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Gabapentinoids in Pain Setting

Poupak Rahimzadeh*

Department of Anesthesiology and Pain, Iran University of Medical Sciences, Tehran, Iran

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Surgical incision induces central and peripheral sensitization and hyperalgesia, and if remain untreated may lead to chronic postoperative pain after surgery. Antihyperalgesic drugs improve postoperative pain by preventing the development of central sensitization [1]. The development of newer agents available for postoperative pain control creates possibilities for better combinations in multimodal analgesia.

The pain especially in cases of being in high intensity and long duration can have a destructive and intense effect on the mood, personality, and social relationships of a person. Long duration of pain causes concomitant depression, fatigue, anxiety, sleep disturbances, and decreased overall physical functioning. It is speculated that CNS regeneration induced sensitivity may result in potentiation of postoperative pain [2-4].

Anticonvulsants reduce the frequency and increase the time between convulsive attacks grow. Gabapentinoids such as gabapentin and pregabalin are anticonvulant which have been widely used for pain control in different medical situations. These aminobutyric acid analogues have shown analgesic anti –nociceptive effects [5-7].

Gabapentin is a GABA analogue and its possible mechanism of actions are binding to the alpha-2 delta subunit of the presynaptic voltage gated-calcium channels and inhibiting calcium release. It also has interaction with NMDA receptor and causes reduction in substance P and glutamate which could show preventive effects on central nervous system excitability by this mechanism of action. Its positive effects on neuropathic and postoperative pain control have been evaluated in different studies. Gabapentin is the precursor of pregabalin the other discussed drug.

Pregabalin is a structural analogue of gamma-aminobutyric acid (GABA). It acts by presynaptic binding to the α -2-λ subunit of voltage-gated calcium channels that are widely distributed in the spinal cord and brain. This mechanism in pre and post-synaptic membranes leads to inhibition of excitatory neurotransmitters release. Compared with gabapentin, pregabalin due to its better fat solubility and transmission in blood-brain barrier is a more favorable replacement for this drug, with better pharmacokinetic properties and because of less hepatic metabolism, drug interactions are lower with pregabalin. Pregabalin in the treatment of neuropathic pain, incisional pain, aches and inflammatory pain induced by formalin has been used effectively. In cases of acute pain after surgery, by reducing the tissue damage induced dorsal horn neurons excitation, pregabalin plays its important role in treatment of acute pain and also causes an altered physiology on deep dorsal horn wide dynamic range neurons, which makes it an appropriate choice in chronic pain management setting as well [8-10]. However, hypersensitivity was suppressed by antinociceptive actions of pregabalin, suggesting descending facilitation phenomenon in pain pathway. Since the most patients have preoperative stress and anxiety, using pegabaline as an anxiolytic agent can be effective also. In different Studies these drugs have reduced the need for opioids for instances in the treatment of pain after spinal fusion surgery, eye surgeries, laparascopic surgeries and dental pain have been useful. Many evidences suggest that perioperative usage of them is efficacious for attenuation of the haemodynamic response to laryngoscopy and intubation, and preventing chronic post-surgical pain, postoperative nausea and vomiting, and delirium. Since safe postoperative pain control is essential, role of gabapentinoids as a sole drug or an analgesic adjuvant for multimodal analgesia in acute pain control is in progress [11-17].

In neuropathic pain control, post-herpetic neuralgia, phantom pain, allodynia, low back pain, cancer pain and diabetic polyneuropathy these drugs have been used effectively.

Preoperative and pre-emptive prescripion of these drugs before beginning of surgical stimuli and onset of inflammatory trauma have shown a decrease in sensitization degree of nervous system neurons and multiple studies have investigated these effects. Pregabalin has shown a more reasonable pharmacokinetic profile than gabapentin, including dose-independent absorption and is more potent than gabapentin while producing fewer adverse effects [14-17].

Interestingly matter is from a third part payer perspective point of view which the treatment of pain associated with painful diabetic polyneuropathy and post-herpetic neuralgia with gabapentinoids is a cost-effective intervention for the social security [18,19].

Considering all of mentioned points about these two drugs, one comes to this understanding that these multi-purpose anticonvulsant drugs have found a strong and reliable place in acute and chronic pain setting.

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***Corresponding author:** Poupak Rahimzadeh MD, FIPP, Department of Anesthesiology and Pain, Iran University of Medical Sciences, Tehran, Iran, Tel: +98-912-1064483; Fax: +98-21-665509059; E-mail: p-rahimzadeh@tums.ac.ir

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