Altered Release and Metabolism of Norepinephrine in Superfused Canine Saphenous Veins in the Presence of Halothane and Hypoxia

Gerard S. Kamath, M.D.,* Duane K. Rorie, M.D., Ph.D.,† Gertrude M. Tyce, Ph.D.‡

Background: Hypoxia and halothane are both known to have different effects on the release and disposition of norepinephrine at sympathetic nerve terminals during neurotransmission. In adverse clinical situations, both conditions may be present, but the effects of halothane and hypoxia together are not known. Therefore, studies were made of the effects of low partial pressures of oxygen and of halothane on the release, action, and metabolism of norepinephrine at sympathetic nerve endings in isolated segments of a blood vessel in which halothane is known to affect norepinephrine release and action profoundly.

Methods: Saphenous veins were removed from dogs, suspended for superfusion with Krebs-Ringer solution, and stimulated electrically. The veins were exposed to either 0%, 0.75%, or 1.5% halothane in the presence of 95% O₂, 5% CO₂, or 5% O₂, 5% CO₂, and 96% N₂. Superfusates were collected under basal conditions, during and after electrical field stimulation, and poststimulation. Norepinephrine and its intraneuronal metabolite, 3,4-dihydroxyphenylglycol, were measured in superfusates and in the tissues after superfusion using high-performance liquid chromatography with electrochemical detection.

Results: Halothane decreased 1) evoked release of norepinephrine, 2) contractile response of the smooth muscle to nerve stimulation, 3) formation of 3,4-dihydroxyphenylglycol, and 4) tissue content of norepinephrine. However, hypoxia 1) increased evoked release of norepinephrine but decreased 2) contractile response during nerve stimulation, 3) formation of 3,4-dihydroxyphenylglycol, and 4) tissue content of norepinephrine. When halothane and hypoxia were present together, their effects on 3,4-dihydroxyphenylglycol formation, tissue content of norepinephrine, and the contractile responses appeared to be additive, but norepinephrine release was decreased compared with control concentrations.

Conclusions: Although halothane and hypoxia had similar and additive effects on the intraneuronal metabolism of norepinephrine and on the postjunctional responses of smooth muscle to nerve stimulation, they had opposite effects on norepinephrine release from sympathetic nerve endings. The halothane-induced decrease in norepinephrine release overrode the increased release of norepinephrine caused by hypoxia. (Key words: Anesthetic, volatile: halothane. Metabolism, norepinephrine: 3,4-dihydroxyphenylglycol. Sympathetic nervous system, catecholamines: norepinephrine. Veins: saphenous.)

SEPARATELY, halothane and hypoxia have been shown to affect control of vascular smooth muscle tone by the sympathetic nervous system profoundly. Hypoxia alone has a direct vasodilatory effect on the peripheral vasculature, although paradoxically, it increases the release of norepinephrine from the peripheral neurons and the adrenal medulla and increases central sympathetic discharge. Halothane, unlike hypoxia, decreases norepinephrine release both from sympathetic nerve endings and the adrenal medulla and has an inhibitory effect on sympathetic activity and ganglionic transmission. The effects of halothane under hypoxic conditions on the release of norepinephrine from sympathetic nerves and its subsequent disposition have not been studied previously to our knowledge, and the aim of this study was to determine the effects of these two conditions together at peripheral nerve endings in a blood vessel.

In adverse clinical conditions, hypoxia may occur during halothane anesthesia. At this time, all blood vessels in the body are exposed to these two factors simultaneously. Blood vessels show great diversity in their responses to halothane anesthesia and in their content of norepinephrine, density and pattern of innervation, and junctional cleft size. The saphenous vein was chosen for this study because it is rich in

* Senior Associate Consultant, Department of Anesthesiology.
† Professor and Chairman, Department of Anesthesiology.
‡ Professor, Department of Physiology and Biophysics.


Address reprint requests to Dr. Kamath: Department of Anesthesiology, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905.

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