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The impact of neck and abdominal fat accumulation on the pathogenesis of obstructive sleep apnea

Dear Editor,

Obesity seems to play an important role in the pathogenesis of obstructive sleep apnea (OSA).[1,2] The prevalence of OSA is estimated to be around 5–25% in the adult population,[2–4] reaching up to 45% in obese subjects.[2] However, it is the location of body fat accumulation rather than the total amount which seems to be most relevant in assessing the risk of OSA.[3,5] Neck and visceral fat accumulation has been described as risk factors for OSA in obese patients.[3] Several mechanisms have been proposed for the greater impact of fat accumulated in the abdomen and neck regions in OSA compared with the peripheral ones: reduced pharyngeal lumen size due to fat deposition in the airway walls and increased abdominal pressure in the thorax reducing end-expiratory lung volumes, consequently reducing tracheal traction and increasing collapsibility of the upper airway.[1] Nevertheless the impact of regional fat accumulation on the onset and progression of the disease is unclear and studies investigating this complex association would be helpful for a better management of these patients.

The authors, therefore, designed a prospective cross-sectional study which aimed to analyze and compare the impact of cervical and abdominal fat accumulation on the presence and severity of OSA, in a Portuguese group of individuals with suspected diagnosis.

Overnight polygraphy and CT scan of the neck and abdomen, for the measurement of neck fat area (NFA), subcutaneous abdominal fat area (SFA) and visceral fat area (VFA), were performed on a cohort of subjects attending our sleep laboratory with symptoms of sleep disordered breathing, between October 2013 and May 2014. Body mass index (BMI), neck circumference (NC) and waist circumference (WC) were recorded.

Fifty-two patients were enrolled in the study: the mean ± SD BMI was 32.4 ± 4.3 kg/m^2, 69.2% of the subjects were obese (BMI ≥30 kg/m^2). The subjects with OSA (n = 38, apnea/hypopnea index (AHI) ≥5 h^{-1}) had a greater BMI, WC, NFA and VFA than those without OSA (n = 14, AHI <5 h^{-1}) (Table 1). There was a positive correlation of AHI with BMI (r = 0.490, P < 0.001), VFA (r = 0.417, P = 0.002), WC (r = 0.417, P = 0.002), NFA (r = 0.377, P = 0.007), SFA (r = 0.308, P = 0.026) and NC (r = 0.282, P = 0.04). The BMI, VFA, NFA and WC increased significantly from snorers to severe OSA (Table 2). The multivariate stepwise linear regression analysis was used to analyze the independent factors contributing to AHI: only BMI and VFA were independent risk factors for AHI (model R^2 = 0.303).

Although more marked in OSA group (81.6%), 35,7% of isolated snorers were obese, probably due to the association of obesity with snoring and daytime sleepiness[6] leading to the suspicion of OSA. Among fat measures, VFA and NFA were significantly higher in OSA subjects. Both increased significantly from snorers to severe OSA and were positively correlated with the AHI, although correlation between AHI and NFA was somewhat less strong than with VFA. In multivariate analysis, only BMI and VFA were significantly associated with AHI, suggesting that VFA had a greater impact on the increasing severity of OSA in our sample. The association of OSA with several body habitus measures has been studied and results vary widely among trials. At present, there is no consensus that any one particular habitus phenotype is more important in the pathophysiology of OSA. It is possible that different types of fat distribution are more important in specific subgroups defined by factors such as sex[4,7] or ethnicity.[7,8] Furthermore the impact of body habitus as a predictor of OSA may vary with age.[9]

In this study, we found a significant positive correlation between AHI and the anthropometric measures WC and BMI, but not NC. The reason why NC did not show differences between groups and was not correlated with AHI while NFA did, could probably be due to the greater impact of cervical fat depot compared to NC on the presence and severity of OSA in our sample. Thus, a greater amount of NFA to the same perimeter could lead to a reduction of the size of the cervical airway structures and facilitate upper airway collapse.

The main limitation of our study was the small cohort size; however, this could be offset by the prospective nature of the study which allowed the measurement of anthropometric values by the same professional and control of the timing of when sleep and imaging studies took place.

This study characterizes the distribution of body fat accumulation in our OSA patients, analyzes its association with disease severity, and assesses the location of fat distribution with the greatest impact on the disease. These findings suggest a complex association of interactive effects between visceral fat and OSA, with pathophysiologic and therapeutic implications. Continuous positive airway pressure has proven beneficial in these patients[3] and they could also benefit from personalized nutrition interventions,

Table 1 Patient characteristics and comparisons of the demographics, clinical parameters and the CT scan measurements between the subjects with and without OSA.

