

# Using Pregabalin as Pre-Emptive Multi-Modal Analgesia for Post-Operative Pain Management: A Randomized Controlled Trial-Case Study

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## Abstract

**Statement of the problem:** A prospective, randomized clinical trial (case study) over 40 patients undergoing surgical procedures.

**Methodology and theoretical orientation:** To give Pregabalin (Lyrica) 75 mg 2 h or more before surgery then 75 mg QHS for 3 days postoperative, to be reassessed by acute pain service team if extension needed. Then add Celecoxib (if not contraindicated) 200-400 mg tablet 1 h before surgery then 200 mg BID for 3 days only. Ranitidine 150 mg BID could be added. Surgical site-specific regional analgesia whenever possible, PCA morphine can be used if indicated and as a backup plan for breakthrough pain. Then post-operatively, Pregabalin, Celecoxib, Solpadine 2 tablets Q6 h or TID. Findings: 30 patients came calm pre-op., smooth for GA, RA blocks, other 10 patients little anxious. All patients examined second day; 30 patients had smooth sleep, no pain after regional blocks, needed PCA morphine 1-5 mg (10 patients). Other 10 patients continued only on oral tablets.

**Conclusion and significance:** the new pre-emptive multimodal analgesic combination is safe and effective postoperative. Lyrica regimen may reduce severity of adverse effects of the opioid. Regular review, follow up of patients postoperative by APS team for 4 days is mandatory.

**Keywords:** Pre-emptive analgesia; Pregabalin (Lyrica); Opioids; Celecoxib; Multimodal; Post-operative pain; Acute pain service

## Introduction

Pregabalin sold under the brand name “Lyrica” is used in the treatment of various Neurological disorders like Seizures, Anxiety, Migraine, Central hyperexcitability, etc. Pregabalin is a gamma-aminobutyric acid derivative which acts as Ligand for the Voltage gated  $Ca^{2+}$  channels in the Nervous system [1-4]. This action leads to the decrease in the intake of  $Ca^{2+}$  ion through the  $Ca^{2+}$  Channels hence causing depolarization and thus leads to the decrease in the release of Excitatory Neurotransmitters like Dopamine, Adrenaline and Serotonin etc. To reduce the pain in early postoperative period pre-emptive analgesics is more effective than the comparative analgesic treatment during surgery [5]. Preemptive analgesia is defined as a treatment which starts before surgery to prevent the central sensitization formation which comes by the inflammatory injuries during surgery. It is an antinociceptive treatment averts the formation of altered processing of afferent input, which Intensifies postoperative agony. Many New studies on pre-emptive analgesia will be conducted from past several years; among them many are published [6-8].

## Objectives

Preemptive analgesia: Analgesic regimen before the onset of noxious stimuli (commonly before incision).

## Goals

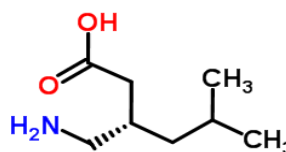
Reduce Central sensitization and Central hyperexcitability of the nervous system, to evaluate the viability of a novel pre-emptive multimodal pain relieving regimen for reducing postoperative torment and complexities.

A prospective, randomized clinical trial case study:

Participants: Patients undergoing surgical procedures (40 Pts).

All patients chosen for Pre-emptive multimodal analgesia treatment group (40 patients) (Figure 1) [9].

## Structure



- IUPAC name: (S)-3-(aminomethyl)-5-methylhexanoic acid
- Molecular Formulae:  $C_8H_{17}NO_2$
- Molecular Weight: 159.229 g/mol
- Drug Category: Anti-convulsion drug.

## Uses

- Muscle pain treatment
- Seizures
- Anesthesia in most of the surgery.

