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Original Research

A Prospective, Randomised, Doubleblind Study To Evaluate Effects Of Oral Pregabalin For Post Operative Analgesia In Total Abdominal Hysterectomy Done Under Combined Spinal And Epidural Anaesthesia

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Abstract:
Background: Post-operative pain management is crucial for patient comfort and recovery following total abdominal hysterectomy (TAH) performed under combined spinal and epidural anesthesia (CSEA). Oral pregabalin has emerged as a potential preemptive analgesic in various surgical procedures, but its efficacy in TAH remains understudied.
Aim and Objectives: To assess the efficacy of oral pregabalin as preemptive analgesia for post-operative pain management in patients undergoing total abdominal hysterectomy under combined spinal and epidural anesthesia.
Materials and Methods: This prospective, randomized, double-blind, placebo-controlled study enrolled 60 ASA grade I and II patients scheduled for elective TAH at RKDF Medical College Hospital and Research Centre. Patients were randomly allocated into Group A (placebo, n = 30) and Group B (pregabalin 75mg, n = 30). Primary outcomes included Visual Analog Scale (VAS) score at first rescue analgesia, onset of sensory and motor block, duration of analgesia, and total requirement of rescue analgesia. Secondary outcomes encompassed hemodynamic parameters and side effects.
Results: Patients receiving pregabalin exhibited significantly lower VAS scores at first rescue analgesia ($p < 0.001$), prolonged duration of analgesia ($p < 0.001$), and reduced total rescue analgesia requirement ($p < 0.001$) compared to placebo. While trends towards earlier sensory and motor block onset were noted in the pregabalin group, the differences were not statistically significant. Hemodynamic parameters remained stable, and the incidence of side effects was comparable between the two groups.
Conclusion: Oral pregabalin as premedication in TAH under CSEA demonstrates efficacy in reducing post-operative pain intensity and analgesic consumption with no significant impact on hemodynamic stability. These findings support the potential role of pregabalin in optimizing perioperative pain management strategies for patients undergoing TAH.
Keywords: Total abdominal hysterectomy, Pregabalin, Combined spinal and epidural anesthesia, Post-operative analgesia, Randomized controlled trial anesthetic management

Introduction

Total abdominal hysterectomy (TAH) is a common surgical procedure performed to address various gynecological conditions such as fibroid uterus and dysfunctional uterine bleeding (DUB). Effective post-operative pain management is essential for patient comfort, early mobilization, and overall recovery.[1, 2] Combined spinal and epidural anesthesia (CSEA) is frequently employed for TAH because it provides rapid onset anesthesia and prolonged post-operative analgesia.[3, 4]

Despite advancements in anesthesia techniques and analgesic medications, post-operative pain remains a significant concern following TAH.[1,3] Traditional

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analgesics such as opioids are associated with adverse effects, including sedation, respiratory depression, nausea, and ileus, which can delay recovery and discharge from the hospital. Therefore, there is a growing interest in exploring alternative analgesic strategies to optimize post-operative pain control and enhance patient satisfaction.[3, 4]

Pregabalin, a gamma-aminobutyric acid analog, has emerged as a promising adjunct in multimodal analgesia regimens. Its mechanism of action involves the modulation of calcium channels in the central nervous system, inhibiting excitatory neurotransmitter release. Pregabalin has demonstrated efficacy in various acute and chronic pain conditions, including post-operative pain, neuropathic pain, and fibromyalgia.[1-3, 5]

Several studies have investigated the role of pregabalin as a preemptive analgesic in various surgical procedures, with mixed results.[2, 3] While some studies have reported significant reductions in post-operative pain scores and opioid consumption, others have found no significant differences compared to placebo. Moreover, the optimal dosage and timing of pregabalin administration remain areas of debate.[1, 3, 4-6]

Limited data are available regarding the efficacy of oral pregabalin as a premedication for post-operative analgesia in the context of TAH performed under CSEA. Therefore, this prospective study aims to fill this gap in the literature by evaluating the effects of oral pregabalin on post-operative pain, onset of sensory and motor block, duration of analgesia, and rescue analgesia requirement in patients undergoing TAH under CSEA. By elucidating the role of pregabalin in this specific surgical setting, we hope to contribute valuable insights into perioperative pain management practices and improve patient outcomes.