	Overall	Snorers (IAH <5)	OSA (IAH ≥5)	*P*-value
Number of subjects	52	14 (26.9%)	38 (73.1%)	
Men:women	36:16	10:4	26:12	N.S.**
Age (years)	54.0 ± 11.0	49.8 ± 10.2	55.5 ± 11.1	N.S.*
BMI (kg/m^2)	32.4 ± 4.3	30.0 ± 1.8	33.3 ± 4.7	$P = 0.001$*
Obese	36 (69.2%)	5 (35.7%)	31 (81.6%)	$P = 0.003$**
NC (cm)	41.4 ± 4.0	40.0 ± 4.3	42.0 ± 3.8	N.S.*
WC (cm)	106 ± 9.6	100.3 ± 7.0	108.9 ± 9.5	$P = 0.001$*
NFA (cm^2)	38.4 ± 21.4	26.8 ± 11.1	42.9 ± 22.9	$P = 0.016$*
VFA (cm^2)	166.7 ± 75.4	115.8 ± 39.7	185.5 ± 77.1	$P < 0.001$*
SFA (cm^2)	276 ± 95.5	245.1 ± 69.6	287.4 ± 101.8	N.S.*

AHI: apnea/hypopnea index; BMI: body mass index; NC: neck circumference; NFA: neck fat area; SFA: subcutaneous fast area; TFA: total fat area; VFA: visceral fat area; WC: waist circumference; OSA: obstructive sleep apnea.
* Student's *t*-test.
** Chi-square.

Table 2 Comparison of BMI, neck and waist circumferences and cervical and abdominal fat areas among snorers and OSA subjects of different severity.

	Snorers	Mild OSA	Moderate OSA	Severe OSA	*P*-value
Number of subjects	14 (26.9%)	12 (23.1%)	14 (26.9%)	12 (23.1%)	–
BMI (kg/m^2)	30.0 ± 1.8	32.9 ± 5.4	31.8 ± 2.4	35.3 ± 5.4	$P = 0.014$
NC (cm)	40.0 ± 4.2	41.1 ± 5.3	42.1 ± 2.1	42.6 ± 3.7	N.S.
WC (cm)	100.3 ± 7.0	107.2 ± 14.7	108.3 ± 6.3	111.3 ± 5.7	$P = 0.022$
NFA (cm^2)	26.8 ± 11.1	36.2 ± 17.6	42.6 ± 25.5	49.9 ± 23.9	$P = 0.042$
VFA (cm^2)	115.8 ± 39.7	170.3 ± 65.6	189.6 ± 95.4	195.9 ± 67.4	$P = 0.019$
SFA (cm^2)	245.1 ± 69.6	264.7 ± 107.0	269.7 ± 93.4	330.6 ± 100.6	N.S.

AHI: apnea/hypopnea index; BMI: body mass index; NC: neck circumference; NFA: neck fat area; SFA: subcutaneous fast area; VFA: visceral fat area; WC: waist circumference; OSA: obstructive sleep apnea.

exercise programs, or even surgical interventions, with the aim of reducing intra-abdominal visceral fat.

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Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter discussed in this manuscript.

Ethical approval

All procedures performed in the study were in accordance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

References

1. Pillar G, Shehadeh N. Abdominal fat and sleep apnea: the chicken or the egg? Diabetes Care. 2008;31 Suppl. 2:S303–9.
2. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea. Chest. 2010;137:711–9.
3. Chin K, Shimize K, Nakamura T, Narai N, Masuzaki H, Ogawa Y, et al. Changes in intraabdominal visceral fat and serum leptin levels in patients with obstructive sleep apnea syndrome following nasal continuous positive airway pressure therapy. Circulation. 1999;100:706–12.
4. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002;165(9):1217–39.
5. Liu KH, Chu WC, To KW, Ko Ng SS, Ngai JC, Chan JW, et al. Mesenteric fat thickness is associated with increased risk of obstructive sleep apnoea. Respirology. 2014;19(1):92–7.
6. Slater G, Pengo MF, Kosky C, Steier J. Obesity as an independent predictor of subjective excessive daytime sleepiness. Respir Med. 2013;107(2):305–9.
7. Bonsignore MR, McNicholas WT, Montserrat JM, Eckel J. Adipose tissue in obesity and obstructive sleep apnoea. Eur Respir J. 2012;39(3):746–67.
8. Li KK, Kushida C, Powell NB, Riley RW, Guilleminault C. Obstructive sleep apnea syndrome: a comparison between Far-East Asian and white men. Laryngoscope. 2000;110 10 (Pt 1): 1689–93.

9. Young T, Shadar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al., Sleep Heart Health Study Research Group. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2001;162(8): 893–900.

