Antinociceptive Properties of Fadolmidine (MPV-2426), a Novel $\alpha_2$-Adrenoceptor Agonist

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ABSTRACT

Fadolmidine (MPV-2426) is a novel $\alpha_2$-adrenoceptor ($\alpha_2$-AR) agonist developed for spinal analgesia. It is highly selective for $\alpha_2$-ARs, but it lacks subtype selectivity. Due to its pharmacokinetic properties, it only poorly penetrates blood-brain barrier or spreads from the site of injection within the central nervous system. By intrathecal (i.t.) administration to laboratory animals, fadolmidine produces dose-dependent antinociception in healthy controls and in models of inflammatory, postoperative and neuropathic pain. Fadolmidine has been effective against various submodalities of pain such as heat pain, mechanical pain, and visceral pain. In general, the antinociceptive potency of fadolmidine, i.t., was equal to that of dexmedetomidine. At antinociceptive i.t. doses fadolmidine did not suppress motoneurons or responses to innocuous stimulation. It produced no hemodynamic depression and considerably less sedation than dexmedetomidine. By peripheral administration fadolmidine had no or only a weak antinociceptive action, except following nerve injury, particularly that of the postganglionic sympathetic nerve fibers. Together these experimental animal studies indicate that i.t. administration of fadolmidine provides a segmentally restricted treatment of somatic and visceral pain, with only minor cardiovascular and sedative side effects. Additionally, peripheral administration of fadolmidine might provide a selective treatment for some hypersensitivity states that involve dysfunction of the sympathetic nervous system.