Research Article

Association between Multiple Oral Complaints and Menopausal Symptoms: An Observational Study

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Abstract

Background: Oral discomfort symptoms such as xerostomia, taste disturbance, and burning sensation occasionally appear simultaneously and may decrease quality of life (QOL). Multiple oral complaints (MOC) may be associated with decreasing levels of female hormones. However, there has been little research to elucidate the relationship between MOC and menopausal symptoms. The purpose of this study was to elucidate the characteristics of participants who complained of xerostomia, taste disturbance, burning sensation, and MOC, and to discuss the association between MOC and menopausal symptoms, using a web-based survey system.

Methods: This study comprised 372 Japanese wom-

-en aged 20-79 years. Participants completed questionnaires covering their experience of xerostomia, taste disturbance, burning sensation, menopausal symptoms, and QOL. A univariate analysis was performed to investigate the relationship between the presence of xerostomia, taste disturbance, burning sensation, and MOC, and each evaluation item. Multiple logistic regression was performed to identify factors associated with MOC.

Results: Xerostomia was the most frequent complaint (39.4%), followed by taste disturbance (16.2%) and burning sensation (9.2%). Nineteen participants (5.1%) had MOC. Multiple logistic regression analysis showed that the number of menopausal symptoms was associated with xerostomia, taste disturbance, burning sensation, and MOC.

Conclusion: This study suggested that multiple oral complaints are related to menopausal symptoms. When treating xerostomia, taste disturbance, and burning sensation, related factors including menopausal symptoms should be considered, which could help improve patients' QOL.

Keywords: Menopause; Oral Discomfort Complaints; Quality of Life; Xerostomia

1. Background

In most women, a wide variety of systemic symptoms, such as hot flashes, sweating, and psychiatric symptoms, appear because of hormonal changes. Xerostomia, taste disturbance, and burning sensation of the oral cavity are common complaints in older women, and these complaints decrease quality of life (QOL) [1]. In fact, 79.5% of physicians have encountered female patients at outpatient facilities complaining of xerostomia, taste disturbance, burning sensation, and temporomandibular disorders [2]. These oral discomfort complaints occasionally appear simultaneously. Many studies have individually reported the etiology of xerostomia and burning sensation [1, 3]. However, few studies have investigated oral complaints that occur in women simultaneously [4-6]. To the best of our knowledge, no studies have examined the factors associated with multiple oral complaints (MOC) in women. If the characteristics of patients who exhibit MOC are clarified, it may lead to early treatment and improvement of the patients' QOL.

Recently, the concept of dryness syndrome [7], also known as dry X syndrome [8], has been promoted. This concept proposes that people who experience dryness in a certain region of the body (e.g., xerostomia) also tend to experience dryness in other regions. A recent survey among Japanese women showed that approximately half experienced dryness in more than two regions of the body (e.g., in the eyes, nose, mouth, skin, or vagina) [7]. Because estrogen receptors are present in the eyes, nose, mouth, and skin, these symptoms could occur simultaneously because of the decreased estrogen levels present during menopause. Additionally, autonomic nervous dysfunction may lead to dryness, because tears and saliva are regulated by the autonomic nervous system. Therefore, there is a possibility that dryness syndrome exists simultaneously with MOC. Detecting the relationship between MOC and dryness syndrome may contribute to improvement in the QOL of patients. The purpose of this study was to elucidate the characteristics of participants who complained of xerostomia, taste disturbance, burning sensation, and MOC, taking the factor of menopausal symptoms and dryness syndrome into account.

2. Subjects and Methods

A web-based questionnaire was administered May, 2018, by an internet research company (Macromill, Tokyo, Japan). This research company has a proprietary automatic online research system called AIRs (Automatic Internet Research System), which instantly collects consumer response data on products and services provided by a variety of companies.

2.1 Participants

Sample size calculation was performed before the study was initiated. Based on an effect size of 0.15, α-value of 0.05, and power of 0.8, the sample size calculation using software (G*power 3.1.9.7, https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower.html) yielded 349 subjects. Considering the likelihood of missing data, we recruited 372 women in the following age groups: 20–29, 30–39, 40–49, 50–59, 60–69, and 70–79 (n = 62 in each age group). All investigations were conducted in accordance with the Guidelines for Biomedical Studies Involving Human Participants (Helsinki Declaration). The Ethics Committee of the Niigata University Faculty of Dentistry approved the study protocol and informed consent was waived (approval number 447).

