IOPscience iopscience.iop.org

Home Search Collections Journals About Contact us My IOPscience

Relationship between volatile sulfur compounds in mouth air and systemic disease

This article has been downloaded from IOPscience. Please scroll down to see the full text article.

2008 J. Breath Res. 2 017012

(http://iopscience.iop.org/1752-7163/2/1/017012)

View the table of contents for this issue, or go to the journal homepage for more

Download details:
IP Address: 147.96.1.236
The article was downloaded on 02/11/2012 at 11:47

Please note that terms and conditions apply.

J. Breath Res. **2** (2008) 017012 (4pp) doi:10.1088/1752-7155/2/1/017012

Relationship between volatile sulfur compounds in mouth air and systemic disease

Shuji Awano[1], Toshihiro Ansai[1], Yutaka Takata[2], Inho Soh[1], Akihiro Yoshida[1], Tomoko Hamasaki[1], Shuntaro Kagiyama[2], Ikuo Nakamichi[2], Kazuo Sonoki[2] and Tadamichi Takehara[1]

[1] Division of Community Oral Health Science, Department of Health Promotion, Kyushu Dental College, 2-6-1 Manazuru, Kokurakita-ku, Kitakyushu 803-8580, Japan
[2] Division of General Internal Medicine, Department of Health Promotion, Kyushu Dental College, 2-6-1 Manazuru, Kokurakita-ku, Kitakyushu 803-8580, Japan

E-mail: awa-shu@kyu-dent.ac.jp

Received 28 October 2007
Accepted for publication 13 February 2008
Published 7 March 2008
Online at stacks.iop.org/JBR/2/017012

Abstract
This study examined the relationship between volatile sulfur compounds (VSCs), including hydrogen sulphide (H_2S), methyl mercaptan (CH_3SH) and dimethyl sulphide [$(CH_3)_2S$], in mouth air of patients and a history of systemic disease. The subjects were 387 residents (174 males and 213 females) of Fukuoka Prefecture, Japan, who participated in an oral and systemic health survey for elderly persons (mean age: 61.8, s.d. 2.8 years). The VSCs were measured using a portable gas chromatograph (OralChroma). The H_2S concentrations were significantly greater in the 132 subjects with a history of hypertension and the 41 subjects with a history of respiratory disease, including pneumonia, pulmonary emphysema and bronchitis, than in those without such a history. The CH_3SH concentrations were significantly greater in those with a history of hypertension. The 16 subjects with a history of cerebrovascular disease, including intracerebral haemorrhage, cerebral infarction, and subarachnoid haemorrhage, and the 58 subjects with a history of liver disease, including hepatitis, alcoholic liver disease, drug-induced liver injury, fatty liver and liver cirrhosis, showed significantly greater $(CH_3)_2S$ concentrations ($p < 0.05$). These results suggest an association between the production of VSCs in mouth air and systemic diseases such as hypertension as well as respiratory, cerebrovascular and liver diseases.

1. Introduction

Halitosis is a common phenomenon which often affects the quality of life (Bosy 1997, Needleman *et al* 2004). Halitosis can be classified according to its site of origin (Delanghe *et al* 1997, Tangerman 2002, Van den Velde *et al* 2007). Halitosis of oral origin is quite well understood. Extra-oral halitosis can originate from the upper respiratory tract and from other sources that are carried by blood and exhaled in the lung (Delanghe *et al* 1997, Tangerman and Winkel 2007). In blood-borne halitosis, malodorous compounds in the bloodstream are carried to the lungs, where they volatilize and enter the breath. Potential sources of blood-borne halitosis include some systemic diseases, metabolic disorders, medication and certain foods (Mitchell 2005, Tangerman *et al* 1994, Tangerman 2002).

