NOVEL LOCAL ANESTHETIC IQB-9302 BLOCKS NEURAL SODIUM CHANNELS IN A VOLTAGE-DEPENDENT MANNER.

Ruiz-Nuño, A., Hernández-Guijo, J.M., Garcia, A.G. and Gandia, L.
Instituto de Farmacologia Teófilo Hernando.
Dpto. Farmacologia y Terapeutica. Fac. Medicina, Univ. Autónoma Madrid.

Whole-cell patch-clamp techniques were used to examine directly the kinetics of sodium current (I_{Na}) block by IQB-9302 (1-methylcyclopropyl)-N-(2,6-dymethyl-phenyl)-2-piperidinecarboxamide), a novel local anesthetic agent in bovine chromaffin cells. IQB-9302 produced a concentration-dependent inhibition of I_{Na}, with an IC_{50} about 100 μM, similar to that of bupivacaine. The blocking effect was fast and reversed after wash-out, with a τ of 32.7±3.7s. I_{Na} was blocked by IQB-9302 in a voltage-dependent manner, the effect being greater at depolarising membrane potentials. IQB-9302 seems to facilitate the inactivation of voltage-dependent sodium channels, producing a hyperpolarizing shift in the inactivation curve of I_{Na}.

We conclude that IQB-9302 is a novel Na^+ channel blocker that shows concentration and voltage-dependence. Its slower reversibility of channel blockade with respect to bupivacaine might explain the more prolonged local anesthetic effects shown for IQB-9302.