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## **Cardiovascular Endocrinology**

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### ***Nicotine E-Cigarette Vapors Exposure Disturbs 11 $\beta$ -Hydroxysteroid Dehydrogenase Type 2 Expression in the Kidney May Contribute to E-Cigarette-Induced Blood Pressure Elevation in Mice***

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Inhalation of electronic (e)-cigarettes containing nicotine may elevate blood pressure (BP), but the underlying mechanisms are poorly understood. 11 $\beta$ -HSD2 is crucial for BP regulation by inactivating glucocorticoids in the kidney. Little is known about the effect of e-cigarettes on 11 $\beta$ -HSD2 and their contribution to the process of BP elevation. To examine the possible effects of e-cigarette vapor exposures on renal 11 $\beta$ -HSD2 and BP, four groups of mice were exposed to aerosolized PBS, nicotine-free or nicotine-containing e-cigarettes, with concurrent exposure to either saline or the nicotine antagonist hexamethonium (Hex). Mouse renal M1 CCD cells were used to identify the effects of nicotine on 11 $\beta$ -HSD2 and its transcription factor C/EBP $\beta$ . Our results showed that mice exposed to e-cigarettes containing nicotine for 4 weeks markedly decreased the

expression and activity of renal 11 $\beta$ -HSD2 and elevated the systolic BP in C57BL/6J mice. Reduction of 11 $\beta$ -HSD2 by nicotine inhalation was accompanied by reduction of renal C/EBP $\beta$  and responded to elevated plasma nicotine levels. In contrast, these effects were not observed in mice exposed to e-cigarettes vapor without nicotine compared to PBS controls. Treatment with Hex significantly decreased the elevated ratio of urinary corticosterone to 11-DHC along with stimulation of renal C/EBP $\beta$  and prevented the raised BP in mice exposed to e-cigarette vapor containing nicotine. Treating CCD M1 cells with vaporized e-cigarettes containing nicotine extract showed comparable effects with those of pure nicotine for suppression of C/EBP $\beta$  and 11 $\beta$ -HSD2, and these effects are blocked by Hex, indicating a mechanistic specificity. Our results indicate that the inhalation of nicotine e-cigarette vapors has potential adverse effects on renal health suggesting that disturbance of renal 11 $\beta$ -HSD2 may contribute to e-cigarette nicotine-induced BP elevation. These findings highlight the potential health risk of e-cigarettes.

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