The main components of human oral malodour are hydrogen sulphide (H_2S), methyl mercaptan (CH_3SH) and dimethyl sulphide [$(CH_3)_2S$], which are categorized as volatile sulfur compounds (VSCs) (Tonzetich 1977). Of these, H_2S and CH_3SH are generally regarded as originating from microbial putrefaction within the oral cavity (Schmidt *et al* 1978, Tangerman and Winkel 2007). In addition, $(CH_3)_2S$ detected in mouth air is thought to originate mainly from the lung and to be related to systemic diseases, although the evidence of a relationship between the $(CH_3)_2S$ level and

 © 2008 IOP Publishing Ltd Printed in the UK

systemic disease is insufficient (Tangerman and Winkel 2007). Moreover, endogenous H_2S is produced in significant amounts in most tissues (Lowicka and Beltowski 2007). The highest rate of production is in the brain, cardiovascular system, liver and kidney. Although H_2S is thought to be associated with several diseases, including hypertension, atherosclerosis and inflammation, further studies are needed to confirm these relationships, and it is unclear whether the endogenous H_2S influences its level in mouth air (Lowicka and Beltowski 2007).

This study examined the relationship between the VSCs in mouth air and a history of systemic disease to determine whether differences in the levels of VSCs in mouth air are related to systemic diseases.

2. Subjects and methods

2.1. Subjects

The subjects were 387 residents (174 males and 213 females) of Fukuoka Prefecture, Japan, who participated in an oral and systemic health survey for elderly persons (mean age ± standard deviation: 61.8 ± 2.8 years). Residents who were 60 or 65 years old and lived in one of four districts were invited to participate in the survey.

The survey was conducted according to the principles expressed in the Helsinki Declaration and was approved by the Human Investigations Committee of Kyushu Dental College. The details of the study protocol were explained to all subjects, and written informed consent was obtained before participation.

2.2. Survey

In the survey, which was performed in 2005, a standardized oral examination was performed. All subjects completed a questionnaire regarding lifestyle and oral and systemic health.

As part of the oral examination, probing depths ⩾4 mm (PD) and bleeding on probing (BOP) were recorded for mesial and distal labial/buccal sites of all teeth, and tongue coating was evaluated as follows: 0, no coating apparent; 1, less than 1/3 of the tongue dorsum area coated; 2, between 1/3 and 2/3 of the surface coated; 3, more than 2/3 of the surface coated. The VSCs [H_2S, CH_3SH and $(CH_3)_2S$] were measured using a portable gas chromatograph (OralChroma: ABILITS, Japan) which was calibrated with standard VSCs, prepared by a permeater (GASTEC, Ayase, Japan) and analytical-grade permeation tube, as previously described (Murata *et al* 2006). Briefly, subjects were instructed to keep their mouths closed and to breathe through the nose for 30 s before the analysis. A 1 mL disposable syringe was inserted into the oral cavity through the lips and teeth, and 1 mL oral air was aspirated by the syringe. Immediately, 0.5 mL oral air from the sample was injected into the portable gas chromatograph.

In the questionnaire, all subjects were questioned about any history of systemic diseases, including sinusitis, adenoid, high lipoprotein serum, tumour, cerebrovascular disease, hypertension, diabetes, heart failure, allergy, respiratory disease and hepatic failure.

Table 1. Oral characteristics of the subjects [mean ± standard deviation (SD)].

Parameters	All $N = 387$	Male $N = 174$	Female $N = 213$
Number of teeth (tooth)	25.8 ± 6.4	26.3 ± 5.9	25.3 ± 6.7
Number of PD (site)	3.5 ± 5.9	4.2 ± 6.2*	2.9 ± 5.5
Number of BOP (site)	2.8 ± 3.8	3.1 ± 3.8	2.6 ± 3.8
H_2S (ng/10 mL)	4.6 ± 7.0	4.6 ± 6.7	4.7 ± 7.2
CH_3SH (ng/10 mL)	3.0 ± 6.1	2.8 ± 5.2	3.2 ± 6.7
$(CH_3)_2S$ (ng/10 mL)	0.8 ± 3.8	0.6 ± 1.8	0.9 ± 4.8
Tongue coat score (0–3)	0.7 ± 0.9	0.8 ± 0.9*	0.6 ± 0.9

N: number of subjects; PD: periodontal pockets of ⩾4 mm; BOP: bleeding on probing; H_2S: concentration of hydrogen sulphide in mouth air; CH_3SH: concentration of methyl mercaptan in mouth air; $(CH_3)_2S$: concentration of dimethyl sulphide.
* $p < 0.05$, unpaired *t*-test (versus females).

