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Research Article

A COMPARATIVE STUDY ON THE EFFECT OF SUGAR-FREE GUM WITH SUGAR-FREE CANDIES ON XEROSTOMIA IN THE PATIENTS UNDERGOING HEMODIALYSISAli Mansouri¹, Aziz Shahraki Vahed¹, Sadegh Dehghanmehr^{2*}, Safoora Nooraie³¹Msc in Nursing, Faculty of Nursing and Midwifery, Zabol University of Medical Science, Zabol, Iran²Student, Student Research Committee, Faculty of Nursing and Midwifery, Zabol University of Medical Sciences, Zabol, Iran³Nursing Expert, Zabol University of Medical Sciences, Zabol, Iran.**Abstract:**

Background: Xerostomia is one of the most significant and the most commonly observed symptoms in patients undergoing hemodialysis, the aim of this study was to compare the effect of sugar-free chewing gum with sugar-free candies in patients undergoing hemodialysis.

Methods: This study was a quasi-experimental study. The patients were examined by xerostomia index (XI). In one intervention group, when thirsty patients used sugar-free chew gum for a week, and in another intervention group they used sugar-free candies for a week. The control group did not receive any intervention. SPSS software version 22 was used to analyze the data.

Results: Based on the results in both groups, sugar-free chewing gum users and sugar free candies users, there was a significant difference between the xerostomia of the patients before and after intervention ($P < 0.05$). Before the intervention, xerostomia of patients was not significantly different in the three groups ($P > 0.05$).

Conclusion: Results of this study, which showed the effects of sugar-free chewing gum and sugarless candy on the reduction of xerostomia in hemodialysis patients, so in a variety of patients whom are suffering from various xerostomia, including those undergoing radiotherapy and hemodialysis, these methods can be used.

Keywords: Sugar Free Chewing Gum, Sugarless Candy, Xerostomia, Hemodialysis

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INTRODUCTION:

Chronic Renal Failure (CRF) is a progressive and irreversible degeneration of the kidney function, in which the body's ability is eliminated to keep metabolism and to balance the water and electrolytes [1]. End-stage renal disease (ESRD) is a form of severe chronic renal disease, and is referred to the irreversible decreasing of kidney function, which results in death if it was not under hemodialysis or kidney transplant [2]. The incidence of ESRD is rising substantially, so that in the USA, number of people over the past few years has been around 10 times higher [3].

Its prevalence in Japan has been estimated more than 2,000 people, in the USA were 1500 and in the European Union 800 of every 1 million people. According to official reports, in our country the annual increase in the ESRD is equivalent to 11%, and the incidence and prevalence rates in Iran is 53 and 250 per million, respectively. In Iran, about 54% of ESRD patients are undergoing hemodialysis and other are undergoing transplantation or peritoneal dialysis [4]. According to other studies and based on the statistics, there were more than 24,000 ESRDs in Iran in 2008 [5]. Although the abundance of treatments for renal replacement is different in various geographic regions, the most common used method is hemodialysis in the most patients [6]. More than 200,000 patients with chronic renal failure in the United States and more than one million people worldwide live through hemodialysis.

Renal patients have a high mortality rate [7]. Over 60,000 people die every year due to chronic renal failure. Chronic renal failure and its treatment can cause systemic tissue problems such as nervous, cardiovascular, respiratory, intracerebral, blood, gastrointestinal, and urinary disorders and affects directly or indirectly on the flow, density and composition of the saliva [8]. The mortality rate of this disease, death per 1000 people has been reported in countries such as the USA, Australia, and New Zealand between 2001 and 2009 [9]. It is estimated that around 10 % of dialysis patients die annually in Iran due to a population of 15,000 hemodialysis patients that about 1,500 dialysis patients die annually [10]. In hemodialysis patients due to the disability of the kidneys in the disposal of water and sodium [11], the volume of urine decreases [12] and the excessive use of fluids leads to edema and overweight [13].