2.2 Questionnaire

Questionnaires covered participant characteristics, QOL, oral symptoms, and menopausal symptoms. Participant characteristics included age, marital status, number of children, employment status, medical history, medication, and sleeping duration. Feelings of dryness of the eyes, nose, skin, and vagina were assessed as: none, mild, moderate, and severe. To evaluate QOL, the Japanese version of the 8-Item Short-Form Health (SF-8) was used [9]. The SF-8 assesses eight health concepts: physical functioning, role (physical), body pain, general health, vitality, social functioning, role (emotional), and mental health. A higher score indicates a better QOL. The following oral symptoms were assessed: levels of xerostomia, dysgeusia, and phantogeusia (experiencing a taste in the mouth in the absence of tastants), burning sensation of the tongue, temporomandibular joint (TMJ) pain, and difficulty in swallowing. They were assessed as: none, mild, moderate, and severe. The duration of these symptoms, whether a consultation with a xerostomia specialist had been sought, the timing of the burning sensation, and any trigger for the burning sensation were documented. Additionally, participants with dysgeusia were asked which tastes they were unable to recognize well. Participants with phantogeusia were asked which tastes they could detect in the absence of tastants in their mouth.

To assess menopausal symptoms, the menopausal symptom checklist for Japanese women was used [10], which differs from the Kuppermann index developed for American women [11]. The Japanese checklist includes 21 items: 'hot flashes of the face or upper body (become hot)', 'sweat easily', 'unable to fall asleep at night', 'fall asleep but often wake at night', 'easily excitable, often irritable', 'always anxious', 'worry about minor things', 'worry and often become depressed', 'lack of energy, easily tired', 'tired feeling of eyes', 'difficulty remembering things or often forgetful', 'dizziness', 'heart pounds quickly', 'tight feeling of chest', 'heavy feeling of the head or frequent headache', 'shoulder or neck stiffness', 'back or lower back pain', 'painful joints at hands and feet', 'cold feeling of the lower back or hands and feet', 'numbness of the hands and feet (fingers, toes)', and 'recently sensitive to sound'; these symptoms were assessed as: none, mild,

moderate, and severe. Finally, the menopausal status and its duration were noted.

2.3 Statistical analysis

Oral symptoms were recognized as present if a participants rated the symptom as severe, moderate, or mild. Participants with dysgeusia or phantogeusia were recognized as having taste disturbance. The presence of three oral symptoms (xerostomia, taste disturbance, and burning sensation) was defined as MOC. The body parts in which participants experienced dryness (eyes, nose, skin, or vagina) were recorded as dryness regions. In the SF-8 analysis, physical component summary (PCS) and mental component summary (MCS) scores were calculated using the Norm-Based Scoring method [12]. A higher PCS or MCS score indicated a better QOL. For Statistical analysis, the prevalence of xerostomia, taste disturbance, burning sensation, and MOC was assessed. A univariate analysis was performed to investigate the relationship between the presence of xerostomia, taste disturbance, burning sensation, and MOC and each evaluation item. Variables that were not normally distributed (assessed using the Shapiro-Wilk normality test) were analyzed using non-parametric tests. The Mann–Whitney U test was used for continuous variables, and the chi-square or Fisher's exact tests were used for categorical variables. A multiple logistic regression model yielding odds ratios and 95% confidence intervals was used to identify factors associated with xerostomia, taste disturbance, burning sensation, and MOC. The model included variables that showed an association in the univariate analysis ($P < 0.05$). In choosing explanatory variables, we considered the correlation of each factor and selected only items with a Spearman's correlation coefficient of 0.7 or more. A stepwise method was used to develop an optimal multivariable logistic model. All analyses were performed using the Statistical Package for the Social Sciences software version 26.0 (IBM, Tokyo, Japan). Statistical significance was set at $P < 0.05$.

3. Results

This survey was conducted using data from 371 women (average age: 49.2 ± 16.5 years) because one woman (aged 42 years) did not answer the questionnaire completely.

3.1 Prevalence of xerostomia, taste disturbance, burning sensation, and MOC

The prevalence of xerostomia, taste disturbance, burning sensation, and MOC is shown in Figure 1. Xerostomia was the most frequent complaint (146, 39.4%), followed by taste disturbance (60, 16.2%), and burning sensation (34, 9.2%). Nineteen participants (5.1%) had all three symptoms. Twenty-nine participants (7.8%) had two oral discomfort complaints. Forty-five participants (6.1%) exhibited the three symptoms of multiple oral complaints, xerostomia, taste disturbance, burning sensation, and multiple oral complaints.

