

# Perioperative Use of Gabapentinoids

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Gabapentin is a second generation anticonvulsant that is effective in the treatment of chronic neuropathic pain. Pregabalin is a structural and functional analogue of gabapentin and may be effective in the treatment of nociceptive inflammatory pain that is resistant to gabapentin. Both drugs bind to the  $\alpha_2\delta$  subunit of voltage-sensitive  $\text{Ca}^{2+}$  channels, which sustain the enhanced release of pain transmitters at the synapses between primary afferent fibres and second-order sensory neurons under conditions of chronic pain. Voltage-gated calcium channels (CaV channels) contain an ion-conducting transmembrane  $\alpha$  subunit, an auxiliary  $\beta$  subunit and an auxiliary  $\alpha_2\delta$  subunit, each coded by separate genes. The therapeutic action of CaV $\alpha_2\delta$  drugs may result both from altering calcium channel traffic and also from the more rapid modulation of synaptic function. Recent work suggests that gabapentin and pregabalin also inhibit the activation of the transcription factor nuclear factor  $\kappa\text{B}$  or NF- $\kappa\text{B}$  by preventing the degradation of cellular I $\kappa\text{B}$ - $\alpha$  and, thereby, reducing the translocation of NF- $\kappa\text{B}$  to the nucleus, which in turn reduces gene transcription for cyclooxygenase-2 and other genes involved in inflammation such as the cytokine, interleukin-6.

Pregabalin in particular represents a remarkable example of a context-dependent analgesic drug that acts at a critical step of nociceptive sensitization. It was not, until recently, thought that these drugs would be useful in acute perioperative conditions. However, a growing body of evidence suggests that perioperative administration is efficacious for postoperative analgesia, preoperative anxiolysis, attenuation of the haemodynamic response to laryngoscopy and intubation, and preventing chronic post-surgical pain, postoperative nausea and vomiting, and delirium. This lecture reviews the pharmacology and clinical trial data describing the efficacy and safety of gabapentin and pregabalin in the setting of perioperative anaesthetic management.

## **References**

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