Table 3 Blood status between antibody-detected and non-detected female subjects

	Antibody non-detected group (n = 13)	Antibody detected group (104)	*P*-vale
Leukocyte (x 10^3/μl)	5.9 ± 1.3	5.8 ± 1.4	0.925
Erythrocyte (x 10^6/μl)	4.2 ± 0.3	4.0 ± 0.4	0.149
Hemoglobin (g/ dl)	12.6 ± 1.1	12.3 ± 1.4	0.253
Hematocrit (%)	39.2 ± 3.2	38.0 ± 3.9	0.205
Platelet (x 10^4/μl)	21.1 ± 5.7	21.1 ± 5.4	0.983
MCV (fl)	93.8 ± 3.7	94.4 ± 4.0	0.698
MCM (pg)	30.2 ± 1.4	30.4 ± 2.6	0.690
MCHC (%)	32.2 ± 0.7	32.4 ± 2.6	0.979
Eosinophil (%)	4.0 ± 2.0	2.5 ± 1.8	0.003*
Basophil (%)	0.8 ± 0.3	0.5 ± 0.3	0.001*
Lymphocyte (%)	33.7 ± 6.9	36.9 ± 6.9	0.214
Monocyte (%)	5.6 ± 1.0	5.6 ± 1.4	0.968
Neutrophil (%)	56.0 ± 8.2	54.5 ± 6.6	0.557

*: Significant difference demonstrated by ANOVA

Table 4 Correlation among PPA level, oral bacteria status, basophil, eosinophil and periodontal status in female

	Correlation	*P* - value
Antibody vs LB	0.297	0.0015*
Antibody vs tS	0.193	0.0433*
Antibody vs MS	0.044	0.6484
tS vs LB	0.328	0.0004*
tS vs MS	0.423	<0.0001*
LB vs MS	0.227	0.0170*
Antibody vs Eosinophil	-0.119	0.2160
Antibody vs Basophil	-0.195	0.0340*
Eosinophil vs Basophil	0.272	0.0029*
AL vs Eosinophil	0.192	0.0439*
BOP vs Eosinophil	0.189	0.0475*
rAL6 vs Eosinophil	0.227	0.0168*

*: Significant differences demonstrated by Correlation Fisher's Test

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「地域住民の口腔保健と全身的な健康状態の関係についての総合研究」

C. 研究協力課題：

「高齢者における慢性的脱水症状と唾液性状との関連について」

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E. 研究目的：

高齢者における慢性的な脱水症は高齢者のQOLに大きく関わっている。また、脱水症状と唾液性状の関連についてはいくつか報告されているが、高齢者における慢性的な脱水状態との関連をみた報告はない。本研究では、高齢者における慢性的脱水症状と唾液性状との関連について調査することを目的としている。

F. 研究方法：

76歳高齢者403名を対象に、血清尿酸値、血清クレアチニン値、血清ナトリウム値、血清カリウム値、血清尿窒素値、刺激唾液流量、唾液牽糸性を測定した。慢性的な脱水症状を示す血清中尿酸値（≥7mg/dl または<7mg/dl）と唾液の流量および牽糸性(糸引き度)との関連を評価した。

G. 研究結果および考察：

牽糸性は、ロジスティック回帰分析により、性別、現在歯数、喫煙経験、刺激唾液流量を調整した後も血清尿酸値と有意な関連（Odds比：2.06、p=0.04）が認められた。また、牽糸性および血清尿酸値は、腎臓機能を示す血清中クレアチニン、尿窒素、ナトリウム、カリウムとと性別で調整した後も有意な関連が認められた。

さらに，本調査では，刺激唾液の牽糸性が、慢性脱水症状を示すマーカーと関連が認められ、さらに腎機能との関連も示された。脱水症状は高齢者に多いここが知られ

ており、全身状態が唾液性状に現れることを示唆している。

H. 研究発表論文：

なし

The relationship between chronic dehydration and saliva conditions in an elderly Japanese population

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Short title: Chronic dehydration and saliva conditions