3.2 Duration of prevalence of xerostomia, taste disturbance, and burning sensation, and details of these symptoms

The average duration of xerostomia was 2.8 ± 5.1 years (range 0–30 years). Only four (1.4%) out of 283 participants who complained of xerostomia had consulted a specialist. Three of these participants consulted internal medicine physicians and one consulted a psychiatrist. The reasons for not seeking a consultation were "not bad enough to see a doctor" (104 participants, 89.7%), "I do not know what department to go to" (15 participants, 12.9%), and "I

think there is no treatment" (8 participants, 6.9%). Details of taste disturbance are shown in Table 1. The complaint of dysgeusia was made by 41 participants (11.1%) and that of phantogeusia by 38 (10.2%). The most disturbed taste was umami (24, 58.5% of with dysgeusia), and the most frequently occurring taste in phantogeusia was bitter (21 participants, 55.3% of participants with phantogeusia). The average duration of the burning sensation was 2.3 ± 2.9 years (range 0–10 years). It was experienced at a variety of times: "no burning sensation during meals or conversation" (18 participants, 52.9% of participants with burning sensation), "burning sensation occurs only during meals" (9 participants, 26.4%), "burning sensation occurs during meals and conversation," (4 participants, 11.7%) and "burning sensation occurs only during conversation" (3 participants, 8.8%). The main triggers for burning sensation were xerostomia (12 participants, 35.2%), psychological stress (9 participants, 26.4%), dental treatment (5 participants, 14.7%), disease (5 participants, 14.7%), medication (3 participants, 8.8%), and unknown (9 participants, 26.4%).

3.3 Characteristics of the participants with xerostomia, taste disturbance, burning sensation, and MOC

The relationships between xerostomia, taste disturbance, burning sensation, MOC, and each factor are shown in Table 2 (Attached at the end of the paper). The prevalence of xerostomia, taste disturbance, burning sensation, and MOC was lower in participants without disease. The use of central nervous system (CNS) agents, number of dryness regions, PCS and MCS, and oral and menopausal symptoms were also significantly related to the occurrence of xerostomia, taste disturbance, and burning sensation. The number of dryness regions, PCS and MCS, and oral and menopausal symptoms were also related to the existence of MOC.

3.4 Factors associated with xerostomia, taste disturbance, burning sensation, and MOC

Table 3 shows the results of logistic regression analyses of factors associated with xerostomia, taste disturbance, burning sensation, and MOC. All analyses were statistically significant ($P < 0.001$), and the discriminant probability was 75.3% for xerostomia, 87.8% for taste disturbance, 93.6% for burning sensation, and 96.4% for MOC ($P < 0.001$). The number of menopausal symptoms was a significant explanatory variable for xerostomia, taste disturbance, burning sensation, and MOC. Other significant explanatory variables were the number of dryness regions and difficulty of swallowing for xerostomia, burning sensation in the mouth and depression for taste disturbance, and taste disturbance, difficulty in swallowing, and TMJ pain for burning sensation.

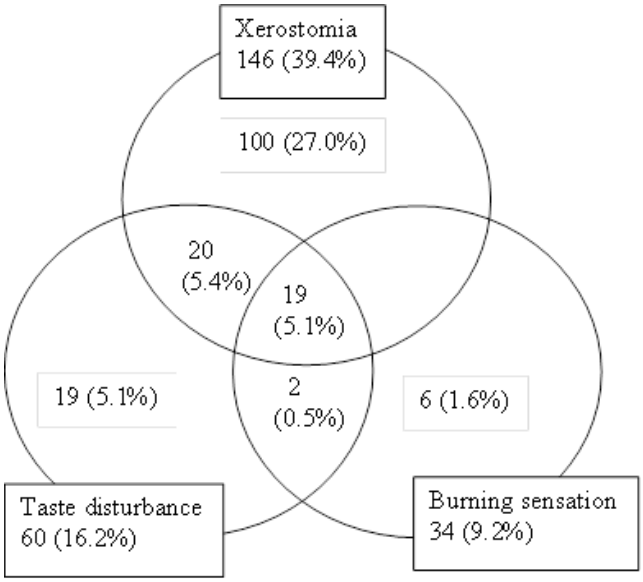

Figure 1: Prevalence of xerostomia, taste disturbance, burning sensation, and multiple oral complaints.

