Department of Dentistry

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General Summary

1. Clinical studies of temporomandibular disorders

We continued our studies of screening questionnaires and evaluation of quality of life in patients with temporomandibular disorders (TMDs).

2. Clinical studies of dentistry for medically compromised patients

We continued our studies of the usefulness of diagnostic equipment for medically compromised patients.

3. Clinical studies of obstructive sleep apnea–hypopnea syndrome

We examined the relationship between body–mass index (BMI) and fatty change of the suprahyoid muscles in patients with obstructive sleep apnea (OSA).

4. Basic studies of growth factors in the oral cavity

We investigated the expression patterns of nerve growth factor (NGF) and NGF receptors in human salivary glands and the secretion of NGF in human saliva.

Research Activities

Clinical studies of TMDs

1. Relationship between TMDs and job content in the employed population of the Tokyo metropolis

Purpose: We previously reported the prevalence of TMDs and factors contributing to TMDs in the employed population of the Tokyo metropolis, based on a survey using a TMD screening questionnaire. Significant factors contributing to TMD identified with multivariate logistic regression analysis were a feeling of fatigue (odds ratio [OR] = 1.55) in men and depression (OR = 1.37) and a feeling of fatigue (OR = 1.30) in women. The purpose of this pilot study was to investigate the sex-related differences in the relationship between job contents and TMDs.

Methods: In 2007 and 2009 we performed a questionnaire survey, with the cooperation of the Tokyo Dental Association, of subjects undergoing dental checks at general dental clinics in Tokyo. Responses were obtained from 244 subjects in 2007 and 76 subjects in 2009 and were used as secondary data for the analysis. We considered subjects who gave any answer other than "0" to the question of commuting time to be employed (256 subjects). The questionnaire included 4 TMD-screening items, sex, age, and 9 job-content items, and the responses were analyzed with multivariate logistic regression analysis.

Results: The mean age did not differ between men and women. In regard to sex differences in job contents, men had a significantly longer driving time, and women had a longer time at home before going to bed (Bonferroni correction value: $p = 0.0062$). The personal computer (PC) operation time did not differ between the sexes. Because multi-

variate logistic regression analysis identified sex as a significant factor (OR = 0.417), we examined the sex-related differences in the relationship between TMD and job contents. The PC operation time showed a significant OR (1.94) for TMD only in women.
Conclusion: Sex-related differences were suggested in the relationship between TMD and job contents. PC-related work was identified as a factor contributing to TMD in women.

2. Criterion-related validity of a questionnaire to assess pain-related limitation of daily functions of Japanese patients with TMDs

Purpose: Reliability and validity are required characteristics of a questionnaire. We devised a questionnaire to assess pain-related limitation of daily functions in Japanese patients with TMDs (LDF-TMDQ) and reported its construct validity and reliability in 2005. In addition, we created a TMD-screening questionnaire and reported its validity in 2007. The purpose of this study was to assess the concurrent validity of the LDF-TMDQ.
Methods: This study was performed as a part of a multicenter joint investigation for a pluralistic evaluation and the effect of the pluralistic treatment on patients with TMD. The 752 subjects used which the existing data as a second document with no missing values at the outpatient clinic of The Jikei University Department of Dentistry from October 2005. We used a specimen LDF-TMDQ and the specimen that I examined of the TMD screening questionnaire for statistical analysis. We used the specimen is different from the specimen which statistical examined of LDF-TMDQ and TMD screening questionnaire. The TMD screening questionnaire was used as an external criterion. The concurrent validity was evaluated with Spearman's correlation coefficient.
Results: The TMD screening questionnaire had a sensitivity of 85.9% and a specificity of 78.1%. Spearman's correlation coefficient was 0.624 ($p<0.001$).
Conclusion: These results support the concurrent validity of the LDF-TMDQ.

3. Simple usage of screening test, quality of life assessment, and a treatment procedure for patients with TMDs

Because TMDs are usually diagnosed by exclusion, knowledge of all diseases manifesting as trismus (persistent contraction of the masseter) and as masticatory disorders is required. However, because dentists treat many patients every day, they might overlook 5 important symptoms for differential diagnosis: nervous system deficiency, a history of trauma, and clinical history taking, an oral aperture of less than 20 mm, and pain in the resting position. Because the understanding of the concept of "pain in the resting position" can differ between dentists and patients, the concept must be explained in plain words that the patient can understand. In a medical interview, confirmation of daily and diurnal variation of symptoms, characteristics of pain (act on onset and time of onset), job contents, sleep condition, and exercise contents are important. Furthermore, behavioral methods of correcting malocclussion, dietary counseling, sleep guidance, monitoring PC use time, mouth-opening exercises, and stress-relieving methods were explained. Advice to healthcare providers on pressure-pain exercises using 2.0 kg of finger pressure, stretch and massage methods in daily life, walking methods, and postural guidance are also important.
There is no treatment without a goal, and function improvements, such as attaining a painless oral aperture of 40 mm and chewing gum for 15 minutes, were suggested treat-

ment goals. Physicians must explain to the patient that the disease is not expressed as a final consultation, but self-care.

Study of dentistry for medically compromised patients

1. Clinical analysis of prothrombin time kits CoaguChek®XS and INRatio®2

Purpose: In our department, the CoaguChek®XS system (F. Hoffmann-La Roche, Ltd., Basel, Switzerland) has been used as a preoperative examination of prothrombin time (PT) for patients taking warfarin potassium. Because the CoaguChek®XS reagent is expensive, we examined whether prothrombin might instead be measured with the INRatio®2 system (Alere, Inc., Waltham, MA, USA). The aim of this study was to compare the PT/international normalized ratio (INR) results measured with CoaguChek®XS and INRatio®2 and to examine the relationship between the 2 systems.