2.3. Statistical analyses

The oral characteristics of males and females, and the concentrations (mean and SD) of VSCs [H_2S, CH_3SH and $(CH_3)_2S$] in mouth air were compared between pairs of groups categorized according to differences in the history of systemic diseases, using unpaired *t*-tests. In addition, halitosis-related parameters between groups categorized according to a history of hepatic failure, respiratory disease, hypertension or cerebrovascular disease were compared using unpaired *t*-tests. The data were analysed using SPSS ver. 11 for Windows (SPSS, Chicago, IL, USA).

3. Results

The oral characteristics of the subjects are summarized in table 1. There were significant differences (unpaired *t*-test; $p < 0.05$) in the PD and tongue coat score between male and female subjects.

The concentrations (mean ± SD) of H_2S, CH_3SH and $(CH_3)_2S$ in mouth air were compared between groups categorized according to differences in the history of systemic diseases (table 2). The percentages of subjects with a history of sinusitis, adenoid, high lipoprotein serum, tumour, cerebrovascular disease, hypertension, diabetes, heart failure, allergy, respiratory disease and liver disease versus total subjects were 6.2, 6.7, 18.0, 5.4, 4.1, 34.1, 10.0, 14.7, 20.6, 10.5 and 14.9%, respectively. The H_2S concentration was significantly ($p < 0.05$) greater in subjects with a history of hypertension or respiratory disease such as pneumonia, pulmonary emphysema and bronchitis than in those without such a history, and the CH_3SH concentration was significantly ($p < 0.01$) greater in subjects with a history of hypertension. The $(CH_3)_2S$ concentration was significantly greater in subjects with a history of cerebrovascular disease, such as intracerebral haemorrhage, cerebral infarction and subarachnoid haemorrhage, and in those with a history of hepatic failure, such as hepatitis, alcoholic liver disease, drug-induced liver injury, fatty liver and liver cirrhosis ($p < 0.001$ and $p < 0.05$, respectively).

Halitosis-related parameters were compared between groups categorized according to a history of hepatic failure, respiratory disease, hypertension or cerebrovascular disease;

Table 2. Comparisons of concentration (mean and SD) of VSCs [H_2S, CH_3SH and $(CH_3)_2S$] in mouth air between two groups categorized according to differences in systemic disease history.

Systemic diseases	(no. of subjects)	H_2S	CH_3SH	$(CH_3)_2S$
Sinusitis	−(363)	4.61 ± 6.87	3.02 ± 6.19	0.78 ± 3.92
	+(24)	6.38 ± 8.91	3.06 ± 5.17	0.38 ± 0.56
Adenoid	−(361)	4.72 ± 7.00	3.13 ± 6.30	0.79 ± 3.92
	+(26)	4.77 ± 7.31	1.55 ± 2.17	0.28 ± 0.72
High lipoprotein serum	−(317)	4.57 ± 6.97	2.93 ± 5.91	0.77 ± 4.05
	+(70)	5.40 ± 7.19	3.43 ± 7.03	0.74 ± 2.46
Tumour	−(366)	4.76 ± 6.99	3.07 ± 6.22	0.78 ± 3.90
	+(21)	4.09 ± 7.60	2.17 ± 4.28	0.51 ± 1.23
Cerebrovascular diseases	−(371)	4.66 ± 6.93	2.90 ± 5.65	0.57 ± 1.49
	+(16)	5.06 ± 8.56	5.27 ± 12.82	4.84 ± 17.16***
Hypertension	−(255)	4.08 ± 6.27	2.38 ± 4.93	0.52 ± 1.50
	+(132)	5.82 ± 8.08*	4.19 ± 7.75*	1.20 ± 6.11
Diabetes	−(348)	4.68 ± 6.90	2.97 ± 6.00	0.78 ± 3.96
	+(39)	4.64 ± 7.77	3.27 ± 6.96	0.47 ± 1.20
Heart failure	−(330)	4.64 ± 6.98	2.81 ± 5.65	0.69 ± 3.89
	+(57)	4.89 ± 7.03	4.04 ± 8.17	1.10 ± 3.10
Allergy	−(307)	4.98 ± 7.28	3.10 ± 6.13	0.77 ± 4.17
	+(80)	3.50 ± 5.57	2.60 ± 6.00	0.70 ± 1.56
Respiratory diseases	−(346)	4.38 ± 6.75	2.91 ± 6.17	0.76 ± 3.97
	+(41)	7.22 ± 8.37*	3.73 ± 5.43	0.66 ± 1.35
Hepatic failures	−(329)	4.66 ± 6.98	2.88 ± 5.62	0.59 ± 1.57
	+(58)	4.78 ± 7.03	3.65 ± 8.31	1.66 ± 9.03*

