

Obstructive Sleep Apnea Hypopnea Syndrome and Pulmonary Embolism: Warfarin Versus Positive Airway Pressure as Determinant

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To the Editor: Xie *et al.* analyzed warfarin doses in pulmonary embolism (PE) and its adverse effects in patients with obstructive sleep apnea hypopnea syndrome (OSAHS). The key findings were that OSAHS patients required a significantly higher dose of warfarin than their non-OSAHS counterparts (4.73 mg vs. 3.61 mg, $P < 0.001$) and that PE recurrence was higher in OSAHS than in non-OSAHS groups after withdrawal of warfarin (21.43% vs. 6.78%, $P = 0.047$). They conclude that OSAHS patients may present with hypercoagulation and relatively high risk of recurrence of PE after cessation of 6-month warfarin treatment. We have read this with great interest.^[1]

However, we consider that there are some controversial aspects that can influence the results and that must be taken into account:

Firstly, there is scarce information such as: Inability to control patient's food intake (leading to the intake of certain foods that can influence warfarin levels), poor compliance, concurrent medications that could decrease the absorption or increase the clearance of warfarin, and consumption of diet rich in Vitamin K. These are the major reasons for warfarin resistance that can influence the results described by authors. Additionally, there is no information if patients received any education program to increase warfarin dosage.^[2]

Secondly, gender difference is an important aspect. There is a higher percentage of men in the OSAHS group, leading to higher body mass index, which could bias the final results. The OSAHS group also has more patients with hypertension, which can increase the risk of PE. In this study, OSAHS patients have a high prevalence of comorbidities associated with PE development. Hence, it would be interesting to evaluate whether OSAHS remain an independent risk factor for PE after covariates adjustment.

Thirdly, there is a prevalent number of nonadherence of OSAHS individuals to home mechanical ventilation with positive airway

pressure (PAP) that could influence the stability of OSAHS and differences among the two groups. Several studies have shown that continuous PAP (CPAP) therapy seems to be related to reduction in mortality risk and cardiovascular events, appearing to be protective in older and male severe obstructive sleep apnoea (OSA) patients.^[3,4] It would be essential to ensure the adherence of individuals to PAP, to assess if this procedure alone is enough to decrease the hypercoagulable state of patients and thereby lower the risk of PE recurrence.

Fourthly, some known risk factors for PE have not been investigated, such as the presence of hemostatic changes and/or inherited thrombophilia, and smoking habits.

Therefore, whether this relationship is casual or a consequence of common risk factors to OSAHS and PE is not totally clear. Part of the answer for the association may lie in common pathways that promote both OSAHS and PE.^[5]

We consider that it would be interesting to conduct similar studies with more characterized groups and better OSAHS control, to assess the maintenance of hypercoagulation state, higher warfarin doses need, and higher risk of PE recurrence in these patients.

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Conflicts of interest

There are no conflicts of interest.

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