Materials and Methods:

This study adopts a prospective, randomized, double-blind, placebo-controlled design to assess the effects of oral pregabalin for post-operative analgesia in TAH performed under CSEA.

Study Site

The study was conducted at RKDF Medical College Hospital and Research Centre in Jatkhedi, Bhopal, Madhya Pradesh, India. The hospital is a tertiary care center that receives patients from urban and rural areas.

Study Population

The study population comprises patients presenting to the Pain Outpatient Department at RKDF Medical College Hospital and Research Centre to manage gynecological conditions necessitating TAH, such as fibroid uterus and DUB. Inclusion and exclusion criteria are as follows:

Inclusion Criteria

- Age between 30 and 80 years.
- Symptom duration of more than 3 months.
- Confirmation of diagnosis through ultrasound, computed tomography guided diagnosis, fine-needle aspiration cytology, or biopsy.
- Patients who refuse surgery or are unfit for surgery due to comorbidities.
- Patients with no significant comorbidities.

Exclusion Criteria

- The patient refused to participate in the study.
- Presence of infection at the surgical site.
- Autoimmune disorders and platelet disorders.
- Use of anticoagulant and antiplatelet medications within 10 days before surgery.
- Use of non-steroidal anti-inflammatory drugs within 2 days before surgery.
- Uncontrolled comorbidities.
- Hemoglobin levels are less than 10 g/dL, and platelet counts are less than 100,000/mL.

Sample Size Calculation

The sample size is determined based on a power analysis using the expected effect size derived from pilot studies and previous literature. With a power of 80% and an alpha error of 0.05, a sample size of 60 patients (30 in each group) is deemed adequate to detect clinically significant differences in post-operative pain outcomes.

Randomization and Blinding

Patients meeting the inclusion criteria are randomly allocated into two groups using computer-generated randomization sequences: Group A (placebo) and Group B (pregabalin 75mg). Allocation concealment is ensured through opaque sealed envelopes. Patients and investigators involved in data collection and analysis are blinded to the treatment assignment to minimize bias.

Intervention

Patients in Group A receive a placebo capsule as premedication one hour before surgery, while patients in Group B receive an oral pregabalin capsule (75mg) following the same protocol.

Anesthesia Technique

All patients undergo CSEA for TAH. Spinal anesthesia is induced using a 25-gauge spinal needle at the L2-3/L3-4 interspace, with 3mL of 0.5% bupivacaine heavy injected. Epidural catheters are placed for post-operative analgesia as per standard practice.

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Outcome Measures

- Visual Analog Scale (VAS) score at the time of first rescue analgesia.
- Mean time to onset of sensory and motor block.
- Duration of analgesia.
- Total requirement of rescue analgesia.
- Hemodynamic parameters (heart rate, blood pressure, oxygen saturation).
- Incidence of side effects (dizziness, sedation, nausea, vomiting).

Data Collection

Data on demographic characteristics, medical history, intraoperative variables, and post-operative outcomes are collected using standardized case report forms. VAS scores are recorded at regular intervals postoperatively, and hemodynamic parameters are monitored continuously.

Statistical Analysis

As applicable, data analysis is performed using appropriate statistical tests, including independent t-tests, Mann-Whitney U tests, and chi-square tests. Descriptive statistics are used to summarize demographic and clinical characteristics. A p-value < 0.05 is considered statistically significant.

Ethical Considerations

The Institutional Ethics Committee of RKDF Medical College Hospital and Research Centre approves the study protocol. Before enrollment, informed consent was obtained from all participants, and patient confidentiality is strictly maintained throughout the study.

Time Frame

The study is conducted over 18 months, during which eligible patients are recruited, interventions are administered, and outcomes are assessed.

Results

Demographic Characteristics

Sixty patients undergoing elective TAH under CSEA were enrolled in the study and randomized into two groups: Group A (placebo, n = 30) and Group B (pregabalin 75mg, n = 30). Table 1 summarizes the demographic characteristics of the study population.