Systemic diseases: a history of systemic diseases.
*$p < 0.05$ and ***$p < 0.001$, all unpaired *t*-test (versus subjects with no history).

Table 3. Comparisons of halitosis-related parameters (mean ± SD) between groups categorized according to a history of hepatic failures, respiratory diseases, hypertension or cerebrovascular diseases that had significantly different concentrations of VSCs.

Systemic disease	(no of subjects)	Teeth	PD	BOP	Tongue coat
Hepatic failures	−(334)	25.7 ± 6.4	3.5 ± 5.7	2.8 ± 3.8	0.7 ± 0.9
	+(59)	26.0 ± 6.2	3.5 ± 6.6	2.6 ± 3.6	0.7 ± 0.9
Respiratory diseases	−(352)	25.8 ± 6.5	3.7 ± 6.1	2.8 ± 3.8	0.7 ± 0.9
	+(41)	26.8 ± 5.1	1.9 ± 2.7	3.2 ± 3.5	0.8 ± 0.9
Hypertension	−(256)	25.8 ± 6.1	3.1 ± 5.6	2.6 ± 3.6	0.7 ± 0.9
	+(137)	25.6 ± 6.8	4.2 ± 6.3	3.2 ± 4.1	0.7 ± 0.9
Cerebrovascular diseases	−(376)	25.9 ± 6.2	3.4 ± 5.7	2.8 ± 3.7	0.7 ± 0.9
	+(16)	23.0 ± 7.1	5.2 ± 7.5	4.1 ± 4.6	0.5 ± 0.7

Systemic diseases: a history of systemic diseases. Teeth: number of teeth. PD: number of periodontal pockets $\geqslant$ 4 mm. BOP: number of bleeding on probing.

these groups had significantly different concentrations of VSCs (table 3). There were no significant differences in number of teeth, PD, BOP and tongue coat score, between any pairs of groups categorized based on disease history (unpaired *t*-tests).

4. Discussion

This study employed a novel portable gas chromatograph for the measurements of concentrations of VSCs in the mouth. A recent study has demonstrated that this portable gas chromatograph can measure the concentrations of H_2S, CH_3SH and $(CH_3)_2S$ in mouth air as well as a gas chromatography system equipped with a flame photometric detector (FPD), which is standard laboratory equipment for the analysis of VSCs, and can be used for the diagnosis of halitosis (Murata *et al* 2006). We also confirmed strong correlations between concentrations of VSCs determined using these two gas chromatography methods in the preliminary examinations of this study (data not shown). Furthermore, the portable gas chromatograph uses metal oxide sensors which can drift and change their sensitivity with use, while the quality of the sensors has been guaranteed for two years according to the instruction manual. In this study, the response reproducibility for the detection of VSCs on multiple uses was preliminarily confirmed using each standard gas.

