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Abstract

A New Pain Killer from the Nature: N-Type Calcium Channels Blockers †

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Abstract: N-type calcium channels (Neuronal-type Calcium channel, Cav2.2) is a member of high voltage activated calcium channels. There are two native small peptides for N-type calcium channels (NTCC) directly which are derived from cone snail, ω-conotoxin-GVIA isolated from Conus geographus and ω-conotoxin-MVIIA (SNX-111, Ziconotide, PrialtTM), from Conus magus which both directly block the α1-ion conducting pore. NTCCs, have been shown to play a key role in nociceptive transmission due to their strategic location, presynaptically in afferent C & Aʒ fiber terminals and postsynaptically in descending neuron. NTCCs, which are highly expressed at the pre-synaptic terminals of nociceptive neurons in dorsal horn of the spinal cord regulate release of the key pro-nociceptive neurotransmitters such as glutamate, substance P, neurokinin A, and CGRP. There have been many preclinical studies demonstrating the effect of different NTCC blockers in various acute, inflammatory and neuropathic animal pain models. In 2004 ziconotide has been approved in US and Europe to be used in clinical practice. Furthermore, many clinical trials have been performed in more than 1000 patients studying the efficacy and safety of ziconotide. IT administrated of ziconotide showed significant decrease in pain scores in patients with malignant and nonmalignant pain which are practically in neuropathic pain characteristic and resistant to IT opioids.

Keywords: (Neuronal-type Calcium channel, Cav2.2); ziconotide; Intrathecal IT; antinociceptive effect