		Dysgeusia (n=41)	Phantogeusia (n=38)
Characteristics	Duration of symptom	2.5 ± 2.8	2.5 ± 2.9
	Age	54.6 ± 15.4	51.2 ± 15.7
Disturbed taste	Sweet	8 (19.5)	1 (2.6)
	Salt	13 (31.7)	8 (21.1)
	Sour	6 (14.6)	11 (28.9)
	Bitter	9 (22.0)	21 (55.3)
	Umami	24 (58.5)	—

Values are represented by number of participants (%) or mean ± SD

Table 1: Details of taste disturbance.

	Xerostomia			**Taste disturbance**			**Burning mouth**			**MOC**		
	no	**yes**	**P**	**No**	**yes**	**P**	**no**	**yes**	**P**	**non-MOC**	**MOC**	**P**
	n=225	**n=146**	**value**	**n=311**	**n=60**	**value**	**n=337**	**n=34**	**value**	**n=352**	**n=19**	**value**
Characteristics												
Age	50.0 ± 16.8	48.0 ± 15.9	0.22	48.6 ± 16.5	52.5 ± 16.1	0.105	49.2 ± 16.6	49.2 ± 15.6	0.986	49.1 ± 16.5	51.6 ± 15.1	0.531
Married	158 (70.2)	95 (65.1)	0.298	213 (68.5)	40 (66.7)	0.781	230 (68.2)	23 (67.6)	0.943	240 (68.2)	13 (68.4)	0.983
Children	150 (66.7)	83 (56.8)	0.056	191 (61.4)	42 (70.0)	0.208	213 (63.2)	20 (58.8)	0.614	222 (63.1)	11 (57.9)	0.649
Employment	102 (45.3)	73 (50.0)	0.379	152 (48.9)	23 (38.3)	0.134	160 (47.5)	15 (44.1)	0.708	166 (47.2)	9 (47.4)	0.986
Medical history												
Hypertension	23 (10.2)	17 (11.6)	0.666	34 (10.9)	6 (10.0)	0.831	33 (9.8)	7 (20.6)	0.053	37 (10.5)	3 (15.8)	0.47
Hyperlipemia	13 (5.8)	11 (7.5)	0.502	20 (6.4)	4 (6.7)	0.946	21 (6.2)	3 (8.8)	0.558	23 (6.5)	1 (5.3)	0.826
Dysautonomia	6 (2.7)	8 (5.5)	0.165	11 (3.5)	3 (5.0)	0.586	12 (3.6)	2 (5.9)	0.498	12 (3.4)	2 (10.5)	0.113
Uterine disease	26 (11.6)	26 (17.8)	0.09	45 (14.5)	7 (11.7)	0.567	45 (13.4)	7 (20.6)	0.247	49 (13.9)	3 (15.8)	0.819
Depression	2 (0.9)	2 (1.4)	0.514	1 (0.3)	3 (5.0)	0.014	3 (0.9)	1 (2.9)	0.32	3 (0.9)	1 (5.3)	0.19
No disease	147 (65.3)	78 (53.4)	0.022	193 (62.1)	32 (53.3)	0.205	209 (62.0)	16 (47.1)	0.089	216 (61.4)	9 (47.4)	0.224
Medication	67 (29.8)	44 (30.1)	0.941	89 (28.6)	22 (36.7)	0.213	97 (28.8)	14 (41.2)	0.133	104 (29.5)	7 (36.8)	0.499
N. of medications	0.4 ± 0.8	0.5 ± 1.0	0.718	0.4 ± 0.9	0.6 ± 1.1	0.191	0.4 ± 0.9	0.6 ± 1.1	0.26	0.4 ± 0.9	0.7 ± 1.3	0.485
CNS agent	5 (2.3)	11 (7.7)	0.014	10 (3.3)	6 (10.5)	0.015	12 (3.6)	4 (12.9)	0.017	14 (4.1)	2 (11.1)	0.158
Sleeping duration	6.5 ± 1.0	6.2 ± 1.0	0.032	6.4 ± 1.0	6.2 ± 1.1	0.173	6.4 ± 1.0	5.9 ± 1.1	0.019	6.4 ± 1.0	5.7 ± 1.1	0.009
N. of dryness lesions	1.0 ± 1.0	2.2 ± 1.2	<0.001	1.3 ± 1.1	2.3 ± 1.4	<0.001	1.4 ± 1.1	2.6 ± 1.3	<0.001	1.4 ± 1.2	2.9 ± 1.3	<0.001
PCS	49.7 ± 6	47.9 ± 7	0.006	49.4 ± 6.2	47.1 ± 7.3	0.015	49.4 ± 6.3	44.6 ± 6.7	<0.001	49.3 ± 6.3	44.1 ± 7.2	0.001
MCS	49.4 ± 6.8	46 ± 8.9	<0.001	48.8 ± 7.5	44.1 ± 8.6	<0.001	48.4 ± 7.8	44.7 ± 7.8	0.003	48.4 ± 7.8	41.5 ± 6.6	<0.001
Oral Symptom												

