often, n (%)	
	Baseline	**EOS**	**Baseline**	**EOS**	**Baseline**	**EOS**	**Baseline**	**EOS**	**Baseline**	**EOS**
Xerostomia Inventory Questionnaires										
I sip liquid to aid in swallowing food	6 (7.1)	32 (38.6)	3 (3.6)	19 (22.9)	29 (34.5)	27 (32.5)	33 (39.3)	5 (6.0)	13 (15.5)	0
My mouth feels dry when eating a meal	5 (6.0)	13 (15.7)	8 (9.5)	38 (45.8)	17 (20.2)	20 (24.1)	35 (41.7)	9 (10.8)	19 (22.6)	3 (3.6)
I get up at night to drink	13 (15.5)	20 (24.1)	7 (8.3)	39 (47.0)	11 (13.1)	12 (14.5)	23 (27.4)	3 (3.6)	30 (35.7)	9 (10.8)
My mouth feels dry	2 (2.4)	15 (18.1)	3 (3.6)	26 (31.3)	32 (38.1)	37 (44.6)	41 (48.8)	5 (6.0)	6 (7.1)	0
I have difficulty in eating dry fruits	7 (8.3)	15 (18.1)	6 (7.1)	24 (28.9)	22 (26.2)	30 (36.2)	29 (34.5)	14 (16.9)	20 (23.8)	0
I suck sweets or cough drops to relieve dry mouth	12 (14.3)	18 (21.7)	6 (7.1)	31 (37.4)	26 (31.0)	20 (24.1)	26 (31.0)	3 (3.6)	14 (16.7)	11 (13.3)
I have difficulties swallowing certain foods	11 (13.1)	17 (20.5)	11 (13.1)	26 (31.3)	19 (22.6)	32 (38.6)	21 (25.0)	5 (6.0)	22 (26.2)	3 (3.6)
The skin of my face feels dry	9 (10.7)	17 (20.5)	8 (9.5)	23 (27.7)	22 (26.2)	31 (37.4)	31 (36.9)	9 (10.8)	14 (16.7)	3 (3.6)
My eyes feel dry	21 (25.0)	30 (36.2)	8 (9.5)	25 (30.1)	17 (20.2)	25 (30.1)	15 (17.9)	2 (2.4)	23 (27.4)	1 (1.2)
My lips feel dry	08 (9.5)	13 (15.7)	8 (9.5)	30 (36.2)	30 (35.7)	31 (37.4)	19 (22.6)	9 (10.8)	19 (22.6)	0
The inside of my nose feels dry	19 (22.6)	01 (1.2)	9 (10.7)	8 (9.6)	12 (14.3)	33 (39.8)	24 (28.6)	27 (32.5)	19 (22.6)	14 (16.9)
Dialysis Thirst Inventory Questionnaires										
Thirst is a problem for me	2 (2.4)	20 (24.1)	04 (4.78)	31 (37.4)	40 (47.6)	28 (33.7)	26 (31.0)	3 (3.6)	12 (14.3)	1 (1.2)
I am thirsty during the day	1 (1.2)	11 (13.3)	03 (3.6)	27 (32.5)	31 (36.9)	33 (39.8)	34 (40.5)	7 (8.4)	15 (17.9)	5 (6.0)
I am thirsty during the night	11 (13.1)	24 (28.9)	13 (15.5)	32 (38.6)	18 (21.4)	15 (18.1)	21 (25.0)	7 (8.4)	21 (25.0)	5 (6.0)
My social life is influenced by my thirst	5 (6.0)	29 (34.9)	21 (25.0)	29 (34.9)	36 (42.9)	24 (28.9)	13 (15.5)	1 (1.2)	9 (10.7)	0
I am thirsty before dialytic session	8 (9.5)	22 (26.5)	10 (11.9)	33 (39.8)	17 (20.2)	20 (24.1)	42 (50.0)	7 (8.4)	7 (8.3)	1 (1.2)
I am thirsty during dialytic session	7 (8.3)	20 (24.1)	14 (40.5)	24 (28.9)	23 (27.4)	30 (36.2)	23 (27.4)	7 (8.4)	17 (20.2)	2 (2.4)
I am thirsty after dialytic session	9 (10.7)	19 (22.9)	8 (9.5)	28 (33.7)	22 (26.2)	27 (32.5)	38 (45.2)	6 (7.2)	7 (8.3)	3 (3.6)

Note: EOS: End of the study.

