Increased pulmonary CO$_2$ excretion in patients with small intestinal bacterial overgrowth (SIBO): Possible implications for COPD

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In this study, we saw a small but highly statistically significant increase in exhaled CO$_2$-percentage in SIBO (4.28 % to 4.35 %, p < 0.0001). This increase corresponds to 0.53 mmHg, or a change in MV of 1.6 L/min. The normal MV at rest is between 5 and 8 L per minute. Bacterial CO$_2$-production in SIBO may therefore account for 20–30 % of the MV needed to keep a steady state, at least in the context of the LBT. This increase should have no effect on otherwise healthy patients but could be relevant in patients with baseline hypercapnia. While further studies appear warranted, it may be reasonable to test patients with hypercapnia for SIBO as a possible contributing factor that would be amenable to intervention.

METHODS
We identified 11,674 consecutive unique subjects who underwent breath testing for SIBO with lactulose as substrate by Commonwealth Laboratories, Salem, MA, from October 2014 to September 2015. Hydrogen and methane concentrations were determined as parts per million (ppm) and CO$_2$ as volume percent of exhaled air. The research was determined to be IRB exempt.

For the 10-sample LBT, subjects were asked to follow a restricted diet in the days preceding the test, then fast for at least 12 h prior to providing the first breath sample. The first breath sample (sample 1) is provided before ingestion of the lactulose solution, then additional breath samples (2–10) are provided at 20 min intervals for 3 h after ingestion of the lactulose solution. We divided the entire source data set into hydrogen-high and low subsets according to the North American consensus criteria (NACC) for breath test interpretation (1), compared the mean CO$_2$ values, and then partitioned the source data set into a high and low-methane subset, with methane status as defined by the NACC, and again compared CO$_2$ values between these two subsets.

RESULTS

Figure 1: Distribution of CO$_2$ values for the entire data set. The shape of the distribution indicates that admixture of room air was minimal and the collection method adequate. A large proportion of adherent room air would make the distribution left-skewed.

Figure 2: Histogram of mean CO$_2$ for the entire data set. The distribution is right-skewed with a mean CO$_2$ of 4.35 ± 0.03 % (SD).

Figure 3: The left panel shows CO$_2$ means separated by subjects who had high-hydrogen (red) and those who had low-hydrogen emissions in blue. The differences are, with the exception of the baseline, all statistically significant. High hydrogen (or SIBO) correlates with high CO$_2$. The mean CO$_2$ for all samples (samples 1–10 combined) of the low-hydrogen subset was 4.28 % (95% CI: 4.27–4.29) and 4.35 % (95% CI: 4.34–4.36) for the high-hydrogen subset (p < 0.0001). The right panel shows CO$_2$ means separated by subjects that had high-methane in red and low-methane in blue. In a reversal of the hydrogen findings, high methane (red) shows a trend towards lower CO$_2$ values. These findings are biologically plausible because methanogenesis consumes CO$_2$. The difference is not statistically significant, presumably because of a competing process: removal of H$_2$ by methanogenesis actually stimulates CO$_2$ production, which allows them to produce more CO$_2$, resulting in a net effect close to zero.

CONCLUSIONS
In this study, we saw a small but highly statistically significant increase in exhaled CO$_2$-percentage in SIBO (4.28 % to 4.35 %, p < 0.0001). This increase corresponds to 0.53 mmHg, or a change in MV of 1.6 L/min. The normal MV at rest is between 5 and 8 L per minute. Bacterial CO$_2$-production in SIBO may therefore account for 20–30 % of the MV needed to keep a steady state, at least in the context of the LBT. This increase should have no effect on otherwise healthy patients but could be relevant in patients with baseline hypercapnia. While further studies appear warranted, it may be reasonable to test patients with hypercapnia for SIBO as a possible contributing factor that would be amenable to intervention.