Xerostomia	—	—	—	107 (34.4)	39 (65.0)	<0.001	120 (35.6)	26 (76.5)	<0.001	127 (36.1)	19 (100.0)	<0.001
Taste disturbance	21 (9.3)	39 (26.7)	<0.001	—	—	—	39 (11.6)	21 (61.8)	<0.001	41 (11.6)	19 (100.0)	<0.001
Burning sensation of tongue	8 (3.6)	26 (17.8)	<0.001	13 (4.2)	21 (35.0)	<0.001	—	—	—	15 (4.3)	19 (100.0)	<0.001
TMJ pain	11 (4.9)	26 (17.8)	<0.001	21 (6.8)	16 (26.7)	<0.001	23 (6.8)	14 (41.2)	<0.001	28 (8.0)	9 (47.4)	<0.001
Difficulty in swallowing	10 (4.4)	36 (24.7)	<0.001	26 (8.4)	20 (33.3)	<0.001	30 (8.9)	16 (47.1)	<0.001	33 (9.4)	13 (68.4)	<0.001
Menopausal symptom												
Hot flushes	50 (22.2)	73 (50.0)	<0.001	91 (29.3)	32 (53.3)	<0.001	102 (30.3)	21 (61.8)	<0.001	110 (31.3)	13 (68.4)	0.001
Sweating	123 (54.7)	104 (71.2)	0.001	185 (59.5)	42 (70.0)	0.126	198 (58.8)	29 (85.3)	0.002	211 (59.9)	16 (84.2)	0.034
Insomnia	108 (48.0)	104 (71.2)	<0.001	173 (55.6)	39 (65.0)	0.179	182 (54.0)	30 (88.2)	<0.001	195 (55.4)	17 (89.5)	0.003
Nocturnal awakening	119 (52.9)	108 (74.0)	<0.001	182 (58.5)	45 (75.0)	0.016	199 (59.1)	28 (82.4)	0.008	209 (59.4)	18 (94.7)	0.002
Irritability	110 (48.9)	110 (75.3)	<0.001	173 (55.6)	47 (78.3)	0.001	190 (56.4)	30 (88.2)	<0.001	202 (57.4)	18 (94.7)	0.001
Anxious	111 (49.3)	112 (76.7)	<0.001	174 (55.9)	49 (81.7)	<0.001	193 (57.3)	30 (88.2)	<0.001	205 (58.2)	18 (94.7)	0.002
Worry	117 (52.0)	115 (78.8)	<0.001	186 (59.8)	46 (76.7)	0.014	203 (60.2)	29 (85.3)	0.004	214 (60.8)	18 (94.7)	0.003
Depression	102 (45.3)	99 (67.8)	<0.001	155 (49.8)	46 (76.7)	<0.001	170 (50.4)	31 (91.2)	<0.001	182 (51.7)	19 (100.0)	<0.001
Easy tired	104 (46.2)	102 (69.9)	<0.001	157 (50.5)	49 (81.7)	<0.001	178 (52.8)	28 (82.4)	0.001	187 (53.1)	19 (100.0)	<0.001
Eyestrain	166 (73.8)	132 (90.4)	<0.001	240 (77.2)	58 (96.7)	0.001	270 (80.1)	28 (82.4)	0.755	279 (79.3)	19 (100.0)	0.027
Forgetfulness	119 (52.9)	111 (76.0)	<0.001	180 (57.9)	50 (83.3)	<0.001	203 (60.2)	27 (79.4)	0.028	212 (60.2)	18 (94.7)	0.003
Dizziness	57 (25.3)	75 (51.4)	<0.001	98 (31.5)	34 (56.7)	<0.001	112 (33.2)	20 (58.8)	0.003	116 (33.0)	16 (84.2)	<0.001
Heart pounding	41 (18.2)	69 (47.3)	<0.001	77 (24.8)	33 (55.0)	<0.001	86 (25.5)	24 (70.6)	<0.001	94 (26.7)	16 (84.2)	<0.001
Chest tightness	31 (13.8)	40 (27.4)	0.001	45 (14.5)	26 (43.3)	<0.001	52 (15.4)	19 (55.9)	<0.001	58 (16.5)	13 (68.4)	<0.001
Headaches	90 (40.0)	86 (58.9)	<0.001	140 (45.0)	36 (60.0)	0.033	151 (44.8)	25 (73.5)	0.001	160 (45.5)	16 (84.2)	0.001
Stiff shoulder	165 (73.3)	134 (91.8)	<0.001	246 (79.1)	53 (88.3)	0.098	266 (78.9)	33 (97.1)	0.011	281 (79.8)	18 (94.7)	0.11
Back ache	130 (57.8)	114 (78.1)	<0.001	198 (63.7)	46 (76.7)	<0.001	212 (62.9)	32 (94.1)	<0.001	226 (64.2)	18 (94.7)	<0.001
Joint pains	70 (31.1)	74 (50.7)	<0.001	103 (33.1)	41 (68.3)	<0.001	115 (34.1)	29 (85.3)	<0.001	126 (35.8)	18 (94.7)	<0.001