## Mode of Action

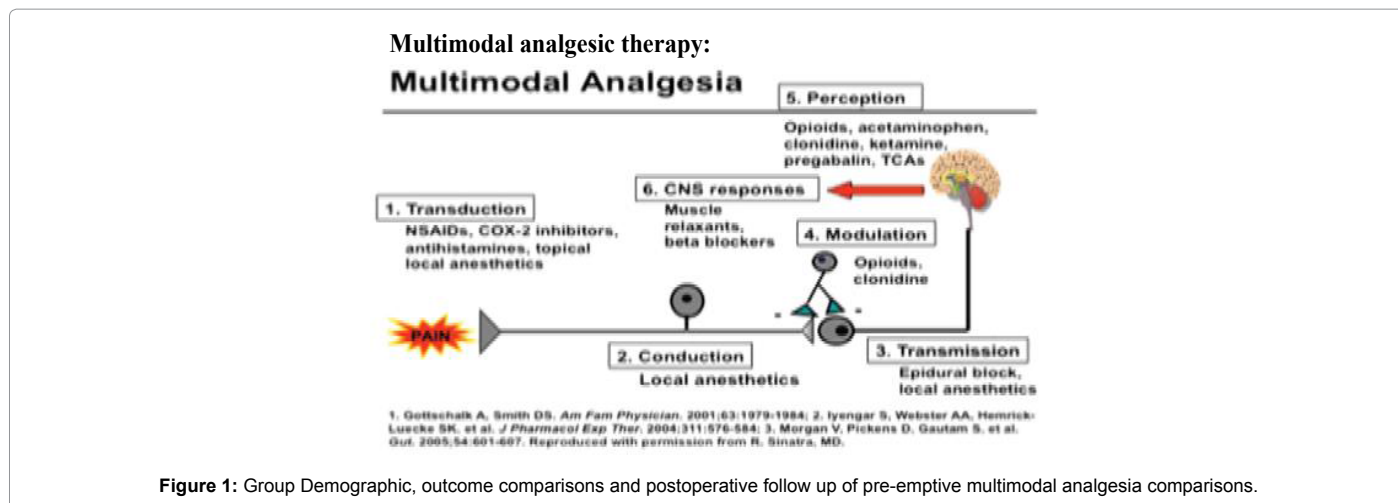
In the voltage-gated calcium channels Pregabalin pre-synaptically binds with alpha-2-delta subunit which is located in the brain and spinal cord. Exact Mode of action is unknown but studies suggest that Pregabalin causes depolarization by inhibiting the Voltage gated

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Demographic	Preemptive multimodal analgesia group (n=40)	Control Group (n=40)	P value
Age	67.9 ± 7.6	66.3 ± 10.0	0.147
BMD	-1.9 ± 1.3	-2.5 ± 0.9	0.107
Intraoperative blood loss	383.0 ± 89.4	400.3 ± 84.9	0.379
Postoperative hemovac drain output	276 ± 111.1	289.3 ± 149.1	0.335
Non-union (Cases)	3	4	0.692
Post-op. Day	Preemptive Multimodal analgesia group (n=40)	Control group (n=40)	P value
Recovery room	5.90 ± 1.10	7.12 ± 1.13	0
After 8 h	5.47 ± 1.17	6.75 ± 1.12	0
Day 1	4.25 ± 0.89	5.52 ± 1.06	0
Day 2	3.62 ± 0.92	5.12 ± 1.13	0
Day 4	3.10 ± 0.92	4.52 ± 0.96	0
Day 7	2.22 ± 0.69	3.65 ± 1.29	0

Table 1: Results for Preemptive multimodal analgesia group in patients (n=40).

Ca<sup>2+</sup> channels in brain tissue which leads to inhibition of excitatory neurotransmitter like adrenaline, Dopamine etc. [10,11]. Some studies also suggest that in mechanism of Pregabalin Noradrenergic and serotonergic pathways are also involved. Meanwhile Pregabalin is an inhibitory neurotransmitter of GABA-Receptor it do not directly bind with GABA, Benzodiazepine or Barbiturate Receptors. 90% Pregabalin will be excreted in unchanged form through urine because it is a plasma Unbound drug [12-14].

### Adverse effect

- Nausea
- Vomiting
- Dry mouth
- Blurred vision
- Dizziness

### Methodology

To give Pregabalin (Lyrica) 75 mg 2 h or more before surgery then 75 mg QHS for 3 days postoperative to be reassessed by APS team if extension needed, no valium with Lyrica [15]. To add Celecoxib (if not contraindicated) 200-400 mg tablet 1 h before surgery then 200 mg BID for 3 days only. Ranitidine 150 mg BID could be added [16-18]. Surgical site-specific regional analgesia whenever possible, PCA morphine can be used if indicated and as a backup plan for breakthrough pain. Then

post-operatively, Pregabalin, Celecoxib, Solpadine 2 tablets Q6 h or TID [19-22].

### Results

30 patients came calm pre-operative, smooth for GA, RA blocks, other 10 patients little anxious. All patients examined second day; 30 patients had smooth sleep, no pain after regional blocks, needed PCA morphine 1-5 mg (10 patients). Other 10 patients continued only on oral tablets shown in Table 1.

### Conclusion

Pregabalin is most effective anaesthetic drug in the treatment of various pains related to nervous system i.e. Epilepsy, Migraine etc. and may show its effect more efficiently than the high doses of many other anaesthetic drugs. The new Preemptive multimodal analgesic combination is safe and effective postoperative. Lyrica regimen may reduce severity of adverse effects of the opioid. Regular review, follow up of patients postoperative by APS team for 4 days is mandatory.

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