Lovastatin Lactone Inhibits Methane Production in Human Stool Homogenates

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BACKGROUND

Research has linked an altered gut microbiome to symptoms of irritable bowel syndrome (IBS). Evidence suggests that methane and colonization with Methanobrevibacter smithii (M. smithii) may be important in the pathogenesis of constipation and constipation-predominant irritable bowel syndrome (C-IBS). The degree of constipation has been shown to be proportional to breath methane levels and is significantly improved with antibiotic elimination of methane. Recent data suggests certain HMG-CoA reductase inhibitors (statins) may reduce methane production by inhibiting methanogenesis of M. smithii.

AIM

This study examines the effects of various statins on methane production in fresh human stool homogenates.

METHODS

I. Five female subjects recruited based on high breath methane production (AVG = 69.6 ppm) provided a total of 8 fresh stool samples each.
II. Samples were homogenized under anaerobic conditions at 37°C in 1XPBS (3ml PBS/2g stool) and divided into stoppered flasks.
III. Assessment 1: Head gas withdrawn through a stopcock was analyzed on a Quintron Model SC gas chromatograph for methane levels; at baseline, then every 30min for 270min.
IV. Nine statins were initially assessed for methane inhibition @ 5mg/g stool; lovastatin lactone & hydroxyacid, pravastatin lactone & hydroxyacid, atorvastatin lactone & hydroxyacid, simvastatin lactone, mevastatin lactone, and resvastatin lactone.
V. Assessment 2: Upon determining lovastatin lactone as the ideal statin, concentrations of 0.04, 0.12, 0.48, 1, 5, and 10 mg/g stool were assessed; at baseline, then every 90min up to 720min.
VI. Assessment 3: Final assessment was performed comparing three forms of lovastatin; lactone, diol, and hydroxyacid.

RESULTS

Lovastatin lactone was identified as the only effective methane inhibitor, significantly inhibiting methane levels by -65% of the control stool (Figure 1). Lovastatin lactone at 5mg/g produced the maximum inhibiting effect, resulting in an average methane level of 3% of the control over time (Figure 2). In a final validation comparison of 3 forms of lovastatin (5mg/g), both the lactone and diol forms proved to be effective (Figure 3). In all assessments, hydroxyacid forms were least able to inhibit methane production.

CONCLUSIONS

Lovastatin lactone and lovastatin diol at concentrations of 5mg/g stool significantly reduce methane production in human stool homogenates. Clinical studies are ongoing to assess the effect of this statin on methane production and IBS-C symptoms in humans.

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