Key words: Chronic dehydration, Saliva condition, Elderly

ABSTRACT

Increases in levels of serum uric acid and several minerals are related to dehydration. Dry mouth is common in the elderly population. This study aimed to identify whether saliva flow rate and salivary spinnbarkeit are sensitive to body hydration markers in a community-dwelling elderly population. A total of 403 subjects aged 76 years participated in the study. Levels of stimulated whole saliva over 3 minutes and spinnbarkeit of saliva were measured. In addition, determinations of serum levels of uric acid, blood urea nitrogen, creatinine, sodium, and potassium were made. The number of teeth and salivary spinnbarkeit (OR=2.06, p=0.04) were significantly associated with the concentration of uric acid according to multiple logistic regression analysis (Pseudo R^2=0.19). In addition, after adjusting for gender by multiple regression analysis, the uric acid concentration and the salivary spinnbarkeit was significantly associated with blood urea nitrogen, potassium, and creatinine levels. Subjects with high uric acid levels had the most elastic saliva. Both serum blood urea nitrogen concentration and serum creatinine concentrations are the most commonly used indicators of renal function. This study suggests that there is a significant relationship between serum uric acid concentration and salivary spinnbarkeit level.

Key words: Chronic dehydration, Saliva condition, Elderly

Dehydration in older adults has been shown to be a reliable predictor of increasing frailty, progressive deterioration in cognitive function, and an overall reduction in quality of life (1). It is also important to understand that increases in concentrations of plasma protein, serum uric acid, and some minerals are related to dehydration (2, 3).

Uric acid is the final oxidation product of purine metabolism in the human body (4). It is produced either by accelerated generation of uric acid through purine metabolism or by impaired excretion in the kidney (5). Gout in humans is associated with abnormal levels of uric acid in the body. Unlike urea and ammonia, uric acid can be excreted as a dry solid (2). It is therefore commonly found in the excretions of animals that live in dry environments (6).

Saliva is essential for the maintenance of oral health. The primary constituent of saliva is water and, traditionally, decreased body water homeostasis has been linked to salivary dysfunction. Dry mouth is common in the elderly population, and makes eating more difficult and increases the cariogenic potential of food (7). Salivary diminution is a known major risk factor for caries among people of any age (8).

Much of the data on the relationship between hydration status and salivary

flow are derived from early physiological experiments. For instance, dehydration induced by a 24-hour period without food and water was shown to reduce parotid saliva flow rate. This evidence suggests that there is a relationship between whole body hydration status and saliva flow rate (9). However, another report showed that metabolic indicators of hydration status are not accurate predictors of parotid salivation (10). Findings of a relationship between saliva and dental disease, and between saliva and dehydration have been observed, but the precise nature of these relationships is unclear and no evidence of a direct link has been found (11). In particular, no study reports a relationship between chronic dehydration and saliva conditions in community-dwelling older adults.

Accordingly, this study was carried out to identify whether saliva flow rate and salivary spinnbarkeit measurements are sensitive to body hydration markers such as uric acid in a community-dwelling elderly Japanese population.

MATERIALS AND METHODS

Subjects

Using a registry of residents in Niigata City in Japan, questionnaires were sent to all 4,542 inhabitants born in 1927, and subjects were informed of the purpose of the survey. The response rate was 81.4% (n=3,695). After dividing respondents by gender, 600 people (the screened population) were randomly selected to have approximately the same number of men and women for the study. Subjects agreed to undergo medical and dental examinations, and all participants signed informed consent forms regarding the protocol. The protocol was reviewed and approved by the Ethics Committee of the Faculty of Dentistry, Niigata University.

Among the screened population, 422 subjects aged 76 year participated in the study. The subjects were examined at local community centers in Niigata City.

Stimulated whole saliva was collected. Subjects chewed a 1-g piece of paraffin wax for 1 minute, and after swallowing once, they expectorated secreted saliva into a test tube. Collection time was 3 minutes and flow rate was calculated. After stimulated whole saliva was collected, salivary spinnbarkeit was immediately measured using the Neva Meter (IMI-001 Ishikawa Ironworks Co. Ltd., Japan). The

Neva Meter has been shown to be able to measure spinnbarkeit of saliva objectively with acceptable reproducibility (12). The meter is based on the principle that electrical resistance becomes infinity at the breaking point of the spinnbarkeit. After a saliva sample is introduced to the bottom reservoir of the device, it is automatically stretched at a constant rate of 5 mm/s. Next, application of an electrical current (5 V) to the liquid induces a microcurrent, which stops at the moment the thread breaks. The device detects the point at which the current stops and then measures the maximum length (in millimeters) of the thread, that is, the spinnbarkeit. Measurements were taken 5 times consecutively and spinnbarkeit was calculated by averaging 3 of 5 values, excluding the highest and lowest readings.