Recently, H_2S has been proposed as a third gaseous mediator to regulate blood pressure in mammals, in addition to nitric oxide and carbon monoxide, which are well-known neurotransmitters involved in regulating blood pressure, vascular tone and inflammation (Lowicka and Beltowski 2007). However, there are no reports on the relationship between H_2S/CH_3SH in mouth air and hypertension or between H_2S and respiratory disease. This study is the first to suggest these relationships. Furthermore, a recent study has reported that periodontitis may be associated with

hypertension (Holmulund *et al* 2006). It is evident that H_2S and CH_3SH in mouth air are produced by oral bacteria and influenced by oral parameters such as periodontal health, tongue coating and saliva. Therefore, the difference in periodontal health of subjects may influence the relationship between H_2S and CH_3SH in mouth air and hypertension. However, in this study, there were no significant differences in halitosis-related parameters including periodontal healthy status such as number of PD and BOP between subjects with and without a history of hypertension. Moreover, there were no significant differences between subjects with and without a history of other diseases. This suggests that differences in periodontal health and the amount of tongue coating may not influence the VSCs regarding the history of systemic disease.

Several studies have reported a relationship between $(CH_3)_2S$ in breath air and hepatic failure such as that in liver cirrhosis (Tangerman *et al* 1994, Tangerman 2002). We also found that an increase of the $(CH_3)_2S$ level in mouth air was related to a history of hepatic failure. In addition, cerebrovascular disease might be linked to the enhancement of $(CH_3)_2S$ in mouth air, although a relationship between $(CH_3)_2S$ and cerebrovascular diseases has not been reported. It might be that $(CH_3)_2S$, like H_2S, is involved in regulating vascular tone.

5. Conclusion

This study demonstrates that VSCs in mouth air are related to a history of systemic disease such as hypertension as well as respiratory, cerebrovascular and hepatic diseases, suggesting that VSC levels are influenced by endogenous gases produced during systemic disease.

Acknowledgments

This research was supported by Kyushu Dental College and by Grants-in-Aid (B) 17390566 (TT) from the Ministry of Education, Culture, Sports, and Technology of Japan. The authors are grateful to Mr Morita (ABILITS and University of Niigata) for supplying the OralChroma used to measure the VSCs in mouth air.

References

Bosy A 1997 Oral malodor: philosophical and practical aspects *J. Can. Dent. Assoc.* **63** 196–201

Delanghe G, Ghyselen J, van Steenberghe D and Feenstra L 1997 Multidisciplinary breath-odour clinic *Lancet* **350** 187

Holmulund A, Holm G and Lind L 2006 Severity of periodontal diseases and number of remaining teeth are related to the prevalence of myocardial infarcion and hypertension in a study based on 4,254 subjects *J. Periodontol.* **77** 1173–8

Lowicka E and Beltowski J 2007 Hydrogen sulfide (H_2S)—the third gas of interest for pharmacologists *Pharmacol. Rep.* **59** 4–24

Mitchell S 2005 Trimethylaminuria (fish-odour syndrome) and oral malodour *Oral. Dis.* **11** (Suppl. 1) 10–13

Murata T, Rahardjo A, Fujiyama Y, Yamaga T, Hanada M, Yaegaki K and Miyazaki H 2006 Development of a compact and simple gas chromatography for oral malodor measurement *J. Periodontol.* **77** 1142–7

Needleman I, McGrath C, Floyd P and Biddle A 2004 Impact of oral health on the life quality of periodontal patients *J. Clin. Periodontol.* **31** 454–7

Schmidt N F, Missan S R and Tarbet W J 1978 The correlation between organoleptic mouth-odor ratings and levels of volatile sulfur compounds *Oral. Surg. Oral. Med. Oral. Pathol.* **45** 560–7

Tangerman A 2002 Halitosis in medicine: a review *Int. Dent. J.* **52** (Suppl 3) 201–6

Tangerman A, Meuwese-Arends M T and Jansen J B 1994 Cause and composition of foetor hepaticus *Lancet* **343** 483

Tangerman A and Winkel E G 2007 Intra- and extra-oral halitosis: finding of a new form of extra-oral blood-borne halitosis caused by dimethyl sulphide *J. Clin. Periodontol.* **34** 748–55

Tonzetich J 1977 Production and origin of oral malodor: a review of mechanisms and methods of analysis *J. Periodontol.* **48** 13–20

Van den Velde S, Quirynen M, van Hee P and van Steenberghe D 2007 Differences between alveolar air and mouth air *Anal. Chem.* **79** 3425–9