Title : HYPOOSMOTIC NEURAL SWELLING AND ELECTROLYTE DEPLETION AS POTENTIATORS OF LOCAL ANESTHETIC BLOCK

Authors : B. Raymond Fink, M.D., D.F. Calkins, B.S., J. Barsa, M.D.

Affiliation: Department of Anesthesiology, University of Washington RN-10, Seattle, Washington, 98195

Rabbit vagus nerve immersed in hypoosmotic (0.6 isoosmotic) physiological medium swells and becomes reversibly non-conducting in about 35 min, but in only 10 min if lidocaine 100 micromolar (0.003 g percent) is added. In contrast, in isoosmotic medium 100 μM lidocaine only slows conduction slightly and does not decrease the amplitude of the C-potential. (Anesthesiology, in press). Both hypoosmotic swelling and partial electrolyte depletion of the nerve occur and may contribute to the potentiated local anesthetic block. The main objective of the present report is to demonstrate which of these factors is the more important.

Weighed nerves with sheath intact were incubated at 37.5°C on an electrode array in various solutions bubbled with O_2 or 5% CO_2 - 95% O_2. The solutions contained $NaHCO_3$ and NaCl as follows (mM): 0 and 0, 24 and 0, 24 and 24, 24 and 48, plus sucrose to a total osmotic strength (O.S.) of 1.0, 0.8 or 0.6 of isotonic (isotonic = 250 mosmolar) adjusted to pH 7.45. The time to 50% depression of the C-fiber component of the compound action potential ($t_{0.5}$) was measured photographically by raising the array out of the solution and stimulating supramaximally for 10 sec at 1 Hz, every 5 or 10 min. After $t_{0.5}$ was determined the nerve was reweighed, frozen, and subsequently analyzed for sodium and potassium content by flame photometry. At least two nerves were studied at each condition; also unincubated isoosmotic controls.

Control levels of total neural sodium and potassium were 125.8 ± 16.7 and 42.6 ± 5.0 mmol/kg wet nerve respectively (± S.D., n = 39). The neural weight gain percent averaged 1.1 ± 2.9, 15.2 ± 2.6, 24.3 ± 2.8 at O.S.: 1.0, 0.8 and 0.6 respectively, (n = 8, 8, 7, $p < 0.001$). Other mean measurements are summarized in fig. 1. In anesthetic-free hypoosmotic solutions (O.S.: 0.8 or 0.6), $t_{0.5}$ was not related to the sodium salt content of the medium but decreased with decreasing O.S.. In osmotic strength 1.0, $t_{0.5}$ was paradoxically prolonged at the two lowest salt contents of the medium. Lidocaine 100 μM in O.S. 0.6, decreased $t_{0.5}$ to about 6 min, irrespective of the external sodium concentration. Conduction velocity at $t_{0.5}$ was about 50% slower when depression was caused by osmotic swelling plus electrolyte depletion than when caused by electrolyte depletion alone or by lidocaine alone (600 μM). Absence or presence of KCl 4 mM or $CaCl_2$ 2 mM in the ambient solution did not noticeably affect the results. Replicates agreed as shown in the figure.

Under the conditions of these experiments hypoosmotic swelling was apparently much more important than neural electrolyte depletion in depressing impulse conduction. The results confirm that hypoosmotic neural swelling markedly potentiates the blocking action of lidocaine. The cause of the paradoxical persistence of conduction in isoosmotic solutions containing little or no sodium is unknown. We speculate that associated inhibition of ($Na^+ + K^+$) activated ATPase may slow down pumping of sodium from inside the axon to the outside and so prolong the use of this store to replenish the transmembrane sodium excitability gradient. The excess slowing of conduction by hypoosmotic swelling at $t_{0.5}$ suggests that hypoosmotic conduction block may involve an additional mechanism that is not implicated in block by lidocaine or by electrolyte depletion.

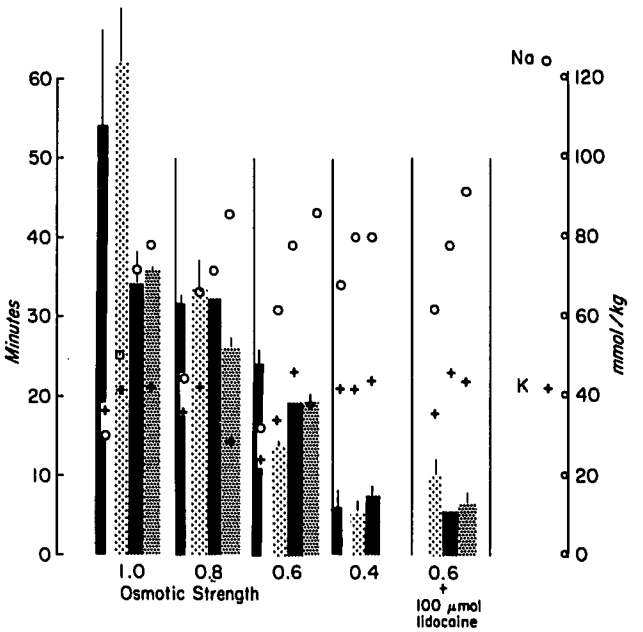

Fig. 1. Mean time to 50% depression of amplitude of C-fiber action potential in various concentrations of sodium chloride and various total osmolarities.

	$NaHCO_3$ (mM)	NaCl (mM)
■	0	0
▒	24	0
▨	24	24
▩	24	48

o Neural sodium content at end of incubation

\+ Neural potassium content at end of incubation

Control levels are shown at extreme right

The black lines at the top of the bars indicate the half range of each replicate pair of observations.

Supported by Grant No. GM-15991-10S1, National Institute of Health, USPHS