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Title : ULTRASTRUCTURAL IMPLICATIONS IN INTRAVENOUS REGIONAL ANESTHESIA

Authors : B.C. Wang, M.D., D.E. Hillman, Ph.D., S. Chen Ph.D, and
H. Turndorf, M.D.

Affiliation : New York University School of Medicine, Department of Anesthesiology
and Department of Physiology and Biophysics, 560 First Avenue, New
York, New York 10016

Introduction. Since the clinical investigation by Foldes and McNall in 1952, 2-chloroprocaine has been widely used for epidural anesthesia and nerve blocks. Theoretically the rapid hydrolysis by plasma pseudocholinesterase plus rapid onset, lack of tachyphylaxis, and minimal systemic toxicity make 2-chloroprocaine a favorable drug for intravenous regional anesthesia. However, clinical reports revealed frequent phlebitis following its use. To investigate the basic mechanism of the aforementioned phlebitis, we used electron microscopy to study the endothelial ultrastructural changes in the guinea pig inferior vena cava following injection of (0.5%) procaine, lidocaine and 2-chloroprocaine.

Methods. Guinea pigs were exsanguinated under anesthesia, and the entire vascular system was washed with 30 ml of saline with an exit opening in the left auricle in order to obtain a blood-free preparation. A clamp was then placed on the inferior vena cava between the heart and the diaphragm. 5 ml of the test drugs in clinical concentration was injected separately into the inferior vena cava above the clamp and allowed the drug to stand for 2 minutes. Perfusion was carried out with 1% paraformaldehyde and 1% glutaraldehyde in 0.08 M phosphate buffer through the aorta, followed by removal of the clamp and continued for 20 minutes. The segment above the clamp served as drug treatment while the segment below served as the control. Both were postfixed

in osmium tetroxide and followed by usual procedures for scanning and transmission electron microscopy. Scanning electron microscopy was used to qualitatively analyze large areas of the endothelium while transmission electron micrographs in thin sections allowed study of the membrane and internal structures.

Results. All three drugs showed membrane lysis on transmission electron microscopy. Injury was more pronounced with 2-chloroprocaine showing membrane leakage with swelling of cells. Scanning electron microscopy showed that the entire smooth surface of the endothelial cells was transformed into small globules. Only patchy areas of the above described transformation were observed with procaine, and least with lidocaine.

Discussion. 2-chloroprocaine causes more reaction on the vena cava endothelium of the guinea pig, than procaine and lidocaine. This may help to explain the higher incidence of phlebitis with intravenous regional anesthesia using 2-chloroprocaine in clinical practice. Measures to protect the vascular endothelium from damage by local anesthetic agents, especially 2-chloroprocaine, deserve exploration.

References.
Foldes, F.F. and McNall, P.G.: 2-Chloroprocaine: a new local anesthetic agent. *Anesthesiology*, 13:287 (May, 1952).