Blood measurements

Determinations of serum concentrations of uric acid were used as a marker of dehydration. Dehydration was defined as uric acid ≥7 mg/dl. In addition, serum concentrations of blood urea nitrogen, creatinine, sodium, and potassium as measures of kidney function were measured at a commercial laboratory (BML, Inc, Japan).

We also measured the number of remaining teeth. A personal interview was performed to obtain the bulk of information regarding sensation of dry mouth

(no, sometimes, always) and smoking habits (no, past, or current).

Data interpretation

A total of 403 subjects were included in our analysis after 19 subjects who did not complete the interview were excluded. Using analysis of variance, we compared smoking habits, the number of remaining teeth, stimulated salivary flow rate (ml/3 min), and salivary spinnbarkeit (cm) according to the sensation of dry mouth (no, sometimes, and always). We compared the salivary spinnbarkeit and stimulated salivary flow rate among those with high (≥7mg/dl) and low (<7mg/dl) uric acid concentrations using the student's *t*-test with two-sided *p*-values. We used multiple logistic regression analysis to evaluate the relationship between uric acid concentration and saliva condition. The concentration of serum uric acid (0: <7mg/dl, 1: ≥7mg/dl) was selected as the dependent variable. Five variables (gender [1: male, 2: female], the number of remaining teeth, smoking habit [0: no, 1: past or current], salivary spinnbarkeit, and stimulated salivary flow rate) were used as independent variables in the model. Finally, multiple linear regression analysis was performed to evaluate the relationship between the salivary and dehydration markers (stimulated saliva flow rate, salivary spinnbarkeit, serum uric acid concentration) and kidney function markers (blood urea nitrogen, serum

concentrations of sodium, potassium, and creatinine). Each salivary or dehydration marker was used as a dependent variable. The kidney function markers as well as gender were used as independent variables.

A p value <0.05 was considered statistically significant.

RESULTS

Table 1 shows the relationship between gender, smoking habits, the number of remaining teeth, and saliva characteristics of subjects according to the sensation of dry mouth. There were significant differences in stimulated salivary flow rate (p=0.04) among subjects who reported a dry mouth (never, sometimes, and always) by analysis of variance. The values were lowest in subjects who reported they always had the sensation of a dry mouth.

In addition, we evaluated the difference in the salivary spinnbarkeit or stimulated salivary flow rate between those with high (≥7mg/dl) and low (<7mg/dl) uric acid concentrations. The salivary spinnbarkeit was higher and stimulated salivary flow rate was lower in the subjects with uric acid levels ≥7 mg/dl (figure 1). In particular, the salivary spinnbarkeit was significantly lower for those with uric acid levels <7mg/dl (1.9 [SD: 0.37] cm) compared with those with uric acid levels ≥7 mg/dl (2.11 [SD: 0.62] cm; p = 0.004).

The results of multiple logistic regression analysis are presented in table 2. Gender (odds ratio [OR]=0.03; p=0.002) and salivary spinnbarkeit (OR=2.06; p=0.04) were significantly associated with the concentration of uric acid (Pseudo R^2=0.19; p<0.001).

As shown in table 3, after adjusting for gender, the salivary spinnbarkeit was significantly associated with serum concentrations of blood urea nitrogen (Std. Coef.=0.15, p=0.002), potassium (Std. Coef.=0.12, p=0.01), and creatinine (Std. Coef.=0.29, p<0.001). In addition, the uric acid concentration was significantly associated with serum concentrations of blood urea nitrogen (Std. Coef.=0.26, p<0.001), sodium (Std. Coef.=0.11, p=0.02), potassium (Std. Coef.=0.20, p<0.001), and creatinine (Std. Coef.=0.29, p<0.001).

DISCUSSION

To our knowledge, this is the first study to clarify the relationship between salivary conditions and body hydration.

In this study, serum uric acid concentrations, used as a marker of dehydration, were significantly associated with salivary spinnbarkeit. Subjects with high uric acid concentrations showed highly elastic saliva. In addition, both the serum uric acid concentration and salivary spinnbarkeit were significantly associated with serum blood urea nitrogen, serum potassium, and serum creatinine concentrations.

Serum blood urea nitrogen and serum creatinine concentrations are the most commonly used indicators of renal function. A rise in blood creatinine levels is observed with marked damage to functioning nephrons (13). Furthermore, the most common cause of an elevated blood urea nitrogen concentration is due to a temporary condition such as dehydration or malnutrition (14, 15). Therefore, our findings might demonstrate that older adults who are dehydrated showed highly elastic saliva, which was associated with renal function.

