Reviewer's report

**Title:** Effects of CPAP on nitrate and norepinephrine in severe and mild/moderate sleep apnea

**Version:** 2  **Date:** 29 June 2012

**Reviewer:** Jose Loredo

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Abstract: should be modified as appropriate based on the comments below.

Methods:

Study population: delete “Arterial hypertension was not a reason for exclusion.” This statement is redundant.

Study design: need to mention that the Epworth Sleepiness Scale was administered.

CPAP Therapy: Please provide the auto-CPAP settings. Were they individualized?

Statistical analyses: Since there was such a large difference in BMI between groups and obesity has a significantly impact on sympathetic nervous system activity, it will be important to control for BMI when comparing U-NE and NOx levels. Consider dividing the groups into BMI categories (BMI < 30 and # 30) when comparing between group using ANOVA and post hoc analyses to better assess the role of obesity versus RDI in U-NE and NOx. Stratification as recommended carries the risk of a reduction in power, but it is needed to parse the effect of BMI.

Results:

How many subjects were on antihypertensive medications and what type?

Under comments for Table 1:

a) No need to include NOx and U-NE values in table 1 since these are found in figures 1 and 2.

b) Recommend including key values of NOx and U-NE in the figure legends with level of significance.

c) Need to describe in the text that severe apneics also had more severe oxygen desaturation than mild-moderate apneics.

d) Consider changing “24h Mean BP” for “24h MAP” (mean arterial pressure).

e) Consider providing the 90th or 95th percentile CPAP pressure rather than the mean CPAP pressure.

Consider deleting: “Baseline sleep parameters of both groups were consistent with the diagnosis of OSA severity.” from the first paragraph.
After CPAP: “This difference was not found in patients with mild-moderate OSA (p = 0.054).” Need to consider that this is a borderline significant finding and that most likely it did not reach full significance due to low statistical power. A higher sample population would probably result in a p < 0.05. The overnight NOx pattern in mild-moderate and severe OSA groups look very similar (See Figure 1). From the data presented it appears to this Reviewer that the both groups had a rise in NOx when treated with CPAP, although the mild-moderate OSA group rise in NOx was of borderline statistical significance.

Discussion:
NOx deficiency: need to modify as appropriate – see comments on After CPAP above.

Blood pressure: “The absence of response of one clinical parameter (BP) and two biological markers (NOx and U-NE) to CPAP therapy could be explained by a ceiling effect, as patients with mild-moderate OSA had baseline NOx, U-NE and BP values similar to those of patients with severe OSA after CPAP treatment.” The data presented is not consistent with a “ceiling effect.” Instead is suggestive that physiological effects of mild-moderate OSA may not be disruptive enough to stimulate a rise in U-NE and BP. In other words, may not be disruptive enough to stimulate the sympathetic nervous system as does severe OSA. A ceiling effect occurs when the parameter being examined is high and further stimulation no longer results in an increase in that parameter. This is not a floor effect either. Please modify Discussion comments.

Limitations: The following limitations should be included and consider making a limitations section: Unable to generalize to women. RDI included RERAs and difficult to compared with literature using AHI. Subjects continued to use antihypertensive medications which could have confounded results. Low sample population.