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Factors Influencing the Xerostomia Symptoms in the Patients with Temporomandibular Disorders

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Purpose: This study investigated factors influencing the xerostomia symptoms in the patients with temporomandibular disorders (TMDs).

Methods: Eighty-six participants over the age of twenty were randomly enrolled from patients with TMDs. The patients were diagnosed by Diagnostic Criteria-TMD (DC-TMD). Intensity of the pain and level of stress of the patients were recorded using TMD pain visual analogue scale (VAS) and stress VAS, respectively. The Symptom Checklist-90-Revised (SCL-90R), dry mouth symptom questionnaire, unstimulated salivary flow rate (USFR) and oral moisture were measured.

Results: The patients who had above the mean of the TMD pain VAS had significantly higher scores on the stress VAS, subjective dry mouth symptoms and T-score of somatization. The patients who suffered from pain more than three months had significantly higher TMD pain VAS, subjective dry mouth symptoms and T-score of somatization. There were no significant differences in xerostomic symptoms according to the diagnosis of TMDs. Moreover, TMD pain VAS and the stress VAS did not correlated to USFR and oral moisture.

Conclusions: The level of individuals' TMD pain and stress significantly affect their subjective dry mouth symptoms, however, it did not affect USFR and oral moisture.

Key Words: Oral moisture; Stress; Temporomandibular disorders; Xerostomia

INTRODUCTION

Temporomandibular disorders (TMDs) are musculoskeletal disorders associated with the temporomandibular joint pathology and the function of the masticatory system. Occlusal factors, trauma, emotional stress, deep pain input and parafunctional activities are suggested as major etiologic factors in TMDs.[1] In particular, it is well known that psychological factors play a significant role in the etiology and maintenance of TMDs. People who have a high incidence of exposure to stressful life events[2] and increased levels of anxiety and stress-related somatic symptoms[3] are reported more prevalent in TMD patients.

Stress is known to be closely related to reinforcement of parafunctional activities, especially bruxism.[4] Stress seems to alter the activity of muscle through either gamma efferent system to the muscle spindle or by means of sympathetic effect to the muscle tissues or related structures.[5-9] Therefore, it is likely that stress may be considerably related to the masticatory muscle pain and the joint problems such as localized muscle soreness, disc displacement, and even osteoarthritis. Moreover, it is generally accepted that stress is also associated with xerostomia. According to the study of Bergdahl and Bergdahl,[10] subjective oral dryness and reduced unstimulated salivary flow rate (USFR) were significantly associated with depression, trait anxiety, perceived stress, and state anxiety. Kim[11] also reported that the job stress itself could be a causative factor of xerostomia.

Based on these findings, we hypothesized that TMD itself and xerostomic condition might be directly correlated, and investigated the stress as intersection of these two diseases. A study showed the relationship between the orofacial pain and xerostomia,[12] but studies on the relationship between TMDs and xerostomia are still insufficient. The objective of this study is to investigate the relationship between the TMDs and xerostomia and reveal specific factors influencing the xerostomia symptoms in the patients with TMDs using Symptom Checklist-90-Revised (SCL-90R), dry mouth symptom questionnaire, USFR and oral moisture.

MATERIALS AND METHODS

1. Subjects

Eighty-six participants over the age of twenty were randomly enrolled from patients who visited the Department of Oral Medicine at Kyungpook National University Hospital (Daegu, Korea) with TMDs from June to July 2016. Individuals with a history of taking any medication during two weeks before their visit and with rheumatoid arthritis or congenital musculoskeletal problems were excluded in this study. Patients who are not able to fill out SCL-90R were excluded, as well. All subjects were provided with a full explanation of the protocol and written informed consent has been obtained before the study began. This study was approved by Kyungpook National University Hospital's Institutional Review Board (IRB No. 2016-05-007-001).

2. Measurements

1) General information

Smoking and drinking status of the patients were recorded. The patients were asked "To what extend do you have stress?" for evaluating their stress and "To what extend do you have pain on TMJ or surrounding structures?" for evaluating the severity of except TMD pain. Above two inquiries were assessed by visual analogue scale (VAS).

2) Diagnosis of TMDs

Diagnosis of TMDs was made in a basis of the patient's chief complaints, clinical examination, clinical history, and radiological examinations using Diagnostic Criteria for TMD (DC-TMD).[13,14] Diagnosis was categorized into 1) joint, 2) muscle, and 3) mixed problems (muscle problems along with joint ones). If the patient had more than three-month history of pain, he or she was categorized as chronic group. If the participant had no pain, only joint sounds, or having pain within three months, then he or she was categorized as acute group.

3) Dry mouth symptom questionnaire

The dry mouth symptom questionnaire[15] was used to evaluate subjective xerostomia symptoms. It is composed of ten questions and divided into two parts. One is composed of six questions to evaluate the degree of dry mouth using VAS and the other is composed of four questions to evaluate the behavioral aspects of dry mouth using the Likert scale. The participants were asked to fill in the questionnaire. We used each scores and the sum of the VAS of six

Table 1. Dry mouth symptom questionnaires

Question	Abbreviated form	Evaluation
Six questions to evaluate the degree of dry mouth		
1. Do you feel your mouth dry during the night, or when you wake up?	Dry-PM	VAS (0-100)
2. Do you feel your mouth dry during the day?	Dry-day	
3. Does your mouth feel dry when eating a meal?	Dry-eat	
4. Do you have any difficulty in swallowing?	Dif-swal	
5. Do you feel that the amount of saliva in your mouth seems to be little?	Am-sal	
6. Then, what extent do you feel your life discomfort caused by dry-mouth symptoms?	Eff-Life	
Four questions to evaluate the behavioral aspects of dry mouth		
7. Have you ever waken up at night because your mouth is dry?	Night-awake	Likert scale (1-5)
8. Do you prepare a cup of water to sip beside your bed before you go to sleep?	H_2O-bed	
9. Do you sip liquids to help while swallowing dry foods?	Sip-liq	Likert scale (1-4)
10. Do you chew gums or eat candies because your mouth is dry?	Gum-candy	

VAS, visual analogue scale.

questions to evaluate the degree of dry mouth (Sub-sum6) for the statistical analysis. The questionnaire and the abbreviated form are shown at Table 1.

4) Unstimulated salivary flow rate

Patients were instructed to drool the saliva for 10 minutes into a centrifuge tube. After collecting them for ten minutes, the volume of saliva was measured. According to the criteria proposed by Ericsson and Hardwick,[16] severe hyposalivation was defined as an USFR <1 mL/10 min, normal salivation was defined as an USFR ≥2.5 mL/10 min, and the in-between was classified as low salivation group.

5) Oral moisture

Oral moisture in the subject's mouth was measured to compare with subjective oral dryness and USFR. The investigator measured oral moisture on the subject's tongue by using the Oral Moisture Checking Device (Mucus; Life Co., Ltd., Tokyo, Japan).[17,18] It measures moisture of the epithelium in terms of capacitance.[17] According to the criteria of the manufacturers guide line, normal group was defined as oral moisture ≥30%, dry group was defined as oral moisture <25%, and moderate group was defined between the two groups. To reduce errors, the participants asked to swallow the saliva before the test and the investigator measured them five times.

6) Symptom Checklist-90-Revised

SCL-90R, self-report inventory of general psychiatric symptoms, was administered to evaluated psychological status of the participants. SCL-90R consists of ninety questions and is composed of nine symptom dimensions, including somatization (SOM), obsessive-compulsive behavior (O-C), interpersonal sensitivity (I-S), depression (DEP), anxiety (ANX), hostility (HOS), phobic anxiety (PHOB), paranoid ideation (PAR), and psychoticism (PSY). It has also three global indices of functioning including global severity index (GSI), positive symptom distress index (PSDI), and positive symptom total (PST).[19] T-scores are used for the statistical analysis.

3. Statistical Analysis

Statistical analysis of the data was performed using the PASW Statistics 18.0 for Windows (IBM Co., Armonk, NY, USA) including the independent two-sample t-test, ANOVA, chi-square and correlation analysis. A difference of $p<0.05$ was considered statistically significant.

RESULTS

1. Demographic and TMD Profiles of the Patients

The participants were forty males and forty-six females. Of the total patients, 59.3% were in their twenties. Fifty-eight patients were non-smokers and fifty patients were alcohol consumers (Table 2). Around 34% had history of pain for more than three months and there was no sex difference. In the case of male patients, joint pain group and mixed pain group were similar in percentage, whereas female patients had more mixed pain than muscle or joint pain only (Table 3). The average TMD pain VAS was 39.64 out of 100 and the average stress VAS was 49.33 among the

Table 2. Demographic profiles of the participants

Characteristic	Classification	No. (%) of subjects
Gender	Male	40 (46.5)
	Female	46 (53.5)
Age (y)	20-29	51 (59.3)
	30-39	13 (15.1)
	40-49	11 (12.8)
	≥50	11 (12.8)
Smoking	Smoking	19 (22.1)
	Quit-smoking	9 (10.5)
	Non-smoking	58 (67.4)
Alcohol drinking	Drinking	50 (58.1)
	Non-drinking	36 (41.9)

Table 3. Analysis of TMD profiles

TMD profile	Male (n=40)	Female (n=46)	Total (n=86)
Acute	26 (65.0)	31 (67.4)	57 (66.3)
Chronic	14 (35.0)	15 (32.6)	29 (33.7)
Joint	17 (42.5)	2 (4.3)	30 (34.9)
Muscle	6 (15.0)	13 (28.3)	8 (9.3)
Mixed	17 (42.5)	31 (67.4)	48 (55.8)
TMD VAS	42.25	37.37	39.64
Stress VAS	45.88	52.33	49.33

TMD, temporomandibular disorder; VAS, visual analogue scale.
Values are presented as number (%) or mean number only.

all patients. The TMD pain VAS in male and the stress VAS in female were higher than the opposites, but they were no statistically significant (Table 3).

2. Relationship between the TMD Pain VAS and the Other Factors

We divided the participants into two groups by the mean of the TMD pain VAS. The patients who had above the mean of the TMD pain VAS had significantly higher scores on the stress VAS (p=0.003), Sub-sum6 (p=0.000), night-time dryness (Dry-PM, p=0.000), day-time dryness (Dry-day, p=0.000), dryness when eating (Dry-eat, p=0.000), difficulty in swallowing (Dif-swal, p=0.009), lack of the amount of saliva (Am-sal, p=0.013), life discomfort (Eff-life, p=0.001), and T-score of SOM (p=0.023). Within the non-smoking group, the patients who had above the mean of the TMD pain VAS had significantly higher scores on the stress VAS (p=0.015), Sub-sum6 (p=0.000), Dry-PM (p=0.000) Dry-day (p=0.000), Dry-eat (p=0.005), Dif-swal (p=0.016), Eff-life (p=0.005), and T-score of SOM (p=0.028) (Table 4).

3. Relationship between the Diagnostic TMD Profiles and the Other Factors

The patients who had pain for more than three months (chronic group) had significantly higher TMD pain VAS (p=0.002), Sub-sum6 (p=0.010), Dry-PM (p=0.027), Dif-swal

Table 4. Relationship between the TMD pain VAS and the other factors

Variable	By the mean of TMD pain VAS (n=86)			By the mean of TMD pain VAS (n=58, non-smokers only)		
	Above the mean group	Below the mean group	p-value	Above the mean group	Below the mean group	p-value
Stress VAS	56.33	42.33	0.003	54.57	40.73	0.015
Sub-sum6	171.47	68.72	0.000	148.25	50.43	0.000
Dry-PM[a]	49.40	19.79	0.000	42.96	13.63	0.000
Dry-day[a]	38.86	17.02	0.000	35.89	13.33	0.000
Dry-eat[a]	27.72	11.19	0.000	23.00	8.63	0.005
Dif-swal[a]	16.02	5.74	0.009	13.39	3.70	0.016
Am-sal[a]	21.05	9.56	0.013	17.29	7.53	0.087
Eff-life[a]	18.42	5.42	0.001	15.71	3.60	0.005
Night-awake[a]	1.37	1.19	0.240	1.29	1.13	0.213
H_2O-bed[a]	1.74	1.40	0.180	1.75	1.33	0.214
Sip-liq[a]	1.93	1.67	0.165	1.89	1.67	0.330
Gum-candy[a]	1.12	1.02	0.152	1.07	1.00	0.327
USFR (mL/10 min)	2.90	2.43	0.217	2.96	2.39	0.136
Oral moisture (%)	30.28	30.14	0.747	30.47	30.33	0.888
SOM	48.40	44.23	0.023	48.75	43.10	0.028
O-C	45.30	43.60	0.434	45.54	42.50	0.422
I-S	45.40	43.23	0.314	46.57	42.70	0.247
DEP	44.72	43.60	0.604	45.64	42.70	0.379
ANX	45.14	43.16	0.295	46.07	41.43	0.120
HOS	46.70	43.86	0.137	46.29	42.50	0.136
PHOB	47.05	53.12	0.526	47.18	43.03	0.078
PAR	42.72	41.86	0.514	44.18	41.10	0.257
PSY	44.35	42.95	0.348	45.64	41.97	0.305
GSI	44.81	42.21	0.178	45.64	41.00	0.132
PSDI	47.16	44.19	0.073	47.29	43.63	0.105
PST	43.63	40.40	0.155	44.54	38.77	0.115

TMD, temporomandibular disorder; VAS, visual analogue scale; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; USFR, unstimulated salivary flow rate; SOM, somatization; O-C, obsessive-compulsive behavior; I-S, interpersonal sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism; GSI, global severity index; PSDI, positive symptom distress index; PST, positive symptom total.
Values are presented as mean.
Statistical significant at significant level of $p<0.05$
[a]See Table 1 for the explanation of the abbreviated form.

(p=0.047), Am-sal (p=0.025), Eff-life (p=0.016), sip liquid while swallowing dry foods (Sip-liq, p=0.038), and T-score of SOM (p=0.013) than the acute group. In ANOVA analysis of the diagnosis-based three groups (muscle, joint and mixed problem groups), there was a tendency that mixed problem group has higher TMD pain VAS, stress VAS and Sub-sum6 but it was not statistically significant. However, the patients who had muscle components (muscle group and mixed group) had significantly higher scores of SOM (p=0.039) than joint group. There was no significant relationship between the diagnosis of TMDs and the xerostomia related data (Table 5).

4. Relationship between the Stress VAS, SCL-90R and the Other Factors

We divided the participants into two groups by the mean of each items of SCL-90R and the stress VAS. The patients who had above the mean of the stress VAS had significantly higher scores on the TMD Pain VAS (p=0.013), Sub-sum6 (p=0.009), Dry-eat (p=0.001), Dif-swal (p=0.001), SOM (p=0.001), O-C (p=0.000), I-S (p=0.000), DEP (p=0.000), ANX (p=0.000), HOS (p=0.000), PAR (p=0.002), PSY (p=0.001), GSI (p=0.000), PSDI (p=0.000), and PST (p=0.000). Within the non-smoking group, the patients who had above the mean of the stress VAS had significantly higher

Table 5. Relationship between the duration of the pain, the diagnostic profiles and the other factors

Variable	By the duration of the pain			By the diagnostic profiles (two groups)			By the diagnostic profiles (three groups)			
	Acute group	Chronic group	p-value	Joint group	Muscle/mixed group	p-value	Joint group	Muscle group	Mixed group	p-value
TMD pain VAS	34.05	50.62	0.002	33.17	43.11	0.088	33.17	35.75	44.33	0.160
Stress VAS	48.21	51.52	0.474	47.73	50.18	0.625	47.73	48.00	50.54	0.849
Sub-sum6	98.56	162.41	0.010	102.23	129.66	0.270	102.23	64.38	140.54	0.101
Dry-PM[a]	29.96	43.69	0.027	29.47	37.34	0.206	29.47	21.88	39.92	0.100
Dry-day[a]	24.89	33.93	0.105	24.63	29.71	0.361	24.63	19.75	31.38	0.305
Dry-eat[a]	16.51	25.24	0.079	17.97	20.25	0.646	17.97	11.88	21.65	0.456
Dif-swal[a]	7.77	17.00	0.047	9.00	11.89	0.488	9.00	5.75	12.92	0.468
Am-sal[a]	11.37	23.03	0.025	11.47	17.36	0.215	11.47	2.38	19.85	0.050
Eff-life[a]	8.05	19.52	0.016	9.70	13.11	0.425	9.70	2.75	14.83	0.175
Night-awake[a]	1.28	1.28	0.977	1.33	1.25	0.617	1.33	1.13	1.27	0.772
H_2O-bed[a]	1.40	1.90	0.072	1.40	1.66	0.341	1.40	1.50	1.69	0.587
Sip-liq[a]	1.67	2.07	0.038	1.73	1.84	0.585	1.73	1.63	1.88	0.645
Gum-candy[a]	1.07	1.07	0.986	1.03	1.09	0.411	1.03	1.00	1.10	0.473
USFR (mL/10 min)	2.57	2.93	0.496	2.83	2.58	0.529	2.83	2.95	2.52	0.672
Oral moisture (%)	30.34	30.23	0.745	30.00	30.46	0.368	30.00	30.96	30.38	0.428
SOM	44.70	49.48	0.013	44.10	47.50	0.039	44.10	45.50	47.83	0.165
O-C	44.53	44.31	0.925	43.70	44.86	0.611	43.70	43.25	45.13	0.781
I-S	43.46	46.00	0.262	43.37	44.82	0.519	43.37	41.13	45.44	0.426
DEP	44.07	44.34	0.904	43.00	44.79	0.374	43.00	41.63	45.31	0.457
ANX	43.51	45.41	0.341	43.10	44.71	0.416	43.10	43.38	44.94	0.646
HOS	45.11	45.62	0.799	44.37	45.77	0.413	44.37	43.25	46.19	0.540
PHOB	51.79	46.72	0.626	44.50	53.07	0.405	44.50	43.50	54.67	0.576
PAR	41.98	42.90	0.512	42.17	42.36	0.891	42.17	39.50	42.83	0.356
PSY	43.05	44.83	0.259	43.00	44.00	0.522	43.00	41.38	44.44	0.415
GSI	42.86	44.79	0.346	42.27	44.18	0.347	42.27	41.63	44.60	0.442
PSDI	45.79	45.45	0.847	44.23	46.45	0.206	44.23	44.75	46.73	0.360
PST	40.68	44.62	0.127	41.03	42.54	0.497	41.03	39.75	43.00	0.596

TMD, temporomandibular disorder; VAS, visual analogue scale; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; USFR, unstimulated salivary flow rate; SOM, somatization; O-C, obsessive-compulsive behavior; I-S, interpersonal sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism; GSI, global severity index; PSDI, positive symptom distress index; PST, positive symptom total.

Values are presented as mean.

Statistical significant at significant level of $p<0.05$.

[a]See Table 1 for the explanation of the abbreviated form.

Table 6. Relationship between stress VAS and the other factors

Variable	By the mean of stress VAS (n=86)			By the mean of stress VAS (n=58, non-smokers only)		
	Above the mean group	Below the mean group	p-value	Above the mean group	Below the mean group	p-value
TMD pain VAS	45.44	31.58	0.013	41.44	30.75	0.061
Sub-sum6	144.46	86.25	0.009	114.50	73.79	0.045
Dry-PM[a]	39.36	27.97	0.057	29.85	24.88	0.306
Dry-day[a]	31.08	23.58	0.162	27.00	20.29	0.184
Dry-eat[a]	25.50	11.06	0.001	19.68	9.75	0.016
Dif-swal[a]	15.76	4.11	0.001	12.32	2.79	0.004
Am-sal[a]	17.82	11.81	0.206	13.38	10.63	0.470
Eff-life[a]	14.94	7.72	0.057	12.26	5.46	0.049
Night-awake[a]	1.38	1.14	0.090	1.24	1.17	0.528
H_2O-bed[a]	1.56	1.58	0.093	1.47	1.63	0.715
Sip-liq[a]	1.86	1.72	0.462	1.76	1.79	0.899
Gum-candy[a]	1.10	1.03	0.271	1.06	1.00	0.389
USFR (mL/10 min)	2.72	2.59	0.739	2.58	2.65	0.740
Oral moisture (%)	30.04	30.67	0.140	30.08	30.85	0.097
SOM	48.76	42.92	0.001	48.88	41.50	0.003
O-C	48.26	39.17	0.000	48.15	38.04	0.000
I-S	47.98	39.22	0.000	48.88	38.46	0.001
DEP	47.50	39.53	0.000	47.85	38.83	0.001
ANX	47.02	40.17	0.000	46.88	39.13	0.000
HOS	48.14	41.31	0.000	46.82	40.79	0.003
PHOB	47.78	53.28	0.581	47.50	41.54	0.002
PAR	43.84	40.14	0.002	44.21	40.29	0.022
PSY	45.60	40.94	0.001	46.15	40.33	0.007
GSI	46.88	38.83	0.000	46.97	37.96	0.000
PSDI	48.12	42.28	0.000	48.00	41.71	0.005
PST	46.36	35.97	0.000	46.50	34.54	0.000

VAS, visual analogue scale; TMD, temporomandibular disorder; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; USFR, unstimulated salivary flow rate; SOM, somatization; O-C, obsessive-compulsive behavior; I-S, interpersonal sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism; GSI, global severity index; PSDI, positive symptom distress index; PST, positive symptom total.
Values are presented as mean.
Statistical significant at significant level of $p<0.05$.
[a]See Table 1 for the explanation of the abbreviated form.

scores on Sub-sum6 (p=0.045), Dry-eat (p=0.016), Dif-swal (p=0.004), Eff-life (p=0.049), and all SCL-90R scores (Table 6). Among SCL-90R items, SOM (p=0.017), O-C (p=0.046), and PSDI (p=0.037) were significantly related to the TMD pain VAS. The patients who had above the mean of O-C (p=0.020), I-S (p=0.025), DEP (p=0.025), ANX (p=0.011), HOS (p=0.008), PAR (p=0.023), GSI (p=0.029), and PSDI (p=0.008) were significantly higher scores on Sub-sum6. All SCL-90R items were significantly correlated with the stress VAS and p-values were <0.01 (Table 7).

5. Relationship between Smoking, Drinking and the Other Factors

The patients who were non-smokers had significantly lower Dry-PM (p=0.001), Dry-day (p=0.042), Dry-eat (p=0.034), and Sub-sum6 (p=0.012) than smokers and previous smokers. Alcohol consumers had significantly higher frequencies on Night-awake (p=0.016) and other factors are not statistically relevant (Table 8).

6. Correlation between the Subjective Dry Mouth Symptoms and the Objective Factors of Xerostomia (USFR and Oral Moisture)

Pearson's correlation coefficient between Sub-sum6 and

Table 7. Relationship between SCL-90R and the other factors

Variable	p-values (differences between above the mean group and below the mean group)											
	SOM	O-C	I-S	DEP	ANX	HOS	PHOB	PAR	PSY	GSI	PSDI	PST
TMD pain VAS	0.017	0.046	0.294	0.539	0.159	0.421	0.342	0.436	0.399	0.230	0.037	0.734
Stress VAS	0.002	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000
Sub-sum6	0.058	0.020	0.025	0.025	0.011	0.008	0.056	0.023	0.102	0.029	0.008	0.099
Dry-PM[a]	0.258	0.059	0.194	0.171	0.121	0.015	0.322	0.066	0.292	0.204	0.012	0.470
Dry-day[a]	0.078	0.098	0.205	0.090	0.042	0.045	0.085	0.286	0.409	0.128	0.004	0.436
Dry-eat[a]	0.062	0.019	0.010	0.016	0.006	0.018	0.011	0.005	0.075	0.013	0.002	0.053
Dif-swal[a]	0.106	0.031	0.012	0.016	0.018	0.009	0.046	0.013	0.145	0.021	0.107	0.033
Am-sal[a]	0.165	0.047	0.036	0.026	0.011	0.014	0.161	0.058	0.154	0.051	0.063	0.115
Eff-life[a]	0.129	0.055	0.063	0.137	0.044	0.045	0.100	0.136	0.202	0.088	0.132	0.110
Night-awake[a]	0.068	0.293	0.656	0.950	0.977	0.341	0.236	0.245	0.336	0.716	0.243	0.778
H_2O-bed[a]	0.235	0.930	0.278	0.608	0.635	0.922	0.263	0.808	0.051	0.326	0.946	0.381
Sip-liq[a]	0.012	0.117	0.082	0.089	0.018	0.038	0.000	0.052	0.415	0.012	0.045	0.028
Gum-candy[a]	0.103	0.329	0.298	0.607	0.238	0.238	0.067	0.449	0.449	0.284	0.298	0.271
USFR (mL/10 min)	0.497	0.886	0.684	0.963	0.389	0.924	0.156	0.872	0.178	0.865	0.537	0.705
Oral moisture (%)	0.969	0.378	0.265	0.086	0.204	0.391	0.442	0.475	0.493	0.345	0.609	0.875

SCL-90R, Symptom Checklist-90-Revised; SOM, somatization; O-C, obsessive-compulsive behavior; I-S, interpersonal sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism; GSI, global severity index; PSDI, positive symptom distress index; PST, positive symptom total; TMD, temporomandibular disorder; VAS, visual analogue scale; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; USFR, unstimulated salivary flow rate.
Statistical significant at significant level of $p<0.05$.
[a]See Table 1 for the explanation of the abbreviated form.

Table 8. Relationship between smoking, alcohol drinking and the other factors

Variable	Smoking			Alcohol drinking		
	Non-smoker	Smoker/ ex-smoker	p-value	Non-drinker	Drinker	p-value
TMD pain VAS	37.02	45.07	0.215	47.17	50.88	0.418
Stress VAS	47.41	53.29	0.247	36.97	41.56	0.442
Sub-sum6	97.66	166.57	0.012	103.89	131.76	0.246
Dry-PM[a]	27.79	48.68	0.001	28.44	39.02	0.077
Dry-day[a]	24.22	35.64	0.042	22.25	32.04	0.066
Dry-eat[a]	15.57	27.50	0.034	17.64	20.76	0.515
Dif-swal[a]	8.38	16.07	0.120	8.47	12.62	0.273
Am-sal[a]	12.24	21.64	0.097	14.92	15.58	0.890
Eff-life[a]	9.45	17.04	0.128	12.17	11.74	0.918
Night-awake[a]	1.21	1.43	0.303	1.08	1.42	0.016
H_2O-bed[a]	1.53	1.64	0.698	1.56	1.58	0.927
Sip-liq[a]	1.78	1.86	0.681	1.81	1.80	0.976
Gum-candy[a]	1.03	1.14	0.159	1.11	1.04	0.329
USFR (mL/10 min)	2.67	2.67	0.989	2.71	2.64	0.857
Oral moisture (%)	30.40	30.10	0.512	30.27	30.33	0.899

TMD, temporomandibular disorder; VAS, visual analogue scale; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; USFR, unstimulated salivary flow rate.
Values are presented as mean.
Statistical significant at significant level of $p<0.05$.
[a]See Table 1 for the explanation of the abbreviated form.

USFR was very low (–0.150) and not statistically significant (p=0.168). Pearson's correlation coefficient between USFR and oral moisture was 0.319 and that between Sub-sum6 and oral moisture was –0.258 which means somewhat correlated (Table 9).

Table 9. Correlation coefficients among the variables

Variable	TMD pain VAS	Stress VAS	Sub-sum6	USFR (mL/10 min)	Oral moisture (%)
TMD pain VAS	1	-	-	-	-
Stress VAS	0.284**	1	-	-	-
Sub-sum6	0.441**	0.383**	1	-	-
USFR (mL/10 min)	0.081	0.054	−0.150	1	-
Oral moisture (%)	0.075	−0.160	−0.258*	0.319**	1

TMD, temporomandibular disorder; VAS, visual analogue scale; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; USFR, unstimulated salivary flow rate.
Values are presented as Pearson's correlation coefficient (r). r>0.4 (significantly correlated). 0.2<r<0.4 (somewhat correlated).
*p<0.05, **p<0.01.

DISCUSSION

This study showed that the patients who had higher TMD pain VAS had significantly higher stress VAS, T-score of SOM. In particular, the patients who had chronic TMD pain had higher TMD pain VAS and SOM than the acute group. The pain intensity can affect the quality of life and can be a stressor itself. In a study with cancer patients, the pain was greater among patients with greater life stress.[20] Moreover, there is a report that depression and SOM in patients with myofascial pain and arthralgia, which have the chronic nature of disease, were higher than patients with only disk displacement.[21] In this study, the patients of the higher pain intensity and chronic pain had higher stress and higher SOM and we can assume that the results are consistent with the previous studies.

The patients who had higher TMD pain VAS and chronic TMD pain showed significantly higher subjective dry mouth symptoms, On the other hand, the intensity of TMD pain and the duration of TMD were not significantly correlated with objective data such as USFR and oral moisture. It means that there are discrepancy between objective dryness and subjective dry feeling. Regarding the term xerostomia, Sreebny and Vissink[22] described that dry mouth, or xerostomia is subjective complaints instead of statistical ones and some may complain of oral dryness yet have a normal flow rate, and others may have an abnormally low flow rate of whole saliva and not complain of oral dryness. Xerostomia may associate not only with objective factors such as salivary flow or oral moisture, but also with psychological or neurologic factors. We focused on the findings that the duration and the intensity of pain is positively correlated with subjective dry symptoms. In regard to this result, we found several previous studies suggested the possibilities of association between chronic pain and sensory dysfunction.[23-25] Based on these reports, we could hypothesize that continuous chronic pain input may alter the processing of sensation from the oral mucosa, which might be related to enhanced dry sensation of patients. The concept of central sensitization is widely accepted in the field of pain. Central sensitization is the result of complex processes in the peripheral and central nervous systems. Suggested mechanisms of central sensitization are wind-up, classic heterosynaptic central sensitization, homosynaptic potentiation, pre- and post-synaptic transcription changes, and reduction in tonic and phasic inhibition.[26] Among these mechanisms, we assumed that the concept of reduction in tonic and phasic inhibition could be a possible explanation for the relationship between pain severity or duration and subjective oral dryness. If chronic nociceptive input continuously stimulates the peripheral nervous system, it can negatively regulate the central inhibition in the central nervous system. The feeling of dryness is a result of processed mechanical sensory input which is modulated in the central nervous system. The patients with chronic pain input such as chronic TMD pain might have dysregulated inhibitory function, which could be a plausible explanation for these findings.

We showed that USFR and oral moisture could not mirror the subjective dry mouth symptoms and they are not significantly related with the TMD pain VAS, duration of TMD, the stress VAS and SCL-90R in this study. Clinically, USFR is one of the most widely used simple methods diagnosing xerostomia. However, discordance between USFR and subjective xerostomia makes diagnostic difficulty. Several studies reported that the salivary fluid thickness, residual

saliva, salivary composition, evaporation of saliva, swallowing, water flux across the oral mucosa and ion transport properties, besides salivation, can contribute to the sensation of dry mouth.[27-29] In this study, we used oral moisture checking device in addition to USFR as an objective tool. Oral moisture was positively correlated with USFR and had higher correlation coefficient with the subjective xerostomia symptoms than USFR (Table 9). Even if one has enough salivation but there is much more evaporation, then oral moisture could be lowered and it may affect the subjective dry mouth symptoms.[18] Interestingly, the subjects who were shown USFR <1 mL/10 min and oral moisture <25% had significantly higher Sub-sum6 (p=0.049), Am-sal (p=0.030), Eff-life (p=0.029) than the subjects who were shown USFR ≥2.5 mL/10 min and oral moisture ≥30% in this study (Table 10). When we evaluate one's xerostomia symptoms, the use of at least two objective measurements would be more accurate.

There was a study about the correlation of orofacial pain and xerostomia[12] and it showed the patients who had orofacial pain had lower salivary flow rate and had more complaints of xerostomia than the normal control group. However, the diagnosis of orofacial pain was wide-ranged and the medication factor was not excluded, so direct relationship between TMDs and xerostomia was hardly inferred. In this study, only TMD patients were participated and the medication factor which was considered to be highly related to xerostomia symptoms was all excluded. It showed

Table 10. Relationship salivary flow/oral moisture and the other factors (n=54)

Variable	USFR (mL/10 min) and oral moisture (%)		p-value
	USFR ≥2.5 and oral moisture ≥30 (n=33)	USFR <1 and oral moisture <25 (n=21)	
TMD pain VAS	41.55	33.24	0.246
Stress VAS	48.85	50.95	0.744
Sub-sum6	95.55	162.33	0.049
Dry-PM[a]	30.67	39.81	0.219
Dry-day[a]	25.21	34.14	0.212
Dry-eat[a]	15.94	27.48	0.106
Dif-swal[a]	6.42	17.24	0.062
Am-sal[a]	10.36	24.76	0.030
Eff-life[a]	6.94	18.90	0.029
Night-awake[a]	1.12	1.48	0.123
H_2O-bed[a]	1.61	1.62	0.971
Sip-liq[a]	1.76	1.81	0.827
Gum-candy[a]	1.06	1.00	0.430
SOM	47.33	45.33	0.418
O-C	44.03	45.95	0.538
I-S	45.82	43.57	0.426
DEP	44.45	44.86	0.898
ANX	45.33	43.48	0.505
HOS	46.33	45.95	0.899
PHOB	47.15	43.90	0.180
PAR	42.67	42.62	0.980
PSY	44.27	42.48	0.365
GSI	44.42	43.33	0.700
PSDI	45.48	47.10	0.504
PST	43.18	40.62	0.411

USFR, unstimulated salivary flow rate; TMD, temporomandibular disorder; VAS, visual analogue scale; Sub-sum6, the sum of the VAS of six questions to evaluate the degree of dry mouth; SOM, somatization; O-C, obsessive-compulsive behavior; I-S, interpersonal sensitivity; DEP, depression; ANX, anxiety; HOS, hostility; PHOB, phobic anxiety; PAR, paranoid ideation; PSY, psychoticism; GSI, global severity index; PSDI, positive symptom distress index; PST, positive symptom total.

Values are presented as mean.

Statistical significant at significant level of $p<0.05$.

[a]See Table 1 for the explanation of the abbreviated form.

that the higher TMD pain VAS is the higher subjective dry mouth symptoms. Smoking is also very important factor when evaluating xerostomia. When we excluded the smoking and the quit-smoking group, the higher TMD pain VAS group showed the higher subjective dry mouth symptoms, as well. Therefore, we could assume that the intensity of TMD pain and duration of TMD are directly related to the subjective dry mouth symptoms.

Stress is known to be one of the most important causative and maintenance factor of TMDs.[30] Many studies showed the relationship between the stress and the subjective oral dryness.[10,11,31] The patients who had above the mean of the stress VAS had significantly higher scores on the TMD pain VAS and the subjective dry mouth symptoms in this study. The importance of hypothalamic-pituitary-adrenal (HPA) axis in chronic pain is well described in several studies.[32-35] Blackburn-Munro and Blackburn-Munro[33] suggested three possibilities of common etiology between chronic pain and HPA axis. First, immune and neuroendocrine systems shared same adaptation mechanism against to the stress. Second, tonic and phasic pain could activate HPA axis in animal model. Third, several elements of HPA hormone cascade was associated with pain response. Corticotropin-releasing hormone (CRH) and vasopressin are known to be key regulators of pituitary adrenocorticotrophic hormone (ACTH).[34] Under the chronic stress condition, release of CRH is maintained , whereas secretion of vasopressin is significantly increased.[35] The number of increased vasopressin receptors in targeted tissue might be definite factors for responsiveness of corticotropin during chronic stress.[34] Another interesting study revealed that vasopressin may contribute one's thirsty and xerostomia symptoms.[36] A minute molecular biology of vasopressin and xerostomia is not fully understood yet, but the relevance of HPA axis and xerostomia may be certain. It would be an attractive study, if we analyze relationship between vasopressin level and xerostomia-related data for orofacial patients in the future.

We used a simple question to evaluate the participants' stress level. The higher stress VAS group showed the higher TMD pain VAS, all SCL-90R items except phobic anxiety, and Sub-sum6, the two subjective dry-mouth symptoms (Dry-eat, Dif-swal) (Table 6). This simple question may not totally reflect the multidimensional aspects of stress such as physical stress. However, the stress VAS had remarkably significant correlations with SCL-90R (Tables 6, 7) and we could assume that the evaluation of stress with VAS mainly reflects one's psychological status.

When we asked to the TMD patients who visited the our clinic to participate in this study, thirty-five people denied and eighty-six ones agreed to join. If the participants would feel some discomfort on oral dryness, then they might want to evaluate their symptoms. So the rate of agreement among those patients would have been higher. This would be a bias of the study results. Moreover almost sixty percentages of the subjects in this study was in their twenties. We thought that the higher proportion of the younger subjects was because the patients with medication within two weeks were excluded in this study. Even though the participants were not even by age, the actual salivation and oral moisture were not related to the patients' age (data not shown), which supports the previous studies that the salivation is more relevant to the medication than the age itself.[37]

In conclusion, the severity of TMD pain, the duration of TMD pain and stress significantly affect the subjective dry mouth symptoms, but they do not affect the USFR or oral moisture. The TMD patients, who especially have great pain intensity and chronic pain history, might need further evaluation of their subjective xerostomia symptoms. This will help to improve the quality of life of TMD patients by managing their submerged complaints.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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