Coldness	104 (46.2)	98 (67.1)	<0.001	157 (50.5)	45 (75.0)	<0.001	176 (52.2)	26 (76.5)	0.007	186 (52.8)	16 (84.2)	0.007
Numbness	42 (18.7)	52 (35.6)	<0.001	64 (20.6)	30 (50.0)	<0.001	73 (21.7)	21 (61.8)	<0.001	78 (22.2)	16 (84.2)	<0.001
Sound sensitivity	30 (13.3)	59 (40.4)	<0.001	59 (19.0)	30 (50.0)	<0.001	68 (20.2)	21 (61.8)	<0.001	72 (20.5)	17 (89.5)	<0.001
N. of menopausal symptoms	8.8 ± 4.9	13.5 ± 4.9	<0.001	9.9 ± 5.1	14.6 ± 5.3	<0.001	10.1 ± 5.1	16.5 ± 4.6	<0.001	10.2 ± 5.1	18.8 ± 2.9	<0.001
Menopause	107 (48.0)	56 (39.2)	0.098	131 (42.8)	32 (53.3)	0.134	150 (45.0)	13 (39.4)	0.533	155 (44.7)	8 (42.1)	0.827
Duration of menopause years	13.8 ± 7.4	13.7 ± 8.0	0.829	13.7 ± 7.9	14 ± 6.3	0.67	13.8 ± 7.7	12.9 ± 4.6	0.725	13.8 ± 7.7	11.8 ± 4.6	0.547

MOC: multiple oral complaints

CNS: central nervous system

SF-8: eight-item Short-form Health Survey

PCS: physical component summary

MCS: mental component summary

TMJ: temporomandibular joint

Values are represented by number of participants (%) or mean ± SD.

Bold text indicates statistically significant associations ($p < 0.05$).

Table 2: Characteristics of xerostomia, taste disturbance, burning sensation, and existence of the multiple oral complaints.

	Explanatory variables	P-value	OR	95% CI	
				lower	upper
Xerostomia	Number of dryness lesion	<0.001	1.866	1.454	2.396
	Number of menopausal symptoms	<0.001	1.114	1.053	1.178
	Difficulty of swallowing	0.006	0.293	0.122	0.703
Taste disturbance	Number of menopausal symptoms	<0.001	1.150	1.072	1.233
	Burning mouth	<0.001	0.135	0.055	0.327
	Depression	0.031	0.071	0.006	0.791
Burning mouth	Taste disturbance	<0.001	5.809	2.286	14.762
	Number of menopausal symptoms	0.006	1.180	1.050	1.326
	Difficulty of swallowing	0.039	0.344	0.125	0.947
	TMJ pain	0.046	0.333	0.113	0.979
MOC	Number of menopausal symptoms	<0.001	1.773	1.403	2.241

MOC: multiple oral complaints

TMJ: temporomandibular joint

OR: odds ratio

Table 3: Associated factors of xerostomia, taste disturbance, burning sensation, and existence of the multiple oral complaints.

4. Discussion

To the best of our knowledge, this is the first survey to evaluate the factors associated with xerostomia, taste disturbance, burning sensation, and MOC in participants who exhibited these symptoms with menopausal symptoms. This study showed that the number of menopausal symptoms was associated with xerostomia, taste disturbance, burning sensation, and MOC. In the menopausal period, a decrease in the level of female hormones and the appearance of vasomotor symptoms, such as hot flushes and night sweats, are common; sometimes with psychosomatic symptoms [13]. Disturbances of the autonomic nervous system may result in a decrease in the secretion of saliva, which is regulated by the autonomic nervous system. Hyposalivation may be the main cause of xerostomia, and estrogen receptors are present in the salivary glands [14]. Although the mechanism is unknown, there is a possibility that estrogen directly influences the secretion of saliva. The taste threshold is influenced by estrogen hormones in pregnancy. Moreover, decreased salivation leads to dysgeusia, because saliva plays an important role in taste [15]. Many studies have reported a relationship between the presence of burning sensation and female hormones [6]. While hyposalivation may cause burning sensation, psychological stress due to menopausal symptoms may lead to xerostomia, taste disturbance (especially phantogeusia) and burning sensation. The PCS is one of the explanatory variables in burning sensation and MOC. Additionally, the three symptoms of oral discomfort complaints were related to each other. Because this study was conducted by a web-based

