TITLE: LIDOCAINE CONSTRICS OR DILATES RAT ARTERIOLES IN A DOSE-DEPENDENT MANNER

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Introduction. Studies on the peripheral vascular effects of local anesthetics are confusing since they provide evidence for both vasodilating and vasoconstricting actions of these drugs. Most assessments of vasoactivity have employed indirect methods such as calculation of regional vascular resistances, have used only single concentrations of drug or have studied isolated strips of vascular smooth muscle. Therefore, we investigated the dose-related effects of lidocaine on fourth-order arteriolar diameters using an in vivo preparation which allowed us to observe directly the microvasculature in the cremaster muscle of the rat and to study widely varying doses of the drug.

Methods. Male Sprague-Dawley rats (160 ± 5 g) were anesthetized with chloralose, 60 mg/kg, and urethane, 800 mg/kg, and the cremaster muscle was prepared for video microscopy. The muscle was suffused with a balanced salt solution, with or without lidocaine hydrochloride. Temperature, pH, osmolality, PO₂, and PCO₂ of the suffusion solution were controlled in all experiments. An electronic vernier system was used to measure diameters of fourth-order arterioles in the cremaster muscle. Fourth-order arterioles were chosen for study because the precapillary arterioles are the major site of vascular resistance and the most responsive of the microvessels to vasoactive stimuli. Internal diameters were measured every 30 seconds during a 10 min control period, a 10 min period of topical application of lidocaine, and a 10 min recovery period. Lidocaine, 10⁰, 10¹, 10², and 10³ μg/ml were applied in seven animals and lidocaine 10⁴ μg/ml, in four animals. In four additional animals, fourth-order arteriolar diameters were measured every 30 seconds before and during an intravenous infusion of lidocaine (1.2 mg/kg loading dose followed by 0.3 mg·kg⁻¹·min⁻¹ for 30 min). Plasma lidocaine concentrations were measured by gas chromatography after 10⁴ and 10⁵ topical applications and after intravenous infusions.

Results. Heart rate and mean arterial pressure were not significantly different between control and study periods in any group. Topical lidocaine produced biphasic, dose-related changes in arteriolar diameter (Figure). Lidocaine, 10⁰, 10¹, 10², and 10³ μg/ml, constricted arterioles to 88.9 ± 0.9, 79.0 ± 1.3, 67.5 ± 2.4, and 60.1 ± 3.4 percent of control, respectively (p < 0.001 for each). Lidocaine, 10⁴ μg/ml, produced arteriolar dilation to 127.1 ± 7.2 percent of control (p < 0.025). Plasma lidocaine concentrations were 0.6 ± 0.2 μg/ml after 10² μg/ml su sfusion and 1.2 ± 0.16 μg/ml after 10³ μg/ml su sfusion. Intravenous infusion of lidocaine resulted in arteriolar constriction to 91.3 ± 0.9 percent of control (p < 0.001). Mean plasma lidocaine concentration with intravenous infusion was 3.6 ± 0.47 μg/ml.

Discussion. Our data demonstrate a biphasic response to increasing concentrations of topically applied lidocaine. At lesser concentrations, including those which occur in the plasma of patients during intravenous infusion or nerve blocks, dose-related vasoconstriction occurred. Lidocaine, 10⁴ μg/ml, a concentration similar to that which occurs at the site of injection during infiltration, nerve block and epidural anesthesia, produced vasodilation. Animals receiving intravenous lidocaine had a plasma concentration of 3.6 ± 0.47 μg/ml and experienced about the same amount of vasoconstriction as did animals receiving similar concentrations (10⁴ and 10⁵ μg/ml) of lidocaine applied topically. This result suggests that the peripheral circulatory action of lidocaine during systemic concentrations of approximately 3-4 μg/ml is the result of local, not central, actions of the drug since similar peripheral vascular effects were seen when the drug was administered topically or intravenously.

References.