Spinnbarkeit is the thread-forming capacity of mucus under the influence of large-amplitude elastic deformation and it gives information about the internal cohesion forces of the mucus (16). Factors that control mucus spinnbarkeit are the

concentration of mucous glycoproteins, the degree of intermolecular and intramolecular cross-linkings, and the hydration of mucus (17-19). According to another report, the salivary spinnbarkeit was classified as either >2.00 mm (high) or ≤2.00 mm (normal) based on subject's distribution (20). In this report, subjects with uric acid concentrations ≥7 mg/dl showed salivary spinnbarkeit >2.00 cm. Our study indicates that the difference in serum uric acid levels shown between subjects with uric acid levels ≥7mg/dl and those with uric acid levels <7mg/dl might have a meaningful influence on salivary spinnbarkeit.

In terms of the relationship between serum uric acid concentration and salivary spinnbarkeit, an increase in saliva total protein concentration and osmolality during dehydration has been seen to occur (21). The changes in saliva total protein concentration that are related to salivary spinnbarkeit appear to be more sensitive to changes in whole body hydration status (21). However we could not obtain more information from the present study on whether chronic renal failure influenced the concentration of mucous glycoproteins. Further studies are needed to confirm this possibility.

On the other hand, there was no significant relationship between serum uric acid concentration and stimulated salivary flow rate. However, subjects with the

subjective sensation of dry mouth showed a significantly lower salivary flow rate than subjects without this sensation. Even if the evidence suggests that there is a relationship between whole body hydration status and saliva flow rate (9), there might be no relationship between chronic dehydration and saliva flow rate, especially in community-dwelling older adults.

One limitation of this study was that we investigated stimulated saliva as opposed to unstimulated saliva. Unstimulated salivary flow is a measure of the amount of saliva that is constantly secreted in the oral cavity, whereas stimulated salivary flow is a measure of the functional capacity of the gland. Resting salivary flow rate also may be measured in addressing the research question (22).

In conclusion, this study suggests that there is a significant relationship between serum uric acid concentration and salivary spinnbarkeit level.

REFERENCES

1. Warren JL, Bacon WE, Harris T, et al. The burden and outcomes associated with dehydration among US elderly. Am J Pub Health 1994;84:1265-69.

2. Teach SJ, Yates EW, Feld LG. Laboratory predictors of fluid deficit in acutely dehydrated children. Clin Pediatr 1997;36:395-400.

3. Popowski LA, Oppliger RA, Lambert GP, et al. Blood and urinary measures of hydration status during progressive acute dehydration. Med Sci Sports Exerc 2001;33:747-53.

4. Masseoud D, Rott K, Liu-Bryan R, et al. Overview of hyperuricaemia and gout. Curr Pharm Des 2005;11:4117-24.

5. Capasso G, Jaeger P, Robertson WG, et al. Uric acid and the kidney: urate transport, stone disease and progressive renal failure. Curr Pharm Des 2005;11:4153-9.

6. Arad Z, Marder J, Eylath U. Serum electrolyte and enzyme responses to heat stress and dehydration in the fowl (Gallus domesticus). Com Biochem Physiol 1983;74:449-53.

7. Dormenval V, Budtz-Jorgensen E, Mojon P, et al. Nutrition, general health status and oral health status in hospitalized elders. Gerodontology 1995;12:73-80.

8. Harris NO, Garcia-Godoy F. Primary Preventive Dentistry, 6th ed. New Jersey: Pearson Prentice Hall, 2004:341-342.

9. Ship JA, Fischer DJ. The relationship between dehydration and parotid salivary gland function in young and older healthy adults. J Gerontol 1997;52A:M310-M319.

10. Ship JA, Fischer DJ. Metabolic indicators of hydration status in the prediction of parotid salivary gland function. Arch Oral Biol 1999;44:343-50.

11. Smith AJ, Shaw L. Mild dehydration: a risk factor for dental disease? Eur J Clin Nutr 2003;57:575-80.

12. Gohara K, Ansai T, Koseki T, et al. A new automatic device for measuring the spinnbarkeit of saliva: the Neva Meter. J Dent 2004;32:335-8.

13. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol 2005;16:3365-70.

14. Lavizzo-Mourey R, Johnson J, Stolley P. Risk factors for dehydration among elderly nursing home residents. J Am Geriatr Soc 1988;36:213-8.

15. Islam S, Abely M, Alam NH, et al. Water and electrolyte salvage in an animal model of dehydration and malnutrition. J Pediatr Gastroenterol Nutr