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Clinical and functional impact of inhaled antibiotics in a Portuguese Pulmonology Department

To the Editor,

Chronic infection by gram-negative agents is associated with progressive deterioration of lung function and clinical worsening of patients with respiratory disease.[1]

Inhaled antibiotics have been effectively administered with safety and efficacy in these patients, particular in cystic fibrosis, bronchiectasis and in the prevention and treatment of patients with pneumonia, with promising results.[2–4]

Chronic suppressive therapy, the proactive use of an antibiotic regimen rather than the reactive use of antibiotics following patient deterioration, has become the standard of care over the last decade.[5]

Inhaled antimicrobial therapy is frequently used in chronic suppressive regimens, and has the advantage of targeting the site of infection and achieving higher antibiotic sputum concentrations within the airway surface liquid than intravenous antibiotics.[6,7]

Here, the authors evaluate the efficacy and safety of inhaled antibiotics, as continued and support therapy, for patients with respiratory disease chronically colonized with *Pseudomonas aeruginosa*, determine if the administration of antimicrobials in the respiratory tract was associated with clinical and functional improvement in these patients and also verified if the administration of inhaled antibiotics changes the microorganisms' sensitivity profile.

We retrospectively analyzed the demographic and clinical characteristics of patients who inhaled antibiotics during 2013 in the Pulmonology Department of Centro Hospitalar de São João, a hospital in the northern region of Portugal, as well as evaluated the functional differences and the sensitivity profile in the 6 months before and after initiation of inhaled therapy.

A total of 33 patients were on inhaled antibiotics during this period, 54.5% ($n = 18$) were male and 45.5% ($n = 15$) female, with an average age of 35 years (25–54 years). Of these patients, 54.5% ($n = 18$) had cystic fibrosis, 24.2% ($n = 8$) bronchiectasis, 12.1% ($n = 4$) were transplanted lung, 6.1% ($n = 2$) diffuse pulmonary disease and 3% ($n = 1$) had amyotrophic lateral sclerosis. Inhaled colistin was prescribed in 54.5% ($n = 18$) of patients, tobramycin in 42.4% ($n = 14$) and aztreonam in one patient. We found overlapping in the pre-and post-treatment functional assessment (FEV_1: $45.9 \pm 19.6\%$ vs. $47.2 \pm 20.7\%$, $p = 0.43$; FVC: $68.8 \pm 20.4\%$ vs. $69.4 \pm 21.5\%$, $p = 0.75$, IT: $56.1 \pm 15.3\%$ vs. $55.7 \pm 14.9\%$, $p = 0.71$). Nevertheless, considering the different pathologies as cystic fibrosis or non-cystic fibrosis, statistically significant post treatment functional differences were observed (FEV_1: $54.77 \pm 20.61\%$ vs. $39.08 \pm 18.16\%$, $p = 0.038$; FVC: $76.97 \pm 24.25\%$ vs. $61.29 \pm 14.99\%$, $p = 0.046$). Comparing the groups of the two most prescribed antibiotics, there were no clinical and functional significant differences.

Significant clinical improvement was observed, with a reduction in the number of exacerbations and hospitalizations, 6 months after the start of inhaled antibiotic therapy (number of exacerbations: 1.94 ± 0.9 vs. 0.82 ± 0.6, $p < 0.001$, number of hospital admissions: 1.03 ± 1.5 vs. 0.45 ± 0.8, $p = 0.002$). The reduction in the number of exacerbations was more evident in the group non-cystic fibrosis than in the cystic fibrosis patients, and this difference was statistically significant (0.6 ± 0.632 vs. 1.0 ± 0.485, $p = 0.048$, respectively).

About tolerance to the antibiotic prescribed, 84.8% ($n = 28$) of patients did not experience any side effects associated with the drug; however, 5 patients (15.2%) required its suspension due to headache, upper abdominal pain and oral clefts.

All antibiotics prescribed regimens produced a reduction in sputum volume and there was no development of highly resistant strains throughout the study, the inhaled antimicrobial therapy did not change the microorganisms' sensitivity profile.

In the literature several studies showed similar results, clinical improvement, lower risk of acute exacerbations and risk reduction of unscheduled admissions in patients on inhaled antibiotic therapy. In Portugal, epidemiological studies are scarce, with results mainly in ventilator-associated pneumonia.

Although the data collected was only from patients followed in the Pulmonology outpatient clinic, therefore it is not representative of the all population, the results support the benefit of inhaled antibiotics, in maintenance regime, to reduce the number of admissions and exacerbations in patients with colonization by *P. aeruginosa*, without development of resistant strains and, in most patients, without side effects.