survey, objective evaluation, such as the volume of saliva, taste threshold, and estrogen level, could not be assessed. This is a limitation of this study. In future investigations, subjective and objective evaluation should be included.

The number of dryness regions was associated with xerostomia, with statistical significance ($P < 0.001$). Dryness syndrome is a concept in which people who feel dryness in certain regions of the body may feel dryness in other regions. Dryness of the eyes may be caused by Meibomian gland dysfunction for dryness of eyes [16], while dryness of the nose may be caused by primary and secondary rhinitis atrophicans, rhinitis atrophicans with fetors (ozena), and empty nose syndrome [17]. The occurrence of dry skin depends on various extrinsic factors including climate; environment; exposure to soaps, detergents, chemicals or medications; genetics; diseases; hormone imbalances; and aging [18]. The vulva and vaginal walls also become pale and thin and lose their elasticity, resulting in decreased vaginal secretions [19]. Furthermore, estrogen receptors are present in the eyes, nose, skin and vagina, which may be related to dryness in these regions.

Nineteen participants (5.1%) had MOC and 7.4% had two of the three symptoms in this study. Toida *et al*. reported that 13.6% of community-dwelling adults had MOC and 10.4% had two of the complaints [20]. In our present report, the analyzed data was limited to female participants, because our aim was to elucidate the relationship between menopausal symptoms and MOC. Further analysis including male data will engender new discussion about the prevalence of MOC. In this study, we recognized three symptoms – xerostomia, taste disturbance, and burning sensation – as constituting MOC. However, univariate analysis showed that TMJ pain and difficulty in swallowing were significantly related to xerostomia, taste disturbance, burning sensation, and MOC. These three complaints include issues related to the perception of the oral mucosa, the mechanism of induced pain of TMJ, and dysphagia. However, these complaints frequently exist in clinical situations. Comprehensive consideration is needed to further elucidate MOC.

Although there is no consensus regarding the relationship of decreased salivary secretions with age, many studies have reported that the prevalence of xerostomia increases with aging [21]. However, we did not find significant differences in salivary secretions with age. One explanation for this finding is that different questionnaires for assessing xerostomia may have been used, such as the Xerostomia Inventory and the Xerostomia Questionnaire. Triggers for the symptom of burning sensation have been listed in a previous study, and include xerostomia, psychological stress, disease, medication, and dental treatment [22], although the rate of these issues differed.

Most participants did not consult a doctor when they experienced xerostomia. Approximately 13% answered "I do not know what department to go to", and 6.9% stated, "I think there is no treatment." In a women's clinic in Japan, the prevalence rate of physician consultations with patients with oral complaints was 58.5% [2]. Lack of knowledge about the department in which xerostomia is treated and the existence of treatment methods for xerostomia is not limited to community-dwelling participants but also to the physicians. Providing the correct information and publicizing the factors associated with MOC may lead to early detection of the symptoms of MOC and

contribute to improvement of the patients' QOL.

There are two limitations in this study. As mentioned above, because this study was conducted using a web-based survey, objective evaluation was not possible. Another limitation is that the participants were limited to internet users. Previous face-to-face surveys reported the prevalence of oral dryness as 38.8% [23]. These rates were similar to the prevalence reported in our web-based survey (39.4%). Although web-based surveys are increasingly used in the medical field, their use remains contentious.

In conclusion, this study showed that menopausal symptoms may be related to MOC, and the symptoms of MOC may be related to each other. While treating xerostomia, taste disturbance, and burning sensation, the related factors should be considered, which could contribute to improvement in the patients' QOL.

Consent for Publication

We have not reported personal data in this manuscript. Consent for publication is therefore not applicable.

Availability of Data and Materials

All data generated or analysed during this study are included in this published article.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

MY, designed this study, analyzed the data, and wrote the first draft of the manuscript. KI, the corresponding author, designed this study, analyzed the data, wrote the draft of the manuscript, and is responsible for the manuscript. KN, KT, MO, SF and MI discussed the design, analyzed the data, and wrote the draft of the manuscript. All authors read and approved the final manuscript.

