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Title: Bronchial hyperresponsiveness using mannitol in morbid obesity before and after bariatric surgery

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Body: Introduction: The association between bronchial hyperresponsiveness (BHR) and morbid obesity (MO) is common. Objective: To investigate the prevalence of BHR using mannitol (MAN) in patients with MO before and one year after bariatric surgery (BS). Methods: We determined BHR in 70 patients with MO (46±11 yr; BMI, 46±6 kg/m2; 53 females; smokers, [33±26 pack-yr] 59%). BHR(+) was defined as a PD15<635mg. Severe OSA (apnea/hypopnea Index [AHI] ≥ 30 events/h) was present in 31 patients. Results: Before BS, patients had FEV1, 93±15%; FEV1/FVC, 0.83±0.05; bronchodilator test, +4.9±0.7%. Twenty two had BHR(+) (PD15=78 mg) with an FEV1 fall of -20±2%. BMI and central obesity (abdominal circumference and waist-hip-ratio) were higher in patients with BHR(+) than in those BHR(-) ($p<0.05$ each). Likewise, the AHI was higher (53±10 vs 29±5 events/h) in patients with BHR(+) than in those BHR(-) ($p<0.05$). The ratio-dose-response (RDR) to MAN was positively associated with BMI ($r=0.30$, $p<0.05$). There were also associations between AHI and TNF-α, and between the abdominal circumference and TNF-α ($r=0.40$, $p<0.05$ each). After BS, all but one BHR(+) patient, reverted their BHR (PD15 ≥ 635 mg) with an FEV1 fall of -8±2%, and IL-8 levels decreased in all patients ($p<0.05$). Conclusions: In MO the prevalence of BHR with MAN is elevated, which is associated with increased BMI, central obesity and AHI. Our findings suggest that obstructive sleep apnea and central obesity can in MO share a similar pathogenic mechanism related to development of BHR. Supported by FIS PI080311 CIBERES, Almirall and Esteve.