Revisiting Tramadol: A Multi-Modal Agent for Pain Management

Ahmed Barakat

Abstract:

Tramadol is an atypical opioid analgesic with a unique pharmacokinetic and pharmacodynamic profile, with opioidergic, noradrenergic, and serotonergic actions. Tramadol has long been used as a well-tolerated alternative to other drugs in moderate pain because of its opioidergic and monoaminergic activities. However, cumulative evidence has been gathered over the last few years that supports other likely mechanisms and uses of tramadol in pain management. Tramadol has modulatory effects on several mediators involved in pain signaling, such as voltage-gated sodium ion channels, transient receptor potential V1 channels, glutamate receptors, α2-adrenoceptors, adenosine receptors, and mechanisms involving substance P, calcitonin gene-related peptide, prostaglandin E2, and proinflammatory cytokines. Tramadol also modifies the crosstalk between neuronal and non-neuronal cells in peripheral and central sites. Through these molecular effects, tramadol could modulate peripheral and central neuronal hyperexcitability. Given the broad spectrum of molecular targets, tramadol as a unimodal analgesic relieves a broad range of pain types, such as postoperative, low back, and neuropathic pain and that associated with labor, osteoarthritis, fibromyalgia, and cancer. Moreover, tramadol has anxiolytic, antidepressant, and anti-shivering activities that could improve pain management outcomes. The aim of this review was to address these issues in the context of maladaptive physiological and psychological processes that are associated with different pain types.

Keywords:

Tramadol attenuates the hyperexcitability of nociceptive neurons in incisional, inflammatory, and neuropathic pain by interfering with peripheral and central sensitizing mediators. Tramadol has wide applicability in different pain conditions, including postoperative, labor, neuropathic, and low back pain. Tramadol has other applications in pain management aside from the analgesic and anti-hyperalgesic modalities, including antidepressant, anxiolytic and anti-shivering roles.

Published In:

CNS Drugs, Vol. 33, Issue. 5, pp. 481–501