Table 1: Demographic Characteristics of Study Population

Characteristic	Group A (Placebo)	Group B (Pregabalin 75mg)
Age (years)	49.7 ± 7.5	50.3 ± 6.9
	(37-63)	(38-65)
Gender (n, %)		
- Female	30 (100%)	30 (100%)
ASA Grade (n, %)		
- I	22 (73.3%)	24 (80%)
- II	8 (26.7%)	6 (20%)
Body Mass Index (kg/m²)	26.1 ± 3.4	26.5 ± 3.2

Table 2: Visual Analog Scale (VAS) Score at First Rescue Analgesia

Group	VAS Score (Mean ± SD)	p-value
Placebo (Group A)	5.4 ± 1.5	< 0.001
Pregabalin (Group B)	3.8 ± 1.2	

Table 3: Ramsey Sedation Score

Group	Ramsey Score (Mean ± SD)	p-value
Placebo (Group A)	2.3 ± 0.5	0.15
Pregabalin (Group B)	2.7 ± 0.6	

Table 4: Time of Onset of Motor Block

Group	Time of Onset of Motor Block (Mean ± SD)	p-value
Placebo (Group A)	6.2 ± 1.5 minutes	0.251
Pregabalin (Group B)	5.8 ± 1.1 minutes	

Table 5: Time of Onset of Sensory Block

Group	Time of Onset of Sensory Block (Mean ± SD)	p-value
Placebo (Group A)	4.7 ± 1.2 minutes	0.182

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Pregabalin (Group B)	4.3 ± 0.9 minutes	

Table 6: Time to First Rescue Analgesia

Group	Time to First Rescue Analgesia (Mean ± SD)	p-value
Placebo (Group A)	4.5 ± 0.8 hours	< 0.001
Pregabalin (Group B)	7.2 ± 1.2 hours	

Primary Outcome Measures

Visual Analog Scale Score at First Rescue Analgesia:The mean VAS score at the time of first rescue analgesia was significantly lower in Group B (3.8 ± 1.2) compared to Group A (5.4 ± 1.5) ($p < 0.001$).

Time to Onset of Sensory and Motor Block:The mean time to onset of sensory block was 4.7 ± 1.2 minutes in Group A and 4.3 ± 0.9 minutes in Group B, with no statistically significant difference ($p = 0.182$). Similarly, the mean time to onset of motor block was 6.2 ± 1.5 minutes in Group A and 5.8 ± 1.1 minutes in Group B, with no significant difference ($p = 0.251$).

Duration of Analgesia:The duration of analgesia was significantly longer in Group B (7.9 ± 1.6 hours) compared to Group A (5.6 ± 1.3 hours) ($p < 0.001$).

Table 7: Intraoperative Variables

Variable	Group A (Placebo)	Group B (Pregabalin 75mg)
Duration of Surgery (minutes)	95.6 ± 12.3	92.8 ± 10.7
Intraoperative Blood Loss (ml)	180 ± 30	175 ± 25
Volume of Intravenous Fluids (ml)	1200 ± 150	1225 ± 140
Incidence of Intraoperative Hypotension	5 (16.7%)	3 (10%)
Incidence of Intraoperative Bradycardia	2 (6.7%)	1 (3.3%)

Total Requirement of Rescue Analgesia:The total requirement of rescue analgesia was significantly lower in Group B (82.5 ± 15.6 mg) compared to Group A (105.2 ± 18.3 mg) ($p < 0.001$).

Secondary Outcome Measures

Hemodynamic Parameters:Intraoperative and post-operative hemodynamic parameters, including heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation, remained stable and comparable between the two groups ($p > 0.05$).

Side Effects:The incidence of side effects such as dizziness, sedation, nausea, and vomiting was higher in Group B compared to Group A, although the difference was not statistically significant ($p > 0.05$).

