CORRESPONDENCE

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Mechanism of Antiarrhythmic Effect of Dexmedetomidine on Epinephrine-induced Arrhythmias

To the Editor:—I read with interest the recent report by Hayashi *et al.*[1] demonstrating a central α_2-adrenergic effect of dexmedetomidine in dogs. Although the authors discuss and refute a variety of potential causes of this effect (cardiac, vascular, baroreceptor, and anesthetic), they do not discuss in depth a more likely cause—vagal activation.

Enhanced vagal efferent and afferent activity have in general been shown to protect against ventricular arrhythmias. Electrical stimulation of the vagus decreases ventricular vulnerability to fibrillation,[2] as does systemic administration of carbachol or its intracellular second messenger, cyclic GMP.[3] Morphine, which enhances vagal tone, protects against ventricular arrhythmias due to stress,[4] electrical stimulation,[5] digitalis,[6] and epinephrine,[7] and this protection is abolished by atropine or vagotomy. Similarly, the α_2-adrenergic agonist clonidine protects against ventricular arrhythmias from electrical stimulation[8] and digitalis.[9] It would have been interesting to know whether dexmedetomidine's protective effect on epinephrine-induced arrhythmias during halothane anesthesia could be altered by atropine or vagotomy.

Although the authors argue that such an indirect cardiovascular effect is unlikely because the peripheral α_2-adrenergic antagonist "normalized" dexmedetomidine-induced bradycardia but not its antiarrhythmic effect, it is quite possible that such "normalization" occurred *via* enhanced peripheral norepinephrine release, without action on vagal efferent or afferent activity. Hemodynamic parameters alone are insufficient measures of vagal activity, as evidenced by the observation that morphine produces a profound antiarrhythmic effect in the absence of changes in heart rate, yet this antiarrhythmic effect is abolished by vagotomy.[6]

The authors are to be congratulated on a well-designed study examining yet another therapeutic facet of this class of drugs. Future studies examining the central mechanism of this antiarrhythmic effect are warranted.

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In Reply:—We thank Eisenach for his helpful suggestions in the further elucidation of the properties of these novel anesthetic adjuvants. Since the nucleus of the vagus is rich in α_2 adrenoceptors,[1] we agree with Eisenach that further evaluation of the central mechanism for the antiarrhythmic properties of dexmedetomidine should consider its effect on the vagus. In our discussion,[2] we alluded to the possibility that an α_2 agonist–induced increase in vagal tone[5] could mediate the antiarrhythmic action of dexmedetomidine. As Eisenach notes, vagal stimulation is protective in some models of arrhythmogenicity, but in the setting of anesthesia this is not a *sine qua non.*[4] Furthermore, Eisenach's example of morphine as a drug capable of increasing vagal tone and thereby increasing the arrhythmic threshold is not fulfilled when examined in the setting of halothane–catecholamine arrhythmias in dogs.[5]

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