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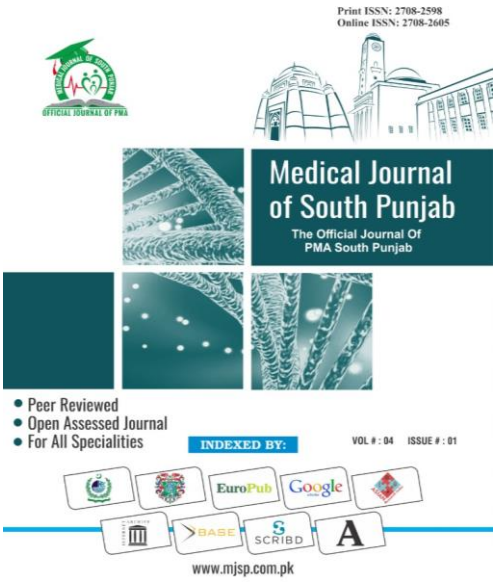

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Original Article

Analgesic efficacy and safety of Duloxetine premedication in patients undergoing hysterectomy

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ABSTRACT

Objective: *to evaluate the effect of Duloxetine on postoperative pain management in patients who underwent hysterectomy, researchers conducted a study to assess the drug's efficacy and its impact on pain levels following the surgical procedure.*

Methods: *Study was prospective cohort conducted at Nishtar Hospital, Multan from March 2023 to February 2024. The study included undergoing abdominal hysterectomy for conditions such as endometriosis, ovarian or cervix cancer, fibroids, or abnormal vaginal bleeding after failed alternative treatments. Postoperative pain was assessed with VAS every 15 mins for 45 mins in recovery, then at 2, 4, and 24 hours. Pethidine (25 mg IV) was given for VAS > 4, along with acetaminophen (1 g IV every 6 hours). QOR-40 scores were assessed after 24 hours. Adverse effects of DLX were monitored. Vital signs were checked at specific intervals throughout the perioperative period.*

Results: *The mean pain score at recovery for Duloxetine group was less than Placebo group as 3.11±0.88 and 9.94±1.04, respectively. (p<0.001). The mean pain score at ward for Duloxetine group was less than Placebo group as 2.58±0.68 and 4.93±0.64, respectively. (p<0.001). The mean QOR-40 score of Duloxetine group was greater than Placebo group as 161.55±15.08 and 129.23±11.18, respectively. (p<0.001). The mean consumption of opioids in both the groups was almost equal, (p>0.050).*

Conclusion: *DLX, a drug commonly used in multimodal anesthesia, has been found to significantly improve postoperative pain management and enhance the quality of recovery in patients undergoing abdominal hysterectomy.*

Keywords: *Abdominal hysterectomy, Duloxetine, Post-operative pain, Multimodal analgesia, QQR-40.*

1. INTRODUCTION

Postoperative pain, stemming from tissue damage, visceral dilatation, or the underlying condition, is widely regarded as one of the most discomforting complications following surgery[1]. Effective management of postoperative pain not only enhances patient satisfaction but also contributes to shorter hospital stays[2]. Various methods such as intravenous opioids, NSAIDs, and local anesthesia are utilized for postoperative pain control, each with its accompanying set of side effects[3].

Before the introduction of multimodal analgesic strategies, opioids stood as the primary analgesic solution, often accompanied by numerous side effects[4]. Multimodal analgesia now offers a balanced approach, combining various drugs in moderation to attain effective postoperative pain control while minimizing adverse effects[5]. Among the drugs introduced to reduce opioid consumption and hasten patient recovery are antidepressants like Serotonin-norepinephrine reuptake inhibitors[6].

Preoperative consumption of the SNRI medication DLX has demonstrated promising effects in postoperative pain management, leading to reduced opioid intake and facilitating anticipated recovery[7]. Previous research conducted in gynecological operations, known for inducing moderate to severe postoperative pain, has yielded successful outcomes in analgesia with DLX administration[8,9].

The study of 63 patients revealed that DLX effectively reduced opioid consumption and promoted recovery in postoperative abdominal hysterectomy pain management[10]. Despite previous partial investigations into DLX's role in this context, inconsistencies remained, prompting further evaluation of its impact on vital signs and quality of recovery[11].

The findings of this study can be incorporated into clinical practice guidelines for managing postoperative pain in patients undergoing abdominal hysterectomy. Anesthesiologists can consider preoperative administration of duloxetine as a potential strategy to reduce postoperative pain intensity and opioid consumption.

2. METHODOLOGY

A prospective cohort study was conducted at Nishtar Hospital's Anesthesiology department and received approval from the local Ethics Committee [NMU/22/23]. The study included candidates aged 18 to 85, with American Society of Anesthesia (ASA) physical status I or II, undergoing abdominal hysterectomy for conditions such as endometriosis, ovarian or cervix cancer, fibroids, or abnormal vaginal bleeding after failed alternative treatments. Exclusion criteria encompassed individuals on narcotics, painkillers, or steroids, as well as those with specific medical conditions such as heart, liver, or renal failure, uncontrolled hypertension, endocrine disorders, a body mass index exceeding 40, a heart rate below 50, prolonged PR interval (>0.2 milliseconds) or any heart block evident on electrocardiograph, and those diagnosed with convulsions or bipolar disorder.