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Table 4: Treatment satisfaction at the end of the study in patients treated with thirst-quenching lozenges.

Questions	Patient satisfaction, n						
	Extremely dissatisfied	**Very dissatisfied**	**Dissatisfied**	**Somewhat satisfied**	**Satisfied**	**Very satisfied**	**Extremely satisfied**
How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?	0	0	5	8	27	32	11
How satisfied or dissatisfied are you with the way the medication relieves your symptoms?	0	0	3	12	27	28	13
How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?	0	0	3	17	35	22	6
As a result of taking this medication, do you experience any side effects at all?	0	0	0	0	0	0	0
How easy or difficult is it to use the medication in its current form?	0	1	1	5	22	40	14
How easy or difficult is it to plan when you will use the medication each time?	0	1	1	4	40	25	12
How convenient or inconvenient is it to take the medication as instructed?	0	1	0	8	33	27	14
Overall, how confident are you that taking this medication is a good thing for you?	0	5	11	15	17	0	0
How certain are you that the good things about your medication outweigh the bad things?	2	8	16	42	15	0	0
Taking all things into account, how satisfied or dissatisfied are you with this medication?	0	0	4	13	30	23	13
Total	**2**	**16**	**44**	**124**	**246**	**197**	**83**

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Table 5: Mean (SD) fluid consumption from baseline to end of the study in patients treated with thirst-quenching lozenges

Fluid consumption		Mean (SD), mL	
Baseline (Day 7, Visit 1)		718.9 (178.4)	
Treatment (Day 9, Visit 2)		680.7 (214.7)	
Treatment (Day 11, Visit 3)		648.9 (196.7)	
Treatment (Day 14, Visit 4)		658.7 (239.6)	
Treatment (Day 16, Visit 5)		632.9 (229.9)	
Treatment (Day 18, Visit 6)		597.7 (235.2)	
End of study (Day 21, Visit 7)		568.1 (260.2)	
Visit to visit comparison	**Mean difference**	**95% CI**	**p-value**
Visit 2 vs. Visit 3	-38.2	-139.3 to 62.9	0.889
Visit 2 vs. Visit 4	-60.2	-161.3 to 40.9	0.530
Visit 2 vs. Visit 5	-86.0	-187.1 to 15.1	0.147
Visit 2 vs. Visit 6	-121.2	-222.3 to -20.1	0.009[a]
Visit 2 vs. Visit 7	-150.8	-251.9 to -49.7	0.001[a]
Visit 3 vs. Visit 4	-22.0	-123.1 to 79.1	0.989
Visit 3 vs. Visit 5	-47.8	-148.9 to 53.3	0.756
Visit 3 vs. Visit 6	-83.0	-184.1 to 18.1	0.177
Visit 3 vs. Visit 7	-112.6	-213.7 to -11.5	0.019[a]
Visit 4 vs. Visit 5	-25.8	-126.9 to 75.3	0.978
Visit 4 vs. Visit 6	-61.0	-162.1 to 40.1	0.516
Visit 4 vs. Visit 7	-90.6	-191.7 to 10.5	0.109
Visit 5 vs. Visit 6	-35.2	-136.3 to 65.9	0.919
Visit 5 vs. Visit 7	-64.8	-165.9 to 36.3	0.446
Visit 6 vs. Visit 7	-29.6	-130.7 to 71.5	0.960

Note: [a]Statistically significant; CI: Confidence interval; SD: Standard deviation.

its form.

There was a significant reduction in the mean (SD) fluid consumption from 718.9 (178.4) mL at baseline to 568.1 mL (260.2; p = 0.001) at the EOS. Visit to visit comparison showed a reduction in fluid consumption at every visit until EOS (Table 5).

The IDWG was monitored throughout the study. Mean (SD) weight was 62.2 kg (7.9) at the baseline and 62.4 kg (7.9) at the EOS with no significant change (Table 6).

Safety

No serious AEs or deaths were reported in the study. One patient discontinued the study due to diarrhea; however, this resolved later. No major changes were observed in blood glucose levels. The mean (SD) fasting blood glucose was 101.1 (85.1) mg/dL at the baseline and was 90.8 (22.9) mg/dL at the EOS. The mean postprandial glucose level was 124.8 (20.8) mg/dL at baseline and 126.6 (20.8) mg/dL at the EOS.

Discussion

Xerostomia, often encountered in patients on chronic hemodialysis, negatively impacts the patients' QoL due to complications in chewing/swallowing and an increased risk of oral disease [1]. Treatment with sugar-free TQL showed a significant reduction in xerostomia and thirst and a decrease in consumption of fluid. Patients also showed satisfaction with TQL use in reducing dry mouth.

Table 6: Weight distribution throughout the study in patients treated with thirst-quenching lozenges

Visit	Mean (SD) weight[a], Kg
Baseline (Day 7, Visit 1)	62.2 (7.9)
Treatment (Day 9, Visit 2)	62.0 (7.9)
Treatment (Day 11, Visit 3)	62.4 (7.9)
Treatment (Day 14, Visit 4)	62.9 (11.7)
Treatment (Day 16, Visit 5)	62.3 (7.9)
Treatment (Day 18, Visit 6)	62.4 (7.9)
End of the study (Day 21, Visit 7)	62.4 (7.9)

Note: [a]p-value, 0.9683 (no significant difference was observed from baseline to end of the study).

Available treatment options have limited success in terms of alleviating thirst and associated comorbidities in these patients. A few studies, which were conducted to evaluate the efficacy of treatments with pharmacological as well mechanical actions such as pilocarpine, artificial saliva, chewing gum, and acupressure in patients with xerostomia on hemodialysis, were inconclusive and/or contradictory for xerostomia symptoms (such as salivary flow and impact on thirst) [14-18]. Clinical benefits have been reported with saliva substitutes in patients with radiotherapy-related xerostomia or with Sjögren syndrome [9-11]. A cross-sectional study in patients on hemodialysis has demonstrated that 2-week treatment with chewing gum and saliva substitute significantly reduced XI (p = 0.024) and DTI (p = 0.015) scores compared to baseline [19]. In contrast, in another study, regular use of sugarless chewing gum for 3 months did not alleviate xerostomia symptoms and thirst in a group of 38 patients on hemodialysis [15].

In a randomized study, patients on chronic hemodialysis who had received liquorice mouthwash showed significant lowering of XI scores at day 5 and day 10 compared to baseline [20]. Another study reported that xerostomia improved in terms of reduced XI score with 4 weeks of treatment with auricular acupressure [18]. Additionally, the other treatment options used for the management of dry mouth and to prevent damage of salivary glands including pilocarpine and cevimeline, reported severe AEs (sweating, vomiting, and diarrhea) [1].

Above studies on xerostomia have shown efficacy with different treatment strategies but not proven as a complete standard-of-care for xerostomia in patients with ESKD undergoing hemodialysis. The current study showed clinical benefits of the TQL for xerostomia, patients' answers to individual questions, which

altogether evaluated overall XI scores, showed that at baseline, higher proportion of the patients required sip of liquid for swallowing food, felt dryness of mouth when eating a meal, frequently drank water during the night, had dryness of mouth, and difficulties in eating dry food. Reduction in all the above individual complications was reported with the lozenges and at the EOS, a high number of patients answered 'never' or 'almost never' for these questions. Similarly, in the DTI questionnaires at baseline, patients opted for 'often' or 'fairly often' in response to the following questions- thirst was a problem, thirsty during the day, thirsty during the night, social life influenced by thirst, thirst before, after, and during the dialytic session. However, at EOS, a high proportion of patients treated with lozenges answered 'never' or 'almost never' for the above complications. Thirst and dry mouth impact the QoL of patients who are on hemodialysis. Thirst can be a sign of disorientation and discomfort in these patients [21]. Previously published studies reported that approximately 80% of the patients are non-adherent with restrictions on liquids, which eventually contributes to IDWG and reduced QoL [22].

Studies have reported a positive correlation among xerostomia, thirst and IDWG; in general, patients on hemodialysis with high levels of thirst and xerostomia, gain more weight between hemodialysis sessions [12,23]. The IDWG results from consumption of salt and liquids between two hemodialysis sessions [24,25]. Non-adherence to the fluid-restricted diet may result in complications, such as congestive heart failure and cardiovascular comorbidity, hypertension, and acute pulmonary edema [12,22]. In the current study, a significant reduction was reported in the mean fluid consumption from baseline to the EOS; mean body weight was consistent throughout the study and none of the patients experienced IDWG. This consistent body weight change observed during the study, despite a significant change in fluid consumption might be due to several other factors including diet which were not controlled during the study.

A strong association between xerostomia and reduced QoL has been reported earlier [26,27]. Our study reported enhanced QoL with the TQL. Overall, a significant difference was observed in the patients who were satisfied with the study treatment versus those who were not satisfied; patient's satisfaction was in terms of relief in condition, relief in symptoms, side effects, timing of medication, and overall confidence on medication and its form. The study is limited by the inherent limitation of being an open-label, single-arm study, with short duration and small sample size. Further long-term head-to-head studies with large sample size are warranted to corroborate the results in this study.

Conclusion

The findings of this study demonstrated that TQLs are effective in lowering symptoms of dry mouth and thirst without any safety concerns. Moreover, a high proportion of patients were satisfied with the treatment outcome of lozenge intervention. Therefore, TQL can serve as supportive care to enhance the QoL in patients with ESKD undergoing hemodialysis.

Conflict of Interest

MS and **AA** declare no conflicts of interests. **SMHN**, **RMK**, **PDP**, **VH**, **SM** and **AM** are employees of the Dr. Reddy's Laboratories Ltd, Hyderabad, India.

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Author Contributions

All authors meet ICMJE criteria and had access to the study data, provided direction and comments on the manuscript, made the final decision about where to publish these data and approved submission to this journal. **MS and AA:** Principal investigators, conducted the study, helped to draft the manuscript and approved the final manuscript. **SMHN:** Principal project leader, conceived study, participated in study design and coordination, analysed the data, helped to draft the manuscript and approved the final manuscript. **VH:** Conceptualized the test compound of the study and helped to draft the manuscript and approved the final manuscript. **SM:** Conceived study, participated in study design and coordination, helped to draft the manuscript and approved the final manuscript. **AM:** Participated in study execution and coordination, helped to draft the manuscript and approved the final manuscript. **PDP** and **RMK:** Analysed the data, helped to draft the manuscript and approved the final manuscript.

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Supplementary Table 1: Xerostomia Inventory Questionnaire.

Sr. No	Question	Responses
1	I sip liquid to aid in swallowing food [1,2]	□Never/almost never, □Occasionally, □Fairly often/very often
2	My mouth feels dry when eating a meal [1,2]	□Never/almost never, □Occasionally, □Fairly often/very often
3	I get up at night to drink [1,2]	□Never/almost never, □Occasionally, □Fairly often/very often
4	My mouth feels dry [1,3]	□Never/almost never, □Occasionally, □Fairly often/very often
5	I have difficulty in eating dry fruits [1,2]	□Never/almost never, □Occasionally, □Fairly often/very often
6	I suck sweets or cough drops to relieve dry mouth [1]	□Never/almost never, □Occasionally, □Fairly often/very often
7	I have difficulties swallowing certain foods [1]	□Never/almost never, □Occasionally, □Fairly often/very often
8	The skin of my face feels dry [1]	□Never/almost never, □Occasionally, □Fairly often/very often
9	My eyes feel dry [1]	□Never/almost never, □Occasionally, □Fairly often/very often
10	My lips feel dry [1]	□Never/almost never, □Occasionally, □Fairly often/very often
11	The inside of my nose feels dry [1]	□Never/almost never, □Occasionally, □Fairly often/very often

Supplementary Table 2: Dialysis Thirst Inventory Questionnaire.

Sr. No	Question	Responses
1	Thirst is a problem for me [4,5]	□Never/almost never, □Occasionally, □Fairly often/very often
2	I am thirsty during the day [4,6]	□Never/almost never, □Occasionally, □Fairly often/very often
3	I am thirsty during the night [4,7]	□Never/almost never, □Occasionally, □Fairly often/very often
4	My social life is influenced by my thirst [4,8]	□Never/almost never, □Occasionally, □Fairly often/very often
5	I am thirsty before dialytic session [4,9]	□Never/almost never, □Occasionally, □Fairly often/very often
6	I am thirsty during dialytic session [4,10]	□Never/almost never, □Occasionally, □Fairly often/very often
7	I am thirsty after dialytic session [4,11]	□Never/almost never, □Occasionally, □Fairly often/very often

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