

CORRESPONDENCE

Anesthesiology
75:1116, 1991

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 stimulation⁸ 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.

JAMES C. EISENACH, M.D.
Associate Professor
Wake Forest University Medical Center

300 South Hawthorne Road
Winston-Salem, North Carolina
27103

REFERENCES

1. Hayashi Y, Sumikawa K, Maze M, Yamatodani A, Kamibayashi T, Kuro M, Yoshiya I: Dexmedetomidine prevents epinephrine-induced arrhythmias through stimulation of central α_2 -adrenoceptors in halothane-anesthetized dogs. *ANESTHESIOLOGY* 75:113–117, 1991
2. Kent KM, Smith ER, Redwood RR, Epstein SE: Electrical stability of acutely ischemic myocardium: Influence of heart rate and vagal stimulation. *Circulation* 47:291–298, 1973
3. Billman GE: Effect of carbachol and cyclic GMP on susceptibility to ventricular fibrillation. *FASEB J* 4:1668–1673, 1990
4. DeSilva RA, Verrier RL, Lown B: The effects of psychological stress and vagal stimulation with morphine on vulnerability to ventricular fibrillation (VF) in the conscious dog. *Am Heart J* 95:197–203, 1978
5. DeSilva RA, Verrier RL, Lown B: Protective effect of the vagotonic action of morphine sulphate on ventricular vulnerability. *Cardiovasc Res* 12:167–172, 1978
6. Rabkin SW: The interrelationship of morphine and the parasympathetic nervous system in digoxin-induced arrhythmias in the guinea-pig. *Clin Exp Pharmacol Physiol* 15:565–573, 1988
7. Leimdorfer: The action of codeine and morphine on cardiac arrhythmias. *Arch Int Pharmacodyn Ther* 100:333–338, 1955
8. Rotenberg FA, Verrier RL, Lown B, Sole MJ: Effects of clonidine on vulnerability to fibrillation in the normal and ischemic canine ventricle. *Eur J Pharmacol* 47:71–79, 1978
9. Gillis RA, Dionne RA, Standaert FG: Suppression by clonidine (ST-155) of cardiac arrhythmias induced by digitalis. *J Pharmacol Exp Ther* 182:218–226, 1972

(Accepted for publication August 25, 1991.)

Anesthesiology
75:1116–1117, 1991

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 tone³ 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

YUKIO HAYASHI, M.D.
Department of Anesthesiology
National Cardiovascular Center
5-7-1 Fujishiro-dai
Osaka 565, Japan

KOJI SUMIKAWA, M.D.
Department of Anesthesiology
Osaka University Medical School
Osaka, Japan