Recommended solutions for reducing the intake of fluids include: administration of angiotensin converting enzyme inhibitors drugs, increasing the frequency of dialysis, limit the amount of sodium intake and cut down protein intake and limit fluid [14]. Intense thirst due to fluid deficiencies and negative symptoms associated with thirst may be led to a lack of compliance with this diet and consequently led to overweight between two dialysis sessions [15,16]. Xerostomia is one of the most common complications that about 10 % of people over 50 years of age and 35 % of adults over 65 years of age are affected. Different causes of reduced saliva secretion and xerostomia include: 375 types of medicines (anti cholinergic, anti-hypertensive medicines, etc.), some diseases (diabetes, Parkinson's disease, etc.), infections, head and neck radiotherapy, menopause, and psychological stresses [17]. Many patients undergoing hemodialysis are susceptible to severe xerostomia. The causes of xerostomia in these patients include dryness of mouth and esophageal mucosa, an increase in angiotensin-2 levels, an increase in sodium levels, an increase in antidiuretic hormone, and an increase in osmolality of the plasma [18]. The most common clinical symptoms in hemodialysis patients are taste changes and stomatitis. Also changes in the flow of saliva will occur [19]. Xerostomia is one of the most common symptoms in hemodialysis patients so that more than 30% of the patients suffer from this complication [18,20]. This complication can affect the quality of life of hemodialysis patients, leading to discomfort, as well as overweight between two dialysis sessions (IVG) [21,22]. There are several ways to treat xerostomia, which are very supportive. For example, in order to relieve the effects and disadvantages caused by thirst, you can use water for the full length of a day or put the ice on the mouth in order to melt gradually.

Treatments such as the use of artificial saliva, prescribing medicines with similar function of Parasympathetic was done such as Pilocarpine Hydrochloride (5 mg, 3 times per day), mouthwash by baking soda, and no alcoholic beverage consumption and so on [23]. But taking medicine will have specific side effects therefore it is necessary to find non-prescriptive and uncomplicated solutions to quench thirst for these patients, so based on harmful and adverse effects of medicine for reducing xerostomia so It seems necessary to find non-pharmacological solutions for these kind of the patients. Non-pharmacological methods that are used

to reduce xerostomia include: limitation of salt intakes, eating raw fruits and vegetables, oral care, sucking hard candies, chewing gum and ice chips [24]. Jagodzinsky in his study said that fluids which consumed by hemodialysis patients to remove dryness of the mouth, led to overweight between dialysis times and chewing gum is a part of the treatment to prevent the complication [25]. Children who use sugar free –chewing gum were made more secretion of saliva compared with their peers. Sugar-free chewing gum has gained specific attention for stimulation of the salivary glands; mechanical restoring the tooth and antibacterial effects [26]. Sugar-free chewing gum improves the flow of saliva and alleviates the xerostomia caused by it. Scientific evidence suggests that chewing gum is a traditional way to prevent oral and dental illness [27]. Stimulation of salivary glands by sugar –free chewing gum has increased 12-14 times higher. The highest amount of saliva was during the first 5-7 minutes of sugar- free chewing gum [28] in a study conducted on cancer patients, it was found that chewing gum led to an increase in the flow of saliva and the reduction of xerostomia due to radiotherapy in cancer patients [6]. It has been suggested that sugar-free chewing gum can help eliminate xerostomia in patients undergoing hemodialysis [7-9]. Sucking candy leads to an increase in the amount of saliva flow by 17 times [29] and improves periodontal condition, increases total antioxidant capacity of saliva, decreases salivary lipid oxidation, and reduce bleeding from the gum and stomatitis [30].

Patients with head and neck cancers undergoing radiotherapy also suffer from reduction in the flow of saliva and xerostomia, which they suck candy to improve the condition [31], also, sucking of lemonade candy after radiotherapy in patients with thyroid cancer reduce the xerostomia of this patients, and patients who immediately start sucking lemon candy recovered faster more than those who used the candy after 24 hours [32]. In a study was done by Jendotier on cancer patients, concluded that patients undergoing radiotherapy can use candy to reduce the xerostomia [33]. Another study has also shown that sucking sugar –free candy can stimulate saliva glands and increase salivation, resulting in decreased xerostomia [34]. In a study by Mazloom and his colleagues, it was also noted that sucking ice chips by hemodialysis patients did not have an effect on the reduction of xerostomia [35], xerostomia has many complications, including cardiovascular problems. Cardiovascular problems are one of the most

common causes of death in patients undergoing hemodialysis. Based on numerous studies It is approved the effect of sugar-free chewing gum on the xerostomia, as well as sucking sugar -free candy to relieve xerostomia in hemodialysis patients so according to the available studies and necessity to find suitable solution for xerostomia in the hemodialysis patients as the common symptoms in these patients, in this study the aim of the researcher is to compare effect of sugar-free chewing gum and candy on xerostomia in the patients undergoing hemodialysis treatment in Zabol City.

MATERIALS AND METHODS:

This is a quasi-experimental study. The aim of this study was to evaluate the comparative study of the effects of sugar-free chewing gum and sugarless candy on the xerostomia in the patients undergoing hemodialysis in Zabol city. The sample size were determined by using the Cochran formula and confidence coefficient of 95% and accuracy of 0.07, and according to Mazloom et al study and his colleagues³⁵ has been determined that it is equivalent to 60 individuals, so among the patients, the subjects who entered the study were randomly divided into three groups: sugar-free chewing gum group (20 people), sugar-free candy group (20 people) and control group (20 people).

The criteria for entry into this study were:

Age between 18 and 65⁴², at least 6 months and at most 8 years treated with hemodialysis, two to three times per week and each time 3 to 4 hours,⁴² Willingness to use the gum or candy, No mental disorder and acute emotional disorders that prevents effective communication. The instrument of this research is a demographic specification form and an instrument for measuring xerostomia index (XI) for examination of patients' xerostomia. The personal profile form includes questions about the individual information and the patient's records which was completed through interviewing and reviewing the case file. The xerostomia index questionnaire (XI) contains 11 questions. Before dialysis, the xerostomia level is measured at the end of pervious dialysis session until the end of current dialysis session based on the Likert scale (1=never, 2=rarely, 3=sometimes, 4=more times and 5=always). Score 11 indicates non-xerostomia and score 55 indicates high xerostomia. The content validity of the xerostomia questionnaire has been confirmed in a study on hemodialysis patient conducted by HajarEbrahmiRigi and Seyed Reza Mazloom in Mashad City.³⁵ The reliability of this tool have been confirmed in this study by re-test and was equal 0.763. First, written informed consent

to participate in the study was taken and the individual profile form was filled out by doing interviews the patient and reviews the patient's record files. Before intervention, Xerostomia was measured in patients by using research tools. Patients in group A used sugar-free chewing gum during their thirst for a week and group B used sugar free- candy. For reminding the intervention on the patients, each morning a text message was sent by the researcher to each research unit's within a week. Patients in the control group did not receive any intervention. After a week, a researcher was presented in the study field and a xerostomia questionnaire gave to the patients and these questionnaires were filled out by patients. It is worth mentioning that patients are being trained about the foods and agents which effect on the xerostomia, and they are asked to follow a trained diet within a week and those who did not comply with these conditions or did not want to continue to collaborate in the study were removed and replaced. The collected data form of individual was analyzed by using descriptive and inferential statistics and SPSS version 22 software.

RESULTS:

In this study, the average age of patients in the chewing gum group was 52.17, in the candy group

51.93 and in the control group was 53.07. In the group of chewing gum, 60% of the research units were women and 40% were men. The candy group consisted of 65% of the women and 35% of the men and in control group 85% of the sample was women and 15% were men. In the chewing gum group, 20 cases (100%), in the candy group, and 17 cases (85%) and in the control group, 15 cases (75%) of research units formed the married. Based on marital status, there was a significant difference between the three groups of patients. The range of changes of the first dialysis history was 1 to 11 years, and in this sense there was no significant difference between the three groups ($P>0.05$). The minimum number of hemodialysis was twice a week, the maximum number was three times a week and was not observed significant differences in the three groups for number of dialysis per week ($P>0.05$).

Xerostomia was compared in each group before and after intervention. Results showed that there was significant difference in xerostomia in the chewing gum and the candy groups before and after the intervention ($P<0.05$) but in the control group there was no significant differences before and after intervention ($P>0.05$)(Table 1).

Table 1: Comparison of mean xerostomia in all three groups before and after the intervention

p-value	Statistical test	After intervention	Beforeintervention	Group	variable
		mean±Standard deviation	mean±Standard deviation		
0.001	wilcoxon	8.12±20.18	9.21±45.12	Chewing gum	xerostomia
0.001	wilcoxon	6.10±25.78	5.95±44.12	candy	
0.44	wilcoxon	7.32±46.61	6.78±42.82	control	

Also, xerostomia was compared in three groups before intervention. Results indicated that there was no significant difference between the three groups before intervention. ($P>0.05$) (Table 2).

