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EDITORIAL

Are the new antiepileptics efficacious for postoperative pain?

Nonopioid compounds acting as analgesics or adjuvants are part of the multimodal analgesic techniques postoperatively, aiming to reduce opioid requirements and improve analgesia. During the last years the new antiepileptic drugs, namely gabapentin and pregabalin, have been used as adjuvants to alleviate postoperative pain and possibly to prevent chronic postoperative pain. Regarding gabapentin there is accumulating evidence showing that this drug may have a place as analgesic not only in neuropathic but also in acute postoperative pain [1-3]. In the present issue Clendenen et al used pregabalin, an antiepileptic with action similar to that of gabapentin, as adjunct to a multimodal analgesic regimen in arthroscopic rotator cuff repair but failed to demonstrate a significant sparing opioid effect or a decrease in pain intensity postoperatively [4].

Pregabalin is a ligand with high affinity to the α_2-δ calcium channels subunit [5]. The drug exhibits analgesic and anxiolytic properties with efficacy for treatment of neuropathic pain as well as anxiety and stress conditions. It is eliminated by the kidney and has a predictable pharmacokinetic profile, rendering its use easy. After oral administration the drug is absorbed rapidly and has an elimination half-life about 6 hours and steady state is obtained in 1 to 2 days of repeated administration. [6].

Randomized controlled trials investigating pregabalin efficacy for postoperative pain are rather limited and controversial. In a randomized, double-blind trial in patients undergoing removal of one or two third molars pain relief and pain intensity were significantly improved after 300 mg of pregabalin when compared to the placebo group and the duration of analgesia was longer than the duration obtained after 400 mg of ibuprofen [7]. Pregabalin 300 mg given to patients undergoing lumbar discectomy 90 minutes before surgery and 150 mg at 12 and 24 hours postoperatively increased the pain tolerance thresholds 24 hours postoperatively and decreased the pain intensity 3 months postoperatively when compared to the placebo [8]. Also pregabalin 300 mg administered before total knee arthroplasty and for the first 14 postoperative days decreased the opioids consumed epidurally and orally during the first postoperative day when compared with the placebo. Patients in the pregabalin group did not report neuropathic pain 3 and 6 months after surgery in contrast to the control group who reported neuropathic pain 8.7% and 5.2% respectively [9].

In contrast, 100 mg of pregabalin given one hour before minor surgery involving the uterus had no effect on postoperative pain or analgesic requirements but were associated with higher incidence of visual disturbance and difficulty to walk [10]. In another randomized controlled trial patients undergoing abdominal hysterectomy received paracetamol 1000 mg plus 300 mg of pregabalin and exhibited the same pain scores with patients who received paracetamol alone [11]. However, these results are not consistent with the results of a randomized controlled trial where in patients undergoing laparoscopic hysterectomy 600 mg of pregabalin given perioperatively decreased the oxycodone consumption when compared to 10 mg of diazepam [12]. A lower single dose of pregabalin, thus 150 mg, given 2 hours before laparoscopic sleeve gastrectomy decreased the morphine consumption over the 24 hours postoperatively to half the dose consumed by the control group [13].

The efficacy of pregabalin regarding the postoperative pain as assessed in the review articles is controversial. This is in contrast to gabapentin for which the data available are more robust. Randomized controlled trials and metaanalysis articles provide good evidence for analgesic and anti-inflammatory effects of gabapentin associated with acute injury [1-3, 14, 15]. Gabapentin is effective in pain after mastectomy accompanied by axillary dissection [14] and in spinal surgery [15], thus procedures involving nerve injury.

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A systematic review of 16 valid randomized controlled trials evaluating the efficacy of perioperative administration of gabapentin demonstrated that the drug exhibits analgesic properties and decreases opioid requirements postoperatively when used in conjunction with opioids [1]. Hurley et al in a meta-analysis including 12 active trials assessing the analgesic effect of gabapentin on postoperative pain reported that the drug is associated with significant decrease in postoperative analgesic requirements and in postoperative pain [2]. According to a meta-analysis of 23 trials the perioperative administration of gabapentin with special reference to the kind of surgery decreases the opioid consumption after spinal surgery and abdominal hysterectomy [3].

Pregabalin studies supporting its role in postoperative acute pain are limited and the evidence supporting its role in acute pain so far is poor [16]. Clendenen's et al results do not support the use of pregabalin in acute postoperative pain. The authors discuss the limitations of their study but beyond these limitations neuaraxial or regional blocks with local anaesthetics may provide adequate postoperative analgesia so adjuvants do not offer any further advantage. It might be interesting the authors to continue pregabalin for a longer period and assess the analgesic requirements and pain intensity.

Though pregabalin has a similar pharmacodynamic profile with gabapentin acting on the α_2-δ subunit of the presynaptic, voltage-dependent calcium channels more studies are required to support or refute its effect on acute postoperative pain. The appropriate dose, the duration of administration after surgery and the type of procedure should be considered before pregabalin will be included as adjuvant in the multimodal analgesia regimes postoperatively. Also assessment of its effect on prevention of postoperative pain is important and should be included in the outcomes of future studies.

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