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References

1. Meurman JH, Tarkkila L, Tiitinen A. The menopause and oral health. Maturitas 63 (2009): 56-62.
2. Matsuki T, Ito K, Funayama S, et al. Questionnaire survey on oral symptoms of menopausal women and cooperation between doctors and dentists. Int J Oral-Med Sci 12 (2013): 21-28.
3. Slebioda Z, Szponar E. Burning mouth syndrome - a common dental problem in perimenopausal women. Przeglad menopauzalny = Menopause review 13 (2014): 198-202.
4. August M. Oral health implications of menopause. Menopause 12 (2005): 123-124.
5. Ben Aryeh H, Gottlieb I, Ish-Shalom S, et al. Oral complaints related to menopause. Maturitas 24 (1996): 185-189.
6. Wardrop RW, Hailes J, Burger H, et al. Oral discomfort at menopause. Oral Surg Oral Med Oral Pathol 67 (1989): 535-540.

7. Ito K, Takamatsu K, Nohno K, et al. Factors associating with mucosal dryness in multiple regions and skin – a web-based study in women. Journal of Obstetrics and Gynaecology Research 43 (2017): 880-886.
8. Partenhauser A, Bernkop-Schnürch A. Mucoadhesive polymers in the treatment of dry X syndrome. Drug Discov Today 21 (2016): 1051-1062.
9. Muraki S, Akune T, Oka H, et al. Health-related quality of life in subjects with low back pain and knee pain in a population-based cohort study of Japanese men: the Research on Osteoarthritis Against Disability study. Spine (Phila Pa 1976) 36 (2011): 1312-1319.
10. Aso T, Uchiyama S, Matsumura Y, et al. A natural S-equol supplement alleviates hot flushes and other menopausal symptoms in equol nonproducing postmenopausal Japanese women. J Womens Health (Larchmt) 21 (2012): 92-100.
11. Kupperman HS, Blatt MH, Wiesbader H, et al. Comparative clinical evaluation of estrogenic preparations by the menopausal and amenorrheal indices. J Clin Endocrinol Metab 13 (1953): 688-703.
12. Sugimoto M, Takegami M, Suzukamo Y, et al. Health-related quality of life in Japanese men with localized prostate cancer: assessment with the SF-8. Int J Urol 15 (2008): 524-528.
13. Augoulea A, Moros M, Lykeridou A, et al. Psychosomatic and vasomotor symptom changes during transition to menopause. Przeglad menopauzalny = Menopause review 18 (2019): 110-115.
14. Välimaa H, Savolainen S, Soukka T, et al. Estrogen receptor-beta is the predominant estrogen receptor subtype in human oral epithelium and salivary glands. J Endocrinol 180 (2004): 55-62.
15. Kaplan MD, Baum BJ. The functions of saliva. Dysphagia 8 (1993): 225-229.
16. Chan T, Chow S, Wan K, et al. Update on the association between dry eye disease and meibomian gland dysfunction. Hong Kong Med 25 (2019): 38-47.
17. Hildenbrand T, Weber R, Brehmer D. Rhinitis sicca, dry nose and atrophic rhinitis: a review of the literature. Eur Arch Otorhinolaryngol 268 (2011): 17-26.
18. Byrne A. Bioengineering and subjective approaches to the clinical evaluation of dry skin. Int J Cosmet Sci 32 (2010): 410-421.
19. Castelo-Branco C, Cancelo MJ, Villero J, et al. Management of post-menopausal vaginal atrophy and atrophic vaginitis. Maturitas 52 (2005): 46-52.
20. Toida M, Nanya Y, Takeda-Kawaguchi T, et al. Oral complaints and stimulated salivary flow rate in 1188 adults. J Oral Pathol Med 39 (2010): 407-419.
21. Nederfors T, Isaksson R, Mornstad H, et al. Prevalence of perceived symptoms of dry mouth in an adult Swedish population--relation to age, sex and pharmacotherapy. Community Dent Oral Epidemiol 25 (1997): 211-216.
22. Kim MJ, Kim J, Kho HS. Comparison between burning mouth syndrome patients with and without psychological problems. Int J Oral Maxillofac Surg 47 (2018): 879-887.

23. Ohara Y, Hirano H, Yoshida H, et al. Ratio and associated factors of dry mouth among community-dwelling elderly Japanese women. Geriatr Gerontol Int 11 (2010): 83-89.