Materials and Methods: Fifty-one patients (31 men and 20 women; mean age, 68 ± 13.9 years) were included in this retrospective study. A single finger puncture provided the retrospective data for 2 examinations; that is, the INR was measured with CoaguChek®XS and INRatio®2 at the same time. Although the INRatio®2 data were not normally distributed, the CoaguChek®XS data were normally distributed. For these reasons, statistical analysis involved paired *t*-tests, linear regression analyses, and determinations of effect size and a sample size.

Results: The mean INR values did not differ between the 2 systems. The adjusted R2 of linear regression was 0.818. The effect size determined with the paired *t*-test was 0.130, which is small. The sample size was 324.

Discussion: Our results suggest that significance can be clarified with a larger sample size. In addition, each member of our department reported that INRatio®2 system required a much larger volume of blood and was more complicated to operate than the CoaguChek®XS system. Although both systems have an equal number of medical remuneration points, the INRatio®2 reagent is less expensive than the CoaguChek®XS reagent.

Consideration: This study did not demonstrate clear differences between the CoaguChek®XS and INRatio®2 systems. We finally decided to continue using the CoaguChek®XS system in our department.

Clinical studies of OSA-hypopnea syndrome

1. BMI and fatty change of the suprahyoid muscles

Purpose: A change in muscle function has been postulated to be associated with the etiology of OSA. Saito et al. have previously reported the effect of obesity on the properties of the lingual muscles (genioglossus and geniohyoid muscles to fat in rats. (*Arch Oral Biol* 2010; 55:803-808). However, such a muscle metamorphosis has not been shown in humans. Here, we show evidence of fatty metamorphosis in the lingual muscles in computed tomography (CT) images of patients suspected to have OSA.

Materials and Methods: The subjects were 66 patients (51 men and 15 women) suspected to have OSA who visited the Tsurumi University School of Dental Medicine from November 2007 through October 2011. All subjects gave informed consent to take part in the study. Subjects underwent CT (Radix Prima scanner, Hitachi Medical Co., Tokyo, Japan) evaluations at the image diagnosis department of the hospital. The tube voltage

used was 120 kV, and the tube current was 50 mA. Exposure time was 1 second. Sex, age, BMI, and apnea-hypopnea index (AHI) were recorded for each patient. The degree of fat-to-muscle metamorphosis was measured with CT. Image-analysis software (Aze Win®, AZE, Japan, Tokyo) was used to set the region of interest (ROI) of 30 mm^2 on the bellies of the lingual muscles. We measured CT levels of 4 ROIs (both sides of the central area and both sides of the posterior area) in the genioglossus muscles and 2 sizes of ROI (both sides of the central area) in the geniohyoid muscles. Values were quantified and compared statistically.

Results: The median values (25% and 75% quartile deviations) were patient's age: 50.00 years old (42 and 61 years); BMI: 24.00 kg/m^2 (22.00 and 26.50 kg/m^2); genioglossus CT levels: 121.55 (88.85 and 135.28), and geniohyoid muscle CT levels: 111.95 (104.28 and 116.25). The results of a multiple regression model were analyzed with the Amos (version 6) software package (Amos Development Corporation, Spring House, PA, USA); the standardized estimates of the BMI were -0.53 ($p = 0.000$) for the genioglossus muscle and -0.40 ($p=0.002$) for the geniohyoid muscle.

Conclusion: Consistent with the report of Saito et al, we found evidence of fatty metamorphosis of the lingual muscles of humans with effects of the BMI. We are planning to investigate the effect of fatty changes of the lingual muscles on OSA.

Basic studies of growth factors in oral cavity

1. Distribution of NGF and its receptors in human salivary glands

Purpose: NGF is a pluripotent mediator present in a range of human tissues. The aim of this study was to investigate the expression pattern of NGF and NGF receptors in human salivary glands and the secretion of NGF in human saliva.

Methods: The distribution of NGF-β, proNGF, and their receptors tyrosine kinase receptor A (TrkA) and p75 neurotrophin receptor ($p75^{NTR}$) was examined qualitatively in human parotid ($n = 6$), submandibular ($n = 3$), sublingual ($n = 3$), and minor salivary glands ($n = 6$) with immunohistochemical methods. Western blotting of unstimulated human whole saliva ($n = 6$) with antibodies reactive with mature NGF-β or proNGF was performed to identify NGF forms.

Results: Intercalated, striated, and collecting ducts in all gland types showed strong staining for proNGF and weak staining for NGF-β in the submandibular, sublingual, and minor salivary glands. TrkA was also strongly expressed in the ducts of all gland types, whereas $p75^{NTR}$ expression was confined mainly to collecting ducts. In acini, no or only weak cytoplasmic staining was seen for any of the markers. Western blotting of saliva showed secretion of several forms of proNGF, but no mature NGF-β was detected.

Conclusion: The ligand proNGF and the receptor TrkA might regulate the functions of duct cells, such as the release of signaling molecules, in an autocrine, paracrine, or solinocrine fashion. Secreted into the oral cavity, salivary proNGF can participate in normal wound healing, as it has been shown to increase the proliferation and migration of oral keratinocytes.

Publications

Nishiyama A*[1]*, Kino K*[1]*, Sugisaki M, Tsukagoshi K*[1] *([1]Tokyo Med Dent Univ). A survey of influence of work environment on temporomandibular disorders-related symptoms in Japan. *Head Face Med.* 2012; **8:** 24.

Naesse EP*[1]*, Schreurs O*[1]*, Messelt E*[1]*, Hayashi K, Schenck K*[1] *([1]Univ Oslo). Distribution of nerve growth factor, pro-nerve growth factor, and their receptors in human salivary glands. *Eur J Oral Sci.* 2013; **121:** 13-20.