It is possible that aldosterone may mediate upper airways inflammation and fibrosis. This, in turn, may contribute to the detrimental effects of fluid overload in patients with OSA and hyperaldosteronism. However, to our knowledge, there are no studies investigating this potential mechanism. It will be important to study this hypothesis in future research, which should provide more basic knowledge on the pathophysiology of both OSA and aldosterone excess.

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Response

We thank Drs Mirrakhimov and Mirrakhimov for their interest in our article¹ and their comments. They point out that additional mechanisms other than fluid overload and rostral fluid shift may be associated with severity of obstructive sleep apnea (OSA) in patients with hyperaldosteronism and high dietary salt intake. Drs Mirrakhimov and Mirrakhimov are correct in hypothesizing that fibrosis and inflammation of the upper airway tissues may also contribute to the severity of OSA, although, as highlighted by them, there are no studies exploring this potential mechanism.

Experiments in animal models indicate that aldosterone excess, in addition to increasing BP, contributes directly to target-organ (heart, brain, and kidney) deterioration by inducing inflammation and perivascular fibrosis.^{2,3} These same studies have been consistent in demonstrating that the pressor, proinflammatory, and profibrotic effects of aldosterone are dependent on concomitant high dietary salt intake.

Clinical studies do suggest that aldosterone blockade reduces the severity of OSA. In a prospective, open-label study, 12 patients with resistant hypertension and moderate to severe OSA (apnea-hypopnea index ≥ 15) received spironolactone in addition to their

previous antihypertensive medications for 8 weeks, after which overnight polysomnography was repeated.⁴ The apnea-hypopnea index was reduced by a mean of about 50% in all patients. This benefit occurred in the setting of increased diuresis, suggesting that aldosterone and sodium-mediated chronic fluid retention is an important mediator of OSA severity. This study is not able to distinguish diuretic vs antiinflammatory/fibrotic effect of mineralocorticoid blockade but does confirm aldosterone as an important mediator of OSA severity at least in patients with resistant hypertension.

In conclusion, we agree that additional mechanisms, other than fluid overload, may be involved in the development of OSA in these patients. Additional experimental and clinical studies are necessary to explore additional mechanisms involved in the development and maintenance of OSA in patients with resistant hypertension, hyperaldosteronism, or both to prospectively test management strategies of OSA.

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