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Efficacy of pregabalin in relieving acute postoperative pain- systemic Review & meta-analysis

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ABSTRACT

Background: Pregabalin is used for postoperative pain management. **Aims and Objectives:** To evaluate efficacy of pregabalin in relieving acute postoperative pain. **Materials and Methods:** 650 studies were assessed, out of which 50 studies with 4012 patients (2212 received pregabalin and 1800 served as control) were included in the final analysis. 45 studies investigated acute pain, and 5 chronic pain. **Results:** Perioperative pregabalin after surgery reduced pain scores, hospital stay, opiod side effects. **Conclusion:** pregabalin has a significant role in relieving acute postoperative pain.

Keywords: meta-analysis, postoperative pain, pregabalin, Nausea,

Introduction

Pregabalin, a γ-aminobutyric acid has property of reducing the dorsal horn neurones excitability after tissue damage. It is usually prescribed for postoperative pain management [1,2].Several studies have been carried out to evaluate the efficacy of perioperative pregabalin in doses 50 to 300 mg. All the studies showed better postoperative analgesia after adminstration of pregabalin[3-5].Few studies used 300 mg of pregabalin and others used in the range of 50–150, 225–300, and 600–750 mg, but whether effects of the drug is due to its dosage or frequency of administration is not yet clear. Several studies investigated role of perioperative pregabalin in relieving acute pain. While few studies evaluated about the efficacy of pregabalin in reducing the preoperative anxiety and chronic pain[6-10].Hence we carried out a systematic review to present an updated meta-analysis of the efficacy of pregabalin in relieving acute postoperative pain and also to find out whether outcomes vary according to dose, frequency of administration of drug and or type of surgery.

Database: The recommendations of the PRISMA statement were followed. We searched MEDLINE (1966–2014), the Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE (1947–2014) for randomized controlled trials (RCTs) that compared pregabalin with controls, in patients undergoing surgery.

Data Search: Databases were searched using the term 'pregabalin' combined with the MESH terms: 'Pain, acute', 'Pain, postoperative', 'Postoperative period', 'Pain, chronic', and 'Analgesics, opioid'.

Inclusion criteria

1. Studies where pregabalin was given prior to surgery and parameters like pain scores, opioid consumption, incidence of persistent pain were reported.
2. Articles of all languages
3. Reference articles in the retrieved studies

Exclusion criteria

1. Studies where pregabalin was given postoperatively
2. Studies in which parameters were not reported

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3. Studies in which controls/placebo was not included
4. Reviews
5. Abstracts
6. Letters to the editor and
7. Retrospective studies

After collecting the articles the articles meeting the inclusion criteria were assessed separately by two authors using the risk of bias table suggested by the Cochrane Collaboration.[11]

The main findings of our meta-analysis were pain scores at 2 and 24 hours, whereas the secondary findings were duration in post-anaesthesia care unit and hospital stay, incidence of persistent pain at 1, 3, 6, and 12 months, preoperative anxiety scores, and side-effects.

Analyses were performed using the Review Manager (RevMan), Version 5.1, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011, and Comprehensive Meta-Analysis Software (version 3.0). Meta-regression was performed using the method of moments.

Results

Out of 650 studies, 50 studies with 4012 patients (2212 received pregabalin and 1800 served as control) were included in the final analysis. 45 studies investigated acute pain, and 5 chronic pain. The characteristics of the included studies are shown in Figure 1, Table 1.

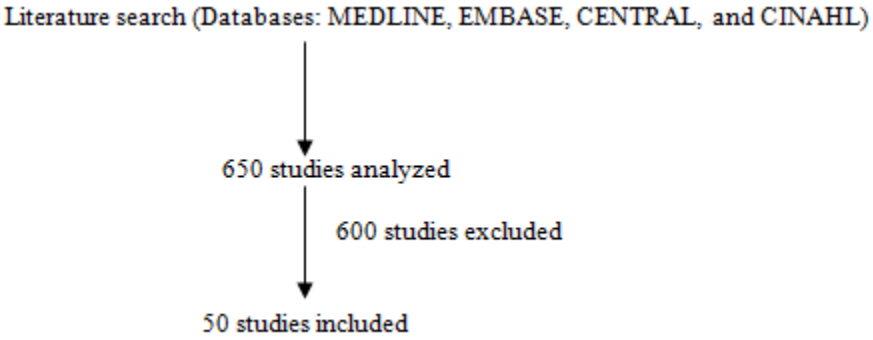

Fig 1: PRISMA flow chart detailing retrieved, excluded, assessed, and included trials

Table 1: Risk of bias table. Low, low risk of bias; high, high risk of bias; unclear, unclear risk of bias

Reference	Randomization sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of outcome assessment
Acin and colleagues	Unclear	High	High	High
Agarwal and colleagues	Low	Low	Low	Low
Alimian and colleagues	Unclear	Low	Low	Low
Balaban and colleagues	Low	Low	Low	Low
Bekawi and colleagues	Low	Low	Low	Low
Bornemann-Cimenti and colleagues	Low	Low	Low	Low
Buvanendran and colleagues	Low	Low	Low	Low

Discussion

We found that the perioperative administration of pregabalin showed a statistically significant lowering in pain scores at rest, pain scores during movement and opioid consumption after surgery when compared with placebo. Opioid related side-effects i,e postoperative nausea and vomiting and pruritus were significantly lowered with pregabalin by 38% and 51%, respectively, relative to placebo after 24 hours of surgery. However there was a significantly higher incidence of sedation (46% increase), dizziness (33% increase), and visual disturbance (3.5 times more likely) relative to placebo. The patients hospital stay was lessened by about 14 hours when compared with patients on placebo. Our findings regarding preoperative anxiety was that there was significantly lower anxiety with pregabalin. Regarding persistent pain, the benefits after 3 months was non conclusive, whereas at 6 and 12 months, there was little benefit[2,3].

The optimal dose or frequency of administration of pregabalin ranged from 50 to 300 mg. We found the drug dosage of 100 –150 and 300 mg but not ≤75 mg at 2 hours after surgery, whereas at 24 hours, no statistically significant differences were detected between the three dose levels. Overall, pregabalin showed opioid sparing of 25% at 24 hours. The impact on pain scores was less pronounced with 19% and 16% reduction in the mean pain scores at rest and on movement at 24 hours, and hence might not be clinically relevant. But there was a reduction in opioid-related side-effects such as post operative nausea and vomiting and pruritus and at the same time increased risk of sedation and dizziness[5-8].

We could do only limited assessment of the impact of sedation on patients' recovery. The duration of hospital stay was reduced with pregabalin administration, but this was only reported in five of the included studies[6-10].

We found that the type of surgery and type of anaesthesia were significant predictors of some of the outcomes. The type of surgery was a significant predictor of pain scores at rest at 2 and 24 hours. This is in accordance with few earlier studies.[12]

The type of anaesthesia also predicted 2 hour pain scores on movement and 24 hour opioid consumption, likely due to the analgesic effect of regional anaesthesia in the early postoperative period.[13-16]

Conclusion

Perioperative pregabalin after surgery reduced pain scores, hospital stay, opiod side effects. We recomend future studies on a larger sample of studies with more parameters to accurately predict the efficacy of pregabalin in reducing postoperative acute persistant pain and other side effects.

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