Eradication of Methane on Breath Testing and Reduction in Intestinal *M. smithii* Levels Result in Improved Insulin Sensitivity and Lipid Profiles in Pre-Diabetic, Obese Subjects

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**BACKGROUND**

The methanogenic archaea are important colonizers of the gastrointestinal tract, and produce methane which can be detected on breath analysis. *Methanobrevibacter smithii* is the most common methanogen in the human gut. Initially it was thought to only inhabit the colon, however, we have recently been the first to show extensive colonization of this microbe in the crucial absorptive part of the small intestine (1). Methanogens are thought to work in conjunction with other microbes in the gut to increase energy harvest for the host, primarily by providing a "hydrogen sink" for hydrogen-producing organisms, thus enhancing the metabolism of these syntrophs (2). We have shown that the presence of methane in the gut itself is associated with a slowing of intestinal transit (3), which may also allow for increased time for absorption of nutrients and enhanced energy harvest.

Our previous research in an already obese population demonstrated that subjects with methane on the breath have a 6.8 kg/m² greater BMI (4). We subsequently expanded this in a general population, and found after multivariate analysis that methane in the presence of hydrogen on breath testing was also associated with a higher BMI in this 792 subject cohort (5).

**AIM**

To examine metabolic parameters before and after antibiotic treatment in obese pre-diabetic subjects with methane positive breath tests. Our aim is to determine whether using an antibiotic to eradicate *M. smithii* (as measured by the surrogate of breath methane) results in improvement in metabolic profile.

**METHODS**

Using ADA criteria we identified 11 pre-diabetic (9F, 2M) obese (BMI 35.2 ± 7.7 kg/m²) methane positive subjects aged 47 ±9 years. Subjects underwent the following:

- Lactulose breath testing
- Oral glucose tolerance testing
- Lipid profile
- Gastric transit analysis

Subjects then received a 10 day course of antibiotics shown to eradicate *M. smithii* in stool (6). The above tests were repeated post intervention. Insulin sensitivity (SI) was calculated using the Modified Minimal Model for OGTT analysis. (7)

**RESULTS**

Breath methane levels correlate with *M. smithii* levels determined by stool PCR:

Breath methane is an acceptable surrogate for detection of intestinal *M. smithii* levels in these subjects. Eradication of breath methane was seen in 8 of 11 subjects (73%). This is in keeping with expected eradication rates. Eradication in these 8 subjects was associated with reduced stool *M. smithii* levels (P<0.05).

**CONCLUSIONS**

Eradication of methane on breath test and reduction in *M. smithii* levels are associated with:

- Improved glucose metabolism and SI improvement of up to 50%  
- Significant improvement in total cholesterol and LDL levels.

Eradication of methane on breath test is a reliable surrogate for *M. smithii* as measured by stool PCR. The potential effects of the antibiotics on other microbes is a confounding issue. However, the lack of change in those who did not eradicate methane suggests that effects beyond *M. smithii* reduction are less likely to be causal.

Further studies are needed to define the mechanisms linking reductions in methanogens to metabolic improvements.

**References**

2. Bauchop T, Mountfort DO. Applied and Environmental Microbiology 42:1103-1110  

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