Unreliability of Breath Methane as a Candidate Indicator of Functional Bowel Disorders

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Background/Aims: The aim of this study was to examine the reproducibility of methane and hydrogen in exhaled air breath after a per-oral load of lactulose.

Methods: Methane was present in the exhaled breath of 21 of 50 healthy subjects recruited by advertisement. Three methane breath tests were performed in 12 women (aged 23.6±0.5 years, mean±SEM) after they consumed 10 g of lactulose dissolved in 300 ml of water. Short- and medium-term reproducibilities were assessed by paired examinations taken 3 and 17 days (median) apart, respectively. Results: High values of coefficients of variation for paired examinations (CVp) indicated a poor short-term reproducibility of parameters characterizing either the methane or hydrogen excretion in breath air: CVp values of the maximum net increments over baseline in methane (max CH4_net), and in hydrogen (max H2_net), were 34% and 41%, respectively. Moreover, the reproducibility consistently deteriorated with increasing time gap between repeat measurements (CVp: 60% for max CH4_net and 64% for max H2_net). Conclusions: The low reproducibility of parameters characterizing quantitative methane breath excretion suggests that caution is necessary when judging the clinical usefulness of the methane breath test after a per-oral lactulose load for the purpose of diagnosing and classifying functional bowel disorders. (Gut and Liver 2008;2:180-185)

Key Words: Breath tests; Hydrogen; Lactulose; Methane; Reproducibility

INTRODUCTION

Measurement of hydrogen concentrations in breath air is a basis for a battery of breath tests currently applied in gastroenterology for the diagnosis of small intestinal bacterial overgrowth or malabsorption of different carbohydrates on the one hand, and the measurement of the orocecal transit time on the other.1-3 Addition of the determination of methane content in the expiratory air may contribute to increase the diagnostic yield in the case of the former group of applications of those breath test.1,2,4

A very promising appears to be a recent finding that a subpopulation of irritable bowel syndrome (IBS) patients with predominant constipation may be detected on the basis of an increment in methane within the breath air after a per oral lactulose load.5,7 Thus that breath test gained a rank of a decision-influencing diagnostic measure because a positive result thereof in an IBS patient would encourage a clinician to undertake a course of an antimicrobial therapy.6,7 More recently a quantitative result of a methane breath test, expressed in terms of an area under a curve of methane concentration in expiratory air after per-oral lactulose load, was advocated a measure of the degree of constipation in IBS patients.8

What may, however, cast some doubt as to the above reasoning is a potential instability of methane elimination with breath air, as previously was signalized by Minocha and Rashid.9 Also, in our Laboratory of Breath Tests, we observed a noticeable inconsistency of a methane-producing status in a number of subjects. Therefore, we decided to undertake a prospective study aiming at the examination of the reproducibility of quantitative parameters
characterizing methane breath air elimination in the course of a breath test involving a per oral lactulose load.

MATERIALS AND METHODS

In response to an advertisement made public at the University, fifty subjects volunteered to participate in the study. At an initial screening with a dedicated gas chromatograph, 21 of them were found to have a fasted breath concentration of methane $\geq$ 1 ppm. After having been made familiar with the aim, protocol and methodology of the study twelve methane-producing females (age 23.6±0.5 [SE] years, body mass index 21.05±0.62 kg · m$^{-2}$) gave a written consent to participate. They declared themselves as being in full health according to the World Health Organisation criteria.$^{10}$ Exclusion criteria comprised use of antibiotics and any other antimicrobial agents currently, as well as within a period of three months preceding the study, a history of an abdominal surgery affecting the anatomical integrity of the digestive tract, except for appendectomy and pregnancy.$^{5-8}$ The research project was conducted according to the Helsinki Declaration and was approved by the Bioethics Committee of the Medical University of Silesia.

1. Study protocol

The research was performed on patients reporting to the laboratory in the morning, after a 12-h overnight fast and abstaining from cigarette smoking (this requirement pertained to three female smokers). Moreover, they were instructed to resign from dietary components which might evoke a rise in basal breath H$_2$ and CH$_4$ concentrations as from the afternoon of the preceding day, which included dishes made of white or red beans, green peas, cabbage, or large amounts of complex carbohydrates.$^{9,11}$ Every volunteer took part at three examination sessions held on separate days. The time gap between two sessions amounted to 3 days (median, range 2-3 days) for a short-term reproducibility (STR), whereas a third session was accomplished at a median of 17 days (range 16-21) apart (medium-term reproducibility, MTR); the order of sessions for the STR/MTR or MTR/STR was randomly assigned to the subjects. The volunteers did not take any medication throughout the whole period of the study involving participation in the three examination sessions.

At the beginning the subjects were requested to perform a thorough 4-min cleaning of their teeth with the use of an antibacterial tooth paste (Colgate Total, Colgate-Palmolive, Poland). Then, after a 15-min rest in a sitting position, necessary for stabilization of the metabolism, a basal probe of expiratory air was collected into an aluminium covered plastic bag of about 1 l capacity (Fisher Analysen Instrumente GmbH, Leipzig, Germany); the procedure of collecting the breath air was standardized: the subjects took in breath and held it for 20 seconds, then steadily blew the air through a mouthpiece equipped with a valve into the bag until full, which was tightly closed with a plastic stopper immediately at the end of the exhalation. At the time point designated “0” the subjects drank 285 still mineral water into which 15 ml of Normae syrup (Molteni Farmaceutici, Italy), containing 10 g lactulose, was added. Next the volunteers were asked to rinse their mouths with tap water. Probes of breath air were collected at 15-min intervals from 30 min and until 4 hour after time zero. The subjects remained fasted during that period. They rested in a comfortably furnished room and were allowed to watch video films.

2. Measurement of breath hydrogen and methane

The H$_2$ and CH$_4$ concentrations in the expiratory breath samples were measured on the day of their collection with a dedicated chromatograph (Microlyzer Model DP, QuinTron Instrument Co., Milwaukee, WI, USA) calibrated with a reference gas containing 49 ppm CH$_4$ and 99 ppm H$_2$ in air (Quingas-2, QuinTron Instrument Co., Milwaukee, WI, USA) according to the manufacturer’s recommendations.

From the curves reflecting the H$_2$ and CH$_4$ concentrations in the breath air the following parameters were derived:

- basal fasted hydrogen (H$_2$$_{bas}$) and methane (CH$_4$$_{bas}$) concentration,
- maximum net increment over baseline in hydrogen (max H$_2$$_{net}$) and methane (max CH$_4$$_{net}$) after per oral lactulose intake (Fig. 1),
- areas under the curves of net increments of hydrogen (AUC H$_2$$_{net}$) and methane (AUC CH$_4$$_{net}$) concentrations (Fig. 1).

3. Statistical analysis

The data obtained were subjected to the Bland and Altman statistic for calculation of the repeatability coefficients.$^{12}$ Moreover, coefficients of variation for paired examinations (CV$_p$) were computed.$^{13}$

RESULTS

From 36 examinations in 12 volunteers, the medians of the basal concentration, the net increment over baseline, the area under the curve of the net increment of the