In an effort to enhance the statistical power of the study, the sample size for each group was increased from to 35 patients, based on a previous study with an alpha of 5% and a power of 90%. Random allocation into either the case or placebo group was facilitated by a computer-generated chart. Prior to the investigation, patients received information regarding the study's methodology and objectives, and written consent was obtained from eligible individuals during preoperative examinations. To maintain blinding, the administering anesthesia personnel were

unaware of the medication method, and assessment of pain severity and vital signs was conducted by personnel independent of the administration process. To standardize recovery times, patients were allowed a 45-minute period in the recovery room.

Patients were randomized into intervention and control groups receiving DLX or placebo respectively. Vital signs were recorded before anesthesia induction. DLX (60 mg) or placebo was administered two hours before anesthesia. General anesthesia was induced with Midazolam, Fentanyl, Atracurium, and Propofol. Maintenance used Isoflurane MAC. Additional Fentanyl was given if heart rate or mean arterial pressure increased >20%. Postoperative pain was assessed with VAS every 15 mins for 45 mins in recovery, then at 2, 4, and 24 hours. Pethidine (25 mg IV) was given for VAS > 4, along with acetaminophen (1 g IV every 6 hours). QOR-40 scores were assessed after 24 hours. Adverse effects of DLX were monitored. Vital signs were checked at specific intervals throughout the perioperative period.

3. RESULTS

Overall, 70 patients were included in this study. The study patients were equally divided into two groups as Placebo 35 (50.0%) and Duloxetine35 (50.0%). Both the study groups were almost equal in terms of age and weight distribution, (p>0.050). There were 30 (85.7%) patients had ASA II in Placebo group and 17 (48.6%) had ASA II in Duloxetine group, (p<0.001). The mean duration of anesthesia of Placebo group was greater than Duloxetine group as 109.22±17.86 minutes and 98.32±7.72 minutes, respectively. (p<0.001). (Table. I).

The mean pain score at recovery for Duloxetine group was less than Placebo group as 3.11±0.88 and 9.94±1.04, respectively. (p<0.001). The mean pain score at ward for Duloxetine group was less than Placebo group as 2.58±0.68 and 4.93±0.64, respectively. (p<0.001). The mean QOR-40 score of Duloxetine group was greater than Placebo group as 161.55±15.08 and 129.23±11.18, respectively. (p<0.001). The mean consumption of opioids in both the groups was almost equal, (p>0.050). (Table. II).

The mean heart rate at pre-operation (p<0.001), at every 15 minutes during surgery (p<0.050), end of surgery (p=0.270), at recovery (p<0.001) and at the discharge (p<0.001) were shown in table III.

Table. I

Demographics and baseline characteristics of both the study groups

Characteristics	Placebo 35 (50.0%)	Duloxetine 35 (50.0%)	p-value
Age (years)	61.62±8.11	63.24±7.45	0.245
<60	18 (51.4)	16 (45.7)	0.632
≥60	17 (48.6)	19 (54.3)	
Weight (kg)	65.48±5.21	62.65±5.58	0.395
ASA			
I	5 (14.3)	18 (51.4)	<0.001
II	30 (85.7)	17 (48.6)	
Duration of anesthesia (min)	109.22±17.86	98.32±7.72	<0.001

Table. II

Distribution of pain score, QOR-40 and opioids consumption of both the study groups

Pain score/opioids consumption	Placebo 35 (50.0%)	Duloxetine 35 (50.0%)	p-value
Recovery	9.94±1.04	3.11±0.88	<0.001
Ward	4.93±0.64	2.58±0.68	<0.001
QOR-40 score	129.23±11.18	161.55±15.08	<0.001
Opioids in recovery unit (mg)	5.71±1.47	4.96±1.74	0.059

Table. III

Distribution heart rate at different time interval of both the study groups

Heart rate (bp/m)	Placebo 35 (50.0%)	Duloxetine 35 (50.0%)	p-value
Pre-operation	88.03±2.02	80.54±3.65	<0.001
1st 15 minutes of surgery	84.85±1.84	78.01±4.52	<0.001
2nd 15 minutes of surgery	82.31±2.66	78.62±6.54	<0.001
3rd 15 minutes of surgery	79.28±2.88	77.78±3.95	0.047
4th 15 minutes of surgery	80.88±2.66	78.88±3.69	0.011
End of surgery	78.34±2.18	79.34±4.86	0.270
In recovery	82.84±3.48	79.20±3.93	<0.001

At discharge from recovery	82.34±2.95	79.48±2.42	<0.001

4. DISCUSSION

Findings in this study revealed that perioperative administration of DLX resulted in a notable reduction in postoperative pain and an improvement in the quality of recovery. Despite experiencing significantly less pain compared to non-DLX recipients, patients who received DLX exhibited similar opioid consumption levels. Moreover, there were no significant differences observed in evaluated standard monitoring between the DLX and non-DLX groups.

Kim et al[12] successfully implemented multimodal analgesia for postoperative pain management, resulting in effective pain control, reduced opioid consumption, and enhanced recovery outcomes. In a study by Sattari et al[13], duloxetine reduced postoperative opioid use insignