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Der Pharmacia Lettre, 2016, 8 (15):37-45
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

The effect of ginger extract on radiotherapy-oriented salivation in patients with xerostomia: A double-blind controlled study

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ABSTRACT

Studies conducted on various properties of ginger showed that it has parasympathetic activity and can stimulate the salivary secretion. This study was aimed to evaluate methanolic ginger extract's effect on the rate of salivary secretion and xerostomia improvement in patients who underwent the radiotherapy in Ahvaz Golestan hospital in 2014(Southwest of Iran). This double-blind intervention trial was conducted on 40 patients with a history of head and neck radiotherapy. Data collection tools included two questionnaires designed using other similar studies. After the preparation of the capsules (500mg) containing total extract of ginger and placebo, the whole saliva of the patients was measured and they were asked to complete the questionnaire of xerostomia symptoms. Then the capsules randomly were given to the two groups of patients and they were asked to take one capsule every six hours. After two weeks, the whole saliva of patients was measured again and they were asked to respond to questions of the first questionnaire again. Furthermore, patients responded the second questionnaire to assess the effects of the drug on xerostomia symptoms. The data were analyzed using SPSS version 20. The saliva secretion level in the ginger group was significantly higher than in the placebo group ($P<0.05$). After two weeks, many of the xerostomia symptoms were healed and patients declared that ginger had positive effects on improvement of their problems. Patients also tend to continue for taking ginger. These findings showed that ginger can improve the xerostomia symptoms through increasing the rate of salivary secretion in these patients.

Keywords: Xerostomia; Hyposalivation; Radiotherapy; Ginger; Saliva.

INTRODUCTION

The field of dentistry is among the most important fields with high applicant volunteers for entering the university in Iran [1-7]. One of the significant aspects of Iran's ancient civilization is pay due attention to the medical knowledge the turning point of which is establishment and development of Academy of Gondishapur (GS) in Khuzestan province of Iran in 1745 (271 AD) [2, 8]. Xerostomia is the subjective feeling of dry mouth that its relative prevalence in the population is about 20 percent, and in most often (but not always) is accompanied by decreased salivation [9]. Some of the most common factors that can decrease the salivation are medications (such as antidepressant drugs, anti-anxiety drugs and diuretics, etc.), some systemic diseases (Sjogren's syndrome, chronic graft versus host syndrome, diabetes, AIDS, hepatitis c), and radiotherapy to the head and neck area [10].

Xerostomia is the most common side effect of radiotherapy to the neck and head area, and radiation therapy, compared with other factors (such as systemic diseases and medications), affects more intensely effect on reducing the flow of saliva [11]. To treat oral squamous cell carcinoma (OSCC) is normally 60 to 70 Gary (Gy) of Ray is

given to the patient while the radiation dose of radiotherapy above 30 Gy can cause severe damage to the salivary glands and usually these glands rarely get their full health again. [10, 12-13]. In a study it was shown that about 64 percent of the people, who had received radiotherapy by conventional method, 22 years after the time of receipt of radiotherapy they were still complaining of moderate to severe Xerostomia [14].

The role of saliva in maintaining the health of soft and hard tissues of the mouth includes: Washing the toxic materials from the oral cavity, adjusting the acidity, buffering the decalcifying acids, the neutralization of toxins and bacterial enzymes, and destruction of microorganisms and remineralization of enamel with its minerals like calcium and phosphorus. The reduction and lack of it creates several problems for patients [15-16, 9-10]. Patients complain of the discomfort and pain in the area of the mouth, difficulty in speaking, chewing and swallowing; furthermore, risk of tooth decay and oral infection goes up in them and ultimately these factors can cause malnutrition and reduction of weight of the patient. Therefore, it can be said that Xerostomia not only lowers the quality of life in some patients who have been saved from cancer, but also affects their health [17]. In order to help these patients and reduce the side effects, some studies have focused on the use of Pilocarpine, artificial saliva, surgery and displacement of the salivary glands from radiation field, use of acupuncture, the use of hyperbaric oxygen and stem cell replacement [10, 14, 18]. Each of these methods has disadvantages that have prevented their widespread use as a treatment for Xerostomia. The use of traditional medicine and natural ingredients are also included in the procedures that some patients may use them to overcome their problems in different countries. For example, Korean red ginseng, and Yukmijihwang- tang ' in In South Korea, Bakumondo-to ' in Japan and ginger in India, are used for patients [19-22].

The rhizome of the plant of Zingiber officinale Roscoe, known as ginger, has been used as a food seasoning and herbal medicine since ancient times. The pharmacological properties of ginger have been studied extensively and anti-inflammatory, anti-fever, properties, antimicrobial, antioxidant, hypoglycemic, anti-hypertensive and anti-nausea and anti-vomiting in pregnant women [23]. and hypercholesterolemia, has been proven. In 2011 in Iran Chamani et al. studied effect of sialogogic characteristics of several plants on rat and found that compared to the rest of the plants, ginger caused a significant increase in the secretion of saliva [24]. However, there are no clinical trials that show whether ginger can reduce the symptoms of dry mouth and increase saliva flow, especially in patients who have undergone radiation therapy in head and neck area or not.

This study was designed to evaluate the effect of four capsules 500 mg of methanol extracts of ginger daily for two weeks (every six hours a capsule) on symptoms of dry mouth in radiotherapy patients. To this end, before and after administration of ginger to patients, subjective symptoms of dry mouth and the unstimulated whole saliva flow rate were evaluated using a questionnaire.

MATERIALS AND METHODS

In the spring of 2014, patients' medical records in the oncology ward of Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran (Southwest of Iran), were reviewed and 71 patients were eligible for the study. According to the exclusion criteria, 31 patients were excluded from the study. Complaints of subjective feelings of dry mouth and having diagnostic criteria of the dry mouth of Fox questionnaire were the inclusion criteria [26]. Other inclusion criteria included age over 18 years, a dose of radiation received over 4,500 cGy, the radiation received during the period 6 to 7 weeks, minor and major salivary glands involvement, one or two sides of the face in the field of radiation, and over the last three months of receiving radiation. Exclusion criteria included being pregnant, diabetes, asthma, Sjogren's syndrome, lack of ability to feed by mouth, using anti-depressant medications, a history of allergy to ginger or corn starch and people who have had recurrence of cancer and residence outside the city of Ahvaz and the lack of consent of the participation in the study. All debates and measurements were conducted in the oncology ward.

This randomized controlled trial study (IRCT2013120915723N1) was approved by the Ethics Committee of AJUMS Research Council with a REC no. 1392.41 and carried out in all stages in conformance with the Declaration of Helsinki .Before the start of the study, all the participants were asked to sign a consent form.

Research flowchart

<table>
<tr><td colspan="4">Patients who are eligible for participation in the study.</td></tr>
<tr><td colspan="4">71</td></tr>
<tr><td colspan="4">Screening of patients (a lack of exclusion criteria)</td></tr>
<tr><td colspan="4">31</td></tr>
<tr><td colspan="4">Randomization 40</td></tr>
<tr><td colspan="2">Ginger group (n=20)
2grams/day for two weeks</td><td colspan="2">Placebo group (n=20) 2grams/day for two weeks</td></tr>
<tr><td colspan="2">After two weeks the 20 patients completed the study and their data were analyzed.</td><td colspan="2">After two weeks the 20 patients completed the study and their data were analyzed.</td></tr>
<tr><td>Analysis of the questionnaire responses</td><td>Saliva weight analysis</td><td>Analysis of the questionnaire responses</td><td>Saliva weight analysis</td></tr>
</table>

Preparation of medicines

To prepare ginger-, and placebo capsules and Rhizome of ginger (*Zingiber officinale*) was purchased from herbal medicines authentic companies in Ahvaz, soaked for 48 hours in methanol, concentrated by using rotary, dried in freeze dryer and became powder. The appropriate formulation of resulting powder was prepared and capsules containing 500 mg of ginger [24]. was ready by capsule filling device. Capsules similar (shape, color, and size) to ginger capsules that contained cornstarch (Osveh Co., Tehran, Iran), were produced as a placebo). In preparation of capsules, at first the rhizome of ginger (Zingiber officinale) was purchased (In late April) from herbal medicines authentic companies in Ahvaz .

Ginger was soaked using a maceration method for 48 hours in methanol solvent and then the extracts were concentrated by rotary and dried in freeze dryer and became powder. The appropriate formulation of resulting powder was prepared and capsules 500mg of ginger was ready by capsule filling device. Capsules similar (shape, color and size) to ginger capsule that contained cornstarch (Osveh Co., Tehran, Iran), was produced as a placebo) [20]. Considering that the extraction method with methanol solvent extracts more bread and little ginger compounds [27], so *ginger* capsules were odorless and in this aspect were also similar to placebo capsules (ginger properties).A total of 40 packages, each of which contains either 60 ginger capsules or 60 placebo capsules were prepared and coded by the pharmacist .The medicine was delivered to the patient by a person who was unaware of the drug code.

Design and evaluation of study

This randomized, double-blind, placebo-controlled clinical trial was designed to investigate the effects of ginger on post-radiotherapy xerostomia. In this session, firstly, patients were asked to answer to a questionnaire, which in addition to demographic profile included 14 questions (six questions that the patient should record his or her question using VAS method and eight questions in the yes or no form) and also unstimulated saliva were collected from the patients. Then, the first based on age and gender and the type of cancer and the use of dental prostheses people were divided into two nearly identical groups in order to receive 4 capsules daily random 500 mg of ginger extract or a placebo for two weeks. A total of 40 packages, each of which contains either 60 ginger capsule or 60 placebo capsules were prepared and coded.

At the end of study, the patient's saliva weight was measured again using the below mentioned method. Patients were asked to fill questionnaire used before treatment. In addition to the questionnaire previously used, a new questionnaire consists of 14 questions (twelve questions with two options: yes or no, and two questions that the patient should respond based on the VAS) were prepared on the basis of previous studies and were filled by the patients [27,28]. The cooperation of patients was determined based on the number of remaining capsule.

Assessment of unstimulated saliva

Unstimulated saliva was measured at the beginning and end of the research. Before the delivery of the medication to the patient to evaluate unstimulated salivary flow rate, the patients ask not to drink, eat, smoke, brush, and put anything in their mouth until 90 minutes before collecting the saliva. The saliva of patients was collected from 9 to 11 in the morning. Then, in a quiet environment, and while the patient was placed in a sitting position, he or she was asked to swallow the saliva in his/her mouth; then he/she must bend his/her head forward, and keep open the eyes and try do not move and allow for discharge his/her saliva into a funnel, which is placed into a graduated cylinder and its weight has already been computed, for five minutes inactively (Libra model and GF300 made by D&A Company with the capability of scaling objects from minimum 0.02gr to maximum up to 310 gr, 1e =%, d = 0.001gr). Then, with a simple calculation by subtracting the weight of the graded tube from the total weight of funnel and saliva, the weight of the secreted saliva was calculated for five minutes [10, 14]. The results were inserted in a form, which the patient's name was written on it. It was carried out in compliance with infection control protocol [17, 28].

Data analysis
The efficacy data, such as the dry mouth (each item or the sum totals of the questionnaire) and USFR were evaluated by per-protocol analysis, because only the pre- and post treatment changes were considered.

Statistical analysis
After the completion of study, data were extracted based on the patient's name and the used drug code; furthermore, data were analyzed by the SPSS version of 15 with the use of the Wilcoxon signed rank test and Binomial test and Mann-Whitney. Then, the codes were decoded. Furthermore, in all analyses, $p < 0.05$ was taken to indicate statistical significance.

RESULTS

Out of 40 patients 28 and 12 subjects were males and females, respectively. The average age was 45 years and the age range was 20 to 70 years. All patients received radiotherapy for cancer of the head and neck and the average duration of radiotherapy was seven weeks and 100% of patients completed the study.

The paired Wilcoxon test showed that the symptoms of dry mouth, difficulty in chewing food, difficulty in swallowing food, oral burning sensation, difficulty in talking, daily and nightly dry mouth feeling, nightly awakening , bad taste in the mouth and Saliva weight in the patient (ginger) group, on the first day (A1, B1, C1,D1, F1, G1,H1, I1, J1,O1) and at the end of the second week (A2, B2, C2,D2, F2, G2,H2,I2, J2,O2) has had a significant difference ($P<0.05$) (tables 1, 2 and 3).

The results of a binomial test to compare the proportions indicated that the ratio of those have who said the use of the drug has a positive impact on the stuck denture and Tend to use medication Improving (T,V) compared to those who have said the drug do not have any positive effect on these items, in the patients group is higher than the control group ($P<0.05$) (Tables 4 and 5.)

Mann-Whitney test showed that the amount of salivation in both the control and the patient groups has significantly increased, but this increase in the patient group was significantly more than the control group ($P<0.01$) (Table 6.)

DISCUSSION

The Eclectic physicians use ginger as a stimulating digestive tonic because they believe that it increases the secretion of saliva and gastric acid, quieted cramping, and dispelled flatus [29]. In the traditional medicine, ginger is used for gastrointestinal disorders as laxative, appetite, Sialogogue, anti- nausea and anti-vomiting, and anti-diarrhea [24, 30, 31, 32]. That different studies have established some of these effects [29, 38, 39, 40].

Considering that Ghayur et al. have shown cholinergic agonist properties of ginger with a hydromethanolic extract and due to the fact that in North America the use of ginger to the extent of two grams per day, as it has been declared, was safe even for pregnant women [29, 36]. , we decided to use this extract two grams daily to assess its effect on dry mouth in patients who have undergone the radiotherapy.

In several studies conducted to evaluate the effect of extracts of the herbal drugs or Pilocarpine on the symptoms of dry mouth, an 8-12 -week intervention time duration has been selected [20, 21, 36]. but the longest period of clinical intervention using ginger was limited to two to three weeks [37, 38]. and its safe has been established. So, we decided to consider a two- week period for this research in order to prevent patients to be exposed to unknown potential complications.

The present study is the first research to examine the effect of ginger on the dryness of the mouth, neck and head area caused by radiotherapy. Factors such as age and sex, the use of prosthetics, radiation field, radiation dose, and type of radiation can affect the amount of mouth dryness of the patients. We tried to unify all these factors between the two study groups. The study's results showed that the amount of non-stimulated salivation and more subjective symptoms of dry mouth have been improved after two weeks of use of ginger in comparison with the control group.
To specify the pharmacological basis of medical use of ginger in gastrointestinal disorders, Ghayur et al. investigated the effect of the aqueous- methanolic extract of ginger on rat-stomach fundus and indicated that ginger has prokinetic activity similar to carbamylcholine chloride that is a cholinergic agonist and an intestinal stimulant, and has a direct cholinergic agonist effect on the post-synaptic M3 receptors, as well [31]. Two medicines of Pilocarpine and Cevimeline that were approved by FDA for treatment of dry mouth are agonists of cholinergic receptors (of course, Cevimeline acts more proprietary than the M1 and m3 receptors) and cause a temporary increase in the flow of saliva [10]. Due to the similarity of the ginger with these drugs, it is likely that the

mechanism of salivation stimulation by ginger is similar to two medicines, which is of course the need for more research to prove it.

It seems that an increase in salivation increases moisture in the mucosa and therefore improves the subjective symptoms of dry mouth. The results of this study showed that most of subjective symptoms of dry mouth have been improved after two weeks of ginger usage. These results are consistent with similar research that evaluated the effect of Pilocarpine on the symptoms of dry mouth in patients who have been undergoing radiotherapy [39, 40, 26]. They showed that Pilocarpine increases salivation and consequently alleviates the symptoms of the patients. Of course, candidiasis is one of the most common infections that is seen in patients with dry mouth and can cause inflammation and make a burning mark and the bad taste feeling in the mouth [17, 10]. Various studies have shown anti-inflammatory and antibacterial and antifungal properties of ginger [41-45].; so, some of the symptoms of the patients may be because of the properties of ginger.

Anyway, it was expected that the increased salivation improves the sense of taste, but the results of this study indicate that the difficulty in the sense of taste before and after the use of ginger has not changed. Based on the study of Tanaka in 2002 [46]. , no relationship existed between the severity of impairment of the sense of taste and the amount of salivation, but those who had received the supplements of zinc in their impaired sense of taste has been improved. Given that patients with head and neck cancers are very likely that they are also malnourished), so we can say that to improve the administration of zinc supplements can help to improve the sense of taste of these patients.
Naturally, this point should also be noted that in a study, Nguyen showed that the mechanism of the taste sensation damage in patients undergoing radiotherapy is loss and the death of progenitor cells of taste bud and the recovery of these cells takes a time from several months to several years [47]; in addition, Zheng et al. [48]. showed that the model of the salivary gland dysfunction differed from the model of damage to the taste bud and main cause of the disorder in the bud in the taste sense is due to damage to the taste buds and not because of the xerostomia in these patients. Using all these articles we can conclude that disorders in the taste sense in the cancer patients are multifactorial and removing a cause is not a warranty to improve the sense of taste; therefore, even improving salivation in patients of this study could not improve the impaired sense of taste. Moreover, some studies can be found in the fields that have shown changes in taste sensation of cancer patients even before starting radiotherapy that indicates other factors apart from taste bud and saliva, such as psychological and nutritional factors) are involved in creating this disorder [49].

Concerning the lack of meeting people and the lack of talking to people and not leaving the house in the control and patient groups the results of this study are similar. One of the reasons for this may include the very much impact of the mental condition of patients on these items is so well that an increase in the secretion of saliva cannot improve these items [50].

Table 1. The measured index and their abbreviation marks

The name of the variable	code	The name of the variable	code	The name of the variable	code	The name of the variable	code	The name of the variable	code
Xerostomia1	A1	oral burning sensation1	F1	grid denture 1	K1	Improving the xerostomia	P	Easy to use medication	Z2
	A2	oral burning sensation2	F2	grid denture2	K2	Reduce the bad taste of the mouth	Q	better Feeling	Z2
	B1	daily dry mouth feeling1	G1	Failure to meet people 1	L1	Removing nightly xerostomia	R1	The impact of the drug on xerostomia	Z3
	B2	daily dry mouth feeling2	G2	Failure to meet people 2	L2	Removing nightly awakening	S		
	C1	Nightly xerostomia1	H1	Non-speaking with people 1	M1	Tend to use medication	T		
	C2	Nightly xerostomia2	H2	Non-speaking with people2	M2	Improving the stuck denture	V		
	D1	nightly awakening1	I1	No leaving the house 1	N1	Improving quality of life	W		
	D2	nightly awakening2	I2	No leaving the house 2	N2	The desire to meet up with others	X		
	E1	bad taste in the mouth1	J1	Saliva weight 1	O1	Increased associated with people	Y		
	E2	bad taste in the mouth2	J2	Saliva weight 2	O2	Increased exit from house	Z1		

Table 2. A comparison between the patient(ginger) group before and after taking the ginger using the paired Wilcoxon test

Parameter	Mean	Std. Deviation	Z Wilcoxon	P-value
A1	74.2500	18.22917	-3.316	**.000
A2	59.0000	19.97367		
B1	67.2500	22.73850	-3.310	**.000
B2	53.5000	27.19810		
C1	64.0000	26.38780	-2.497	**.004
C2	53.0000	28.34932		
D1	52.0000	28.34932	-2.220	*.012
D2	38.5000	32.73096		
E1	38.1579	27.89915	-.513	.321
E2	35.5263	32.05441		
F1	71.7500	24.98816	-2.884	**.001
F2	54.2500	23.24215		
G1	1.1000	.30779	-2.828	**.004
G2	1.5000	.51299		
H1	1.1500	.36635	-2.828	**.004
H2	1.5500	.51042		
I1	1.4500	.51042	-2.449	*.016
I2	1.7500	.44426		
J1	1.2000	.41039	-2.828	**.004
J2	1.6000	.50262		
K1	1.4500	.51042	-1.732	.125
K2	1.6000	.50262		
L1	1.8000	.41039	-.577	.500
L2	1.8500	.36635		
M1	1.7000	.47016	-1.000	.313
M2	1.8000	.41039		
N1	1.8500	.36635	.000	.750
N2	1.8500	.36635		
O1	1.8045	1.45082	-3.920	**.000
O2	3.8560	1.71201		

**. The difference is significant at the 0.05 level and **. the difference is significant at the 0.01 level*

Table 3. A comparison between the control group before and after taking the placebo test with the paired Wilcoxon test

Parameter	Mean	Std. Deviation	Z Wilcoxon	P-value
A1	58.7500	27.61936	-2.722	**.002
A2	44.5000	26.05157		
B1	45.8500	31.44297	-2.542	**.004
B2	35.0000	31.45590		
C1	47.9000	34.26353	-2.092	*.017
C2	37.7500	35.07417		
D1	40.2500	23.70182	-1.696	.053
D2	32.0000	25.56725		
E1	31.9000	26.93247	-1.683	.051
E2	24.0000	24.14866		
F1	53.0000	33.30086	-2.764	**.002
F2	36.5500	30.93537		
G1	1.4500	.51042	-2.000	.063
G2	1.6500	.48936		
H1	1.3000	.47016	-3.000	**.002
H2	1.7500	.44426		
I1	1.7000	.47016	-1.000	.313
I2	1.8000	.41039		
J1	1.6000	.50262	-.816	.344
J2	1.7000	.47016		
K1	1.5000	.51299	-1.000	.313
K2	1.6000	.50262		
L1	1.6500	.48936	-2.236	*.031
L2	1.9000	.30779		
M1	1.5000	.51299	-1.342	.188
M2	1.6500	.48936		
N1	1.7500	.44426	-1.414	.250
N2	1.8500	.36635		
O1	1.3325	1.23213	-3.361	**.000
O2	2.3295	1.45858		

**. The difference is significant at the 0.05 level and **. the difference is significant at the 0.01 level.*

In fact, there are several factors that play a role in the creation of artificial teeth stuck. Saliva plays a role in the denture retention, but only the saliva is not the determining factor in the creation of stuck and stability of the artificial teeth; so, the change in its amount does not create certain the change in the denture retention. Factors such as sufficient tissue to support artificial teeth, sufficient seal in prosthesis borders, type, quality and weight in making the prosthesis play a greater role in stuck and stability of artificial teeth. Inefficiency of each of these can be solely a cause of the prosthesis with the inadequate stuck and stability [51-53]. However, it was expected that the increased salivation improves dental denture stuck, but it seems that other effective factors prevented the occurrence of such a result .

Table 4. The results of a binomial test to compare relative data (ginger groups). Group1: Yes, Group 2: No

		N	Observed Prop.	Exact Sig. (2-tailed)
P	Group 1	12	.60	.503
	Group 2	8	.40	
Q	Group 1	11	.55	.824
	Group 2	9	.45	
R1	Group 1	11	.55	.824
	Group 2	9	.45	
S	Group 1	10	.50	1.000
	Group 2	10	.50	
T	Group 1	15	.75	.041*
	Group 2	5	.25	
V	Group 1	15	.75	.041*
	Group 2	5	.25	
W	Group 1	13	.65	.263
	Group 2	7	.35	
X	Group 1	9	.45	.824
	Group 2	11	.55	
Y	Group 1	13	.65	.263
	Group 2	7	.35	
Z1	Group 1	14	.70	.115
	Group 2	6	.30	
Z2	Group 1	10	.50	1.000
	Group 2	10	.50	
Z3	Group 1	14	.70	.115
	Group 2	6	.30	

**. The difference is significant at the 0.05 level and **. the difference is significant at the 0.01 level.*

Table 5. The results of a binomial test to compare relative data (control group) Group1: Yes, Group 2: No

		N	Observed Prop.	Exact Sig. (2-tailed)
P	Group 1	13	.65	.263
	Group 2	7	.35	
Q	Group 1	12	.60	.503
	Group 2	8	.40	
R1	Group 1	11	.55	.824
	Group 2	9	.45	
S	Group 1	12	.60	.503
	Group 2	8	.40	
T	Group 1	8	.40	.503
	Group 2	12	.60	
V	Group 1	17	.85	.003**
	Group 2	3	.15	
W	Group 1	9	.45	.824
	Group 2	11	.55	
X	Group 1	10	.50	1.000
	Group 2	10	.50	
Y	Group 1	12	.60	.503
	Group 2	8	.40	
Z1	Group 1	15	.75	.041*
	Group 2	5	.25	
Z2	Group 1	5	.25	.041*
	Group 2	15	.75	
Z3	Group 1	6	.30	.115
	Group 2	14	.70	

**. The difference is significant at the 0.05 level and **. the difference is significant at the 0.01 level.*

Table 6. The results of a Mann-Whitney test to compare weight of saliva in two independent groups

	Mean	Std. Deviation	Mean Rank	Mann-Whitney test statistic	P-value
patient groups	2.051	0.659	26.75	75.000	**.000
control group	0.997	0.947	14.25		

***.. The difference is significant at the 0.01 level.*

CONCLUSION

Most patients who have a history of radiotherapy to the head and neck region, due to the placement of the salivary glands in the radiation field, complain of the mouth [54-56]. One of the most widespread methods for treatment of the complication is the use of Pilocarpine for patients, because different studies have proven its effectiveness in these patients [36, 57-58]. Of course the use of Pilocarpine in pulmonary patients, cardiovascular patients and patients with glaucoma with contraindicated narrow-angle [10]. and some of its side effects such as sweating, hot flashes, urination, diarrhea and blurred vision caused that some patients are reluctant to use it, while the use of ginger in the therapeutic dose has had no toxicity and side effect [59]. On the other hand, in vitro, animal and epidemiological studies have shown that ginger and its compounds cause suppression of growth and induction of apoptosis in a variety of cancers of the skin, ovary, colon, Brest, cervical, oral, kidney, prostate, gastric, pancreatic, liver, and brain [60]. and has antioxidant, anti-inflammatory, antimutagenic properties and also other biological activities [61]. properties of ginger). According to these characteristics and due to the positive results of this study in the treatment of dry mouth, more research can be suggested in order to replace the ginger instead of Pilocarpine in the treatment of dry mouth in patients who have undergone radiation.

Failure to check changes in the constituents of saliva following the administration of ginger can be pointed out as one of the weaknesses of the study; however, this requires the advanced laboratory equipment and more time and costs.

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