Table 2: Comparison of the mean of xerostomia in the three groups before intervention

p-value	Statistical test	control	Candy	Chewing gum	Group Variable
		Standard mean±deviation	Standard mean±deviation	Standard mean±deviation	
0.72	Kruskal-wallis	6.78±42.82	5.95±44.12	9.21±45.12	xerostomia

Also, Thexerostomia has been compared in the three groups after intervention. that results showed that there was a significant difference between the three groups. ($P<0.05$). According to the obtained mean and standard deviation of xerostomia in each group,

the lowest mean was related to the chewing gum group and then it is related to sugar-free candy. So sugar-free chewing gum reduce higher level of xerostomia in the hemodialysis patients (Table 3).

Table 3: Comparison of mean xerostomia in the three groups after intervention

p-value	Statistical test	control	candy	Chewing gum	Group variable
0.0001	Kruskal-wallis	Standard mean±deviation	Standard mean±deviation	Standard mean±deviation	xerostomia
		7.32±46.61	6.10±25.78	8.12±20.18	

DISCUSSION:

The results of this study showed that the mean decrease of xerostomia in the sugar-free chewing gum group and sugar-free candy group were significantly more than the control group. Also, the mean reduction of xerostomia in the sugar-free chewing gum group was more than free-sugar candy group, which suggests that in this study, sugar-free chewing gum has a more effect on reducing xerostomia of the patients undergoing hemodialysis, but this is not a big difference, and sugar-free candy also decreases xerostomia significantly in these patients. It is possible that sucking sugar-free candy and sugar-free chewing gum increase blood flow to the saliva glands, as well as stimulate these glands and increase the flow of saliva that can lead to reduced xerostomia [40]. By reviewing similar studies, did not find a study that was similar to our study in addition done studies in this field were limited so that the researcher used this part of the study that is in some way related to the present subject. Dr. Azardarbandi and his colleagues compared the effect of sugar-free chewing gum containing bicarbonate and sugar-free chewing gum on the flow of saliva in 2007. so concluded that both types of chewing gum lead to reduced acidity and increased the flow of saliva and reduced xerostomia [36]. In another study done by Maryam Karami Norgorani in 2010, she compared the effect of ordinary chewing gum with saliva boosting chewing gum. In this study, it was found that both types of chewing gums can greatly increase the flow of saliva but in a specific saliva-boosting chewing gum, the flow of saliva reach to approximately 12 times [37]. The results of two studies are consistent with the present study based on the effect of sugar-free chewing gum on increasing the flow of saliva and resulting in reduced xerostomia. In 2013, Zhang and his colleagues conducted a study on the hemodialysis patients. Zhang concluded that xerostomia in patients undergoing hemodialysis is high and chewing gum can help to reduce it. On the other hand, it has been determined that xerostomia in patients undergoing hemodialysis may be accompanied by various irreversible complications [21]. The present study was also confirmed by the result of this done study and on the other hand was alarmed about the xerostomia complications that one of the most

important complications due to xerostomia is cardiovascular complications [35], which probably the reason for this dangerous side-effect is accumulation of excessive fluids in patients body following taking high levels of water for reducing xerostomia. Kaaejk, in 2016, tested the effect of chewing gum on the flow of saliva and xerostomia in patient under radiotherapy and after taking cisplatin for two weeks. Based on this study, they concluded that 14 of the subjects showed increased the flow of saliva by chewing gum and Chewing gum can increase the amount of saliva that can lead to reduced xerostomia in patients undergoing radiotherapy, especially after cysplatin usage [34] in the other studies have also shown that sugar-free chewing gum regularly can help increase the flow of saliva also by stimulating the taste receptors and reducing the xerostomia, it prevents occurrence of many complications which caused by it [38,39]. In cases such as Rheumatic fever (RF) and various types of malignancies that xerostomia is very common, the effect of chewing gum on decreasing xerostomia has been demonstrated in these patients [14]. ArashAzizi and his colleagues compared the effects of different types of chewing gum with mouthwashes on the the flow of saliva of healthy cases, then concluded that sugar-free Chewing gum can lead to increase in the flow of saliva and decrease of xerostomia [23]. in 2013 Kumar also concluded that sugar-free chewing can lead to increase in the the flow of saliva and reduction of acidity, that followed by measurable reduction in xerostomia and preventing tooth decay [26]. All of these studies are in line with the results of our study and approve it. In 2011, Jogaudzin and his colleagues examined the effect of three months chewing gum on the xerostomia and weight between two dialysis sessions. The results of this study showed that although the number of water-consuming has been decreased, but there was no significant relationship between the numbers of chewing gums with the number of glasses of water. In other words, the study suggests that there is no significant relationship between chewing gum and xerostomia in the hemodialysis patients [25], that is not the align with the result of this study, so it can be because of some causes such as sample size of the study, so that in Jogaudzin study included 38 patients under hemodialysis but in the current study

include 60 patients; duration of treatment with Hemodialysis machine and can mention to other environmental conditions such as weather. Also, factors such as amount of received sodium, reduced potassium levels, rapid increase in urea levels, psychosocial factors, and etc... that is very common in the hemodialysis patients and can be a major cause of thirst for these patients¹⁴ and probably cause of difference between the results of Jogovazine study and the present study is the impact of these side factors on xerostomia of the patients in his study. Lam et al, in a study on patients undergoing radiation therapy for thyroid cancer, found that sucking lemon candy led to reduced xerostomia and even reduced damage of the saliva glands due to radiation, immediately and 24 hours after routine therapy. However, in this study found that sucking candy had more effect after radiation therapy [32]. Lam study also confirms our study concerning the reduction in the intensity and duration of patients' xerostomia. In the another study in patients with thyroid carcinoma found that sucking candy could increase the flow of saliva as well as increased blood flow to the salivary glands, which also led to reduction of salivary glands damage and xerostomia due to radiotherapy, and may also led to accelerated excretion of radioactive materials [40]. Therefore, in these patients, sucking candy also prevents uncontrollable xerostomia, as well as the rapid excretion of the radioactive materials; prevent effect of its accumulation in mouth and body. Yang, in 2010, examined the effect of acupressure on the thirst and xerostomia in hemodialysis patients and concluded that if acupressure is effective in reducing the xerostomia of these patients so²⁰ the results of the Young's study confirms the results of this study and based on these two studies It can be concluded that acupressure and usage of chewing gum and candy have been shown to reduce xerostomia but for achieving a more reliable outcome and finding acupressure mechanisms in reducing xerostomia, more extensive studies is necessary for this field. In the study, Mazloom did not find correlation between the consumption of ice chip, thirst and xerostomia in the hemodialysis patients [35]. Considering that there is a general difference between the intervention of mazloom study and the intervention in this study, and also 49 cases were reported in Mazloom study and due to other factors affecting the thirst and xerostomia of the patients, the results of this two study are different .but It is recommended that more studies should be done on comparing the effects of ice chips and sugar-free chewing gum and candy on xerostomia of the hemodialysis patients and other patients. For the management of xerostomia in

different patients, and even reducing salivary gland damage in patients with head and neck cancers undergoing radiotherapy, some kind of medicines are used such as amphotericin and polycarpic which they have been shown severe and various complications [41] and according to the results of this study and the noticeable impact of sugar-free chewing gum and candy on xerostomia of the hemodialysis patients and no evidence of sugar-free chewing gum and candy complications so they can be used in head & neck cancers under radiotherapy, hemodialysis patients and all those who suffer from xerostomia [40].

CONCLUSION:

This finding has clinical importance in nursing care because control and treatment of xerostomia in the hemodialysis patients without medication is considered as an important health care target and can reduce the complications associated with medicine interventions, in addition use of sugar-free chewing gum and candy, do not take too much cost and time of patients so can be used any place and any time by patients. Even in healthy people these methods can be used so that in those who suffer from sever xerostomia thanks to environmental reasons such as live in hot and dry conditions.

REFERENCES:

1. Aliloo LL, Shakibi A, Shargh A. THE EFFICACY OF HOME CARE EDUCATION ON KNOWLEDGE AND PERFORMANCE OF HEMODIALYSIS RENAL PATIENTS DISCHARGED FROM HOSPITALS. URMIA MEDICAL JOURNAL. 2011; 22(5): 410-15
2. Hadian b, Anbari k, Heidari r. Epidemiologic study of end stage renal disease and related risk factors in patients under hemodialysis in Lorestan province. Yafteh. 2015; 16(3): 44-53.
3. Arefzadeh AR, Lesan-Pezeshki M, Safi S, Khatami MR. The Cost of Hemodialysis. Journal of Medical Council of Islamic Republic of Iran. 2008; 26(1): 76-82.
4. Khazaei Z, Rajabfardi Z, Hatami H, Khodakarim S, Khazaei S, Zobdeh Z. Factors associated with end stage renal disease among hemodialysis patients in Tuyserkan City in 2013. Pajouhan Scientific Journal. 2014; 13(1): 33-41
5. Nafar M, Mousavi SM, Mahdavi-Mazdeh M, et al. Burden of chronic kidney disease in Iran: a screening program is of essential need. Iran J Kidney Dis. 2008; 2(4): 183-192.
6. Singh AK, Brenner BM. Dialysis in the treatment of renal failure. In: Stone RM, Harrison TR, Editors. Harrison's principles of internal medicine. 16th Ed. New York: McGraw Hill, 2005.

7. Rm H, Ta D. Adequency hemodialysis. *Am J kidney Dis.* 1992; 20(2): 106-23.
8. Anuradha BR, Katta S, Kode VS, Praveena C, Sathe N, Sandeep N, Penumarty S. Oral and salivary changes in patients with chronic kidney disease: A clinical and biochemical study. *Journal of Indian Society of Periodontology.* 2015; 19(3): 297-301.
9. Proctor R, Kumar N, Stein A, Moles D, Porter S. Oral and dental aspects of chronic renal failure. *Journal of dental research.* 2005; 84(3): 199-208.
10. Hamshahri. Anuall 1500 hemodialysis patient dies, 2008.
11. Hamad A, Khosrovaneh A, Gupta S, Fazal S, Manis T, Feinfeld DA. Lack of effect of long-term use of angiotensin-converting enzyme inhibitors by hemodialysis patients on thirst and fluid weight gain. *Renal failure.* 2002; 24(4): 461-66.
12. Asadi-Noghabi A, Basampoor R, Zolfaghari M. Special nursing care of ccu-Icu-Dialysis. Tehran: Salemi, 2011.
13. Masajtis-Zagajewska A, Nowicki M. Influence of dual blockade of the renin-angiotensin system on thirst in hemodialysis patients. *Nephron Clinical Practice.* 2009; 112(4): 242-47.
14. Bots CP, Brand HS, Veerman EC, Korevaar JC, Valentijn-Benz M, Bezemer PD, Van Amerongen B. Chewing gum and a saliva substitute alleviate thirst and xerostomia in patients on haemodialysis. *Nephrology Dialysis Transplantation.* 2005; 20(3): 578-84.
15. Bots CP, Brand HS, Veerman EC, Valetijn-Benz M, Van Amerongen BM, Valentijn RM, Amerongen AVN. Interdialytic weight gain in Patients on haemodialysis is associated with dry mouth and thirst. *Kidney Int.* 2004; 66(3): 1162-68
16. Porcu M, Fanton E, Zampieron A. Thirst distress and interdialytic weight gain: a study on a sample of haemodialysis patients. *Journal of renal care.* 2007; 33(4): 179-81.
17. Bakhtiari S, Hosseini SA, Esfandiari F, Alavi K. Comparison of the effect of sugarfree orbit chewing gum & natural turpentine on salivary flow rate & ph. *journal of Dental School.* 2008; 24(4):423-28.
18. Salata RA, Verballis JG, Robinson AG. Cold water stimulation of oropharyngeal receptors in man inhibits release of vasopressin. *The Journal of Clinical Endocrinology & Metabolism.* 1987; 65(3): 561-67.
19. Hajian-Tilaki A, Oliae F, Jenabian N, Hajian-Tilaki K, Motalebnejad M. Oral Health-related Quality of Life and Periodontal and Dental Health Status in Iranian Hemodialysis Patients. *The journal of contemporary dental practice.* 2014; 15(4): 482-90.
20. Yang L-Y, Yates P, Chin C-C, Kao T-K. Effect of acupressure on thirst in hemodialysis patients. *Kidney and Blood Pressure Research.* 2010; 33(4): 260-65
21. Fan W-F, Zhang Q, Luo L-H, Niu J-Y, Gu Y. Study on the clinical significance and related factors of thirst and xerostomia in maintenance hemodialysis patients. *Kidney and Blood Pressure Research.* 2013; 37(4-5): 464-74.
22. Nak M, Sham H, Shaum T. Comparing the two regular gum increased saliva, dry mouth and renal patients on hemodialysis. *Journal of Islamic Dental Association.* 2010; 22(4): 255-61.
23. Azizi A, Lawaf SH, Najafi M. Comparison of the Effect of Different Chewing Gums and one Mouth Wash on the Amount and PH of Saliva in Healthy Individuals. *Journal of Dental Medicine, Shiraz University of Medical Sciences.* 2007; 8(3): 42-9.
24. Porcu M, Fanton E, Zampieron A. Thirst distress and interdialytic weight gain: a study on a sample of haemodialysis patients. *Journal of renal care.* 2007; 33(4): 179-81.
25. Jagodzińska M, Zimmer-Nowicka J, Nowicki M. Three months of regular gum chewing neither alleviates xerostomia nor reduces overhydration in chronic hemodialysis patients. *Journal of Renal Nutrition.* 2011; 21(5): 410-17.
26. Kumar S, Sogi SH, Indushekar K. Comparative evaluation of the effects of xylitol and sugar-free chewing gums on salivary and dental plaque PH in children. *Journal of Indian Society of Pedodontics and Preventive Dentistry.* 2013; 31(4): 240-49.
27. Silva ACVD, Aprile LRO, Dantas RO. Effect of gum chewing on air swallowing, saliva swallowing and belching. *Arquivos de gastroenterologia.* 2015; 52(3): 190-94.
28. Dodds MW, Johnson DA, Yeh CK. Health benefits of saliva: a review. *Journal of dentistry.* 2005; 33(3): 223-33
29. Jensdottir T, Buchwald C, Nauntofte B, Hansen HS, Bardow A. Saliva in relation to dental erosion before and after radiotherapy. *Acta Odontologica Scandinavica.* 2013; 71(3-4): 1008-13.
30. Roodgaryan R, Jenabian N, Moghadamnia AA, Pouramir M. Clinical and biochemical effects of dark chocolate in moderate chronic periodontitis. *Caspian Journal of Dental Research.* 2015; 4(1): 43-9.
31. Jensdottir T, Buchwald C, Nauntofte B, Hansen HS, Bardow A. Erosive potential of calcium-modified acidic candies in irradiated dry mouth patients. *Oral health & preventive dentistry.* 2010; 8(2): 173-78.
32. Lam MG, van Isselt JW. Re: does lemon candy decrease salivary gland damage after radioiodine therapy for thyroid cancer?. *Journal of Nuclear Medicine.* 2005; 46(12): 2118-19.

33. Jensdottir T, Nauntofte B, Buchwald C, Hansen HS, Bardow A. Effects of sucking acidic candies on saliva in unilaterally irradiated pharyngeal cancer patients. *Oral oncology*. 2006; 42(3): 317-22.
34. Kaae JK, Stenfeldt L, Eriksen JG. Xerostomia after Radiotherapy for Oral and Oropharyngeal Cancer: Increasing Salivary Flow with Tasteless Sugar-free Chewing Gum. *Frontiers in oncology*. 2016; 6(4): 111-18.
35. Maslom S, EbrahimiRigiTanha H, Sharifipour F, Zerati A. Effect of ice chips on intensity of thirst and fluid intake in patients undergoing hemodialysis. *Evidence Based Care*. 2013; 3(3): 59-68.
36. Abbasi F, Tohidast-Kurds Z, Darbandi A. Comparison of sugar-free gum and sugar-free gum containing bicarbonate PH of saliva and saliva ordinary oral stimulation, Faculty of Dentistry control, 2007; 15(72): 1-6.
37. Karami-Nogourani M, Hoseinzadeh S, Taheri S. The comparison between the effects of two saliva stimuli and ordinary chewing gums on xerostomia in hemodialysis patients. *The Journal of Islamic Dental Association of IRAN (JIDA)*. 2010; 22(4): 255-61
38. Visvanathan V, Nix P. Managing the patient presenting with xerostomia: A review. *Int J ClinPract*. 2010; 64(3): 404-07.
39. Plemons JM, Al-Hashimi I, Marek CL. Managing xerostomia and salivary gland hypofunction: executive summary of a report from the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc*. 2014; 145(8): 867-73
40. Christou A, Papastavrou E, Merkouris A, Frangos S, Tamana P, Charalambous A. Clinical Studies of Nonpharmacological Methods to Minimize Salivary Gland Damage after Radioiodine Therapy of Differentiated Thyroid Carcinoma: Systematic Review. *Evidence-Based Complementary and Alternative Medicine*. 2016; 30(2016): 47-56.
41. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Schuff KG. American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016; 26(1): 1-133.