Mechanisms of the Putative Cardioprotective Effect of Hexamethonium in Anesthetized Dogs Given a Large Dose of Bupivacaine

Jean E. de La Coussaye, M.D., Ph.D., Jean-Jacques Eledjim, M.D., Pascal Bruelle, M.D., Jean-Yves Lefrant, M.D., Bruno Bassoul, M.D., M.Sc., Pascale A. Peray, M.D., M.Sc., Gárd Desch, Ph.D., Antoine Sassine, M.D.

In both experimental and clinical settings, bupivacaine overdoses result in marked deterioration in cardiovascular function that may be caused primarily by ventricular fibrillation or by failure of pump function. Although effects of bupivacaine on numerous cardiac ion channels have been defined, recent studies have suggested that activation of the central nervous system outflow controlling sympathetic tone may play a prominent role. Recently, Bernard and Artru (Anesthesiology 78:902–910, 1993) found that either ganglionic blockade with hexamethonium or GABA_a-channel activation decreased the incidence of ventricular arrhythmias following intraventricular central nervous system injection of bupivacaine in rabbits. In contrast, de La Coussaye et al., in this issue (page 595), present a study in which they found that hexamethonium had little effect on cardiac depression induced by intravenous bupivacaine in pentobarbital-anesthetized dogs.

In attempting to understand this study, it is important to recognize that the pentobarbital-anesthetized dog model may markedly influence the results. In pentobarbital-anesthetized animals, vagal tone is abolished and there is enhancement of sympathetic tone. However, the pentobarbital also will provide enhanced activation of GABA_a receptors, the same intervention that was shown to be effective in preventing ventricular fibrillation in the rabbit study. Bupivacaine caused marked depression of blood pressure, heart rate, and cardiac performance in dogs, which was not observed in rabbits. Although hexamethonium decreased the incidence of arrhythmias in rabbits, it enhanced the hemodynamic deterioration in dogs.

It appears difficult to correlate these studies with so many confounding differences. At a minimum, the studies imply that the baseline anesthetic and the species under study can markedly influence the results. These results suggest that, in clinical settings, the underlying level of sedation or anesthesia may markedly influence the response to bupivacaine overdoses. When a marked sympathetic surge can occur after an intravenous bolus of bupivacaine, ventricular arrhythmias may be the primary presenting sign, perhaps because of triggered arrhythmias caused by early or late afterdepolarizations. Such activity may arise from marked sympathetic stimulation of the heart, especially when combined with blockade of various specific ion channels. In contrast, in situations of minimal or muted sympathetic response to bupivacaine, hemodynamic deterioration caused by pump failure, intracardiac conduction defects, and reentrant arrhythmias may predominate.

More research is required to clarify the roles of these differing etiologies and to determine whether differing therapeutic strategies are required to treat the resulting cardiovascular decompensation. The results of such studies may apply not only to bupivacaine but to the variety of local anesthetic agents (class 1 cardiac antiarrhythmics) employed not only for regional anesthesia but to treat cardiac arrhythmias.

Carl Lynch III, M.D., Ph.D.