Table 8: Post-operative Outcome Measures

Outcome Measure	Group A (Placebo)	Group B (Pregabalin 75mg)
Time to Ambulation (hours)	12.5 ± 2.1	11.8 ± 1.8
Length of Hospital Stay (days)	2.3 ± 0.4	2.1 ± 0.3
Incidence of Post-operative Nausea and Vomiting	7 (23.3%)	5 (16.7%)
Patient Satisfaction Score (mean ± SD)	8.2 ± 0.9	8.7 ± 0.7

Table 9: Incidence of Side Effects

Side Effect	Group A (Placebo)	Group B (Pregabalin 75mg)
Dizziness (n, %)	4 (13.3%)	8 (26.7%)
Sedation (n, %)	3 (10%)	6 (20%)
Nausea (n, %)	5 (16.7%)	4 (13.3%)
Vomiting (n, %)	2 (6.7%)	3 (10%)

Discussion

The present study investigated the efficacy of oral pregabalin as a preemptive analgesic in patients undergoing TAH under CSEA. The results demonstrated several noteworthy findings that warrant discussion in the context of existing literature.

Effectiveness of Pregabalin in Post-operative Pain Management

Our study found that patients receiving oral pregabalin exhibited significantly lower VAS scores at the time of first rescue analgesia than those receiving placebo. This finding aligns with previous research demonstrating the

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efficacy of pregabalin in reducing post-operative pain intensity across various surgical procedures, including abdominal surgeries.[1, 2] Pregabalin's mechanism of action, involving modulation of calcium channels in the central nervous system, likely contributes to its analgesic effects by reducing excitatory neurotransmitter release.[3]

Duration of Analgesia and Total Analgesic Consumption

Consistent with prior studies, we observed a prolonged duration of analgesia and reduced total requirement of rescue analgesia in patients receiving pregabalin.[4, 5] This suggests that pregabalin may provide sustained post-operative pain relief, thereby decreasing the need for supplemental analgesics and potentially minimizing opioid consumption. Such opioid-sparing effects are particularly relevant in the current opioid epidemic context, where efforts to mitigate opioid-related adverse effects and dependency are paramount.[6]

Onset of Sensory and Motor Block

While our study did not find statistically significant differences in the onset of sensory and motor block between the pregabalin and placebo groups, trends towards earlier onset were noted in the pregabalin group. This finding is consistent with some previous studies [7, 8], although conflicting results have been reported in the literature [9, 10]. The lack of consensus regarding the effect of pregabalin on block onset time may be attributed to variations in study populations, surgical techniques, and dosage regimens.

Incidence of Side Effects

An essential consideration in the use of pregabalin is the incidence of side effects. Our study observed a slightly higher incidence of dizziness and sedation in the pregabalin group, although the difference was not statistically significant. These findings are consistent with the known side effect profile of pregabalin, which includes central nervous system-related adverse effects such as dizziness, sedation, and cognitive impairment.[11]Despite these potential side effects, pregabalin remains a valuable adjunct in multimodal analgesia regimens when used judiciously.

Comparison with Previous Studies

Comparing our results with those of previous studies, it is evident that the efficacy of pregabalin in post-operative pain management varies across different surgical procedures and patient populations. While some studies have reported significant reductions in post-operative pain scores and opioid consumption with pregabalin [12, 13], others have found no significant differences compared to placebo [14, 15]. These discrepancies may be attributed to variations in study design, sample size, dosage regimens, and outcome measures.

Clinical Implications

The findings of our study have several clinical implications for perioperative pain management practices. Oral pregabalin, when administered as premedication in TAH under CSEA, provides effective post-operative analgesia and may reduce the need for rescue analgesics. However, clinicians should weigh the potential benefits of pregabalin against its side effect profile and individual patient factors when making treatment decisions.

Limitations

Several limitations of our study should be acknowledged. Firstly, the relatively small sample size and single-center design may limit the generalizability of our findings. Additionally, using a fixed pregabalin dosage may not account for individual variability in patient response and may have influenced the observed outcomes. Furthermore, the short-term follow-up period in our study precludes the assessment of long-term efficacy and safety outcomes associated with pregabalin use.

Conclusion

Our study provides evidence supporting the efficacy of oral pregabalin as a preemptive analgesic in patients undergoing TAH under CSEA. Pregabalin demonstrated superior post-operative pain control, prolonged duration of analgesia, and reduced total analgesic consumption compared to placebo. These findings underscore the potential role of pregabalin in optimizing perioperative pain management practices. However, further research incorporating larger sample sizes, dose optimization, and long-term follow-up is warranted to validate our findings and elucidate the optimal use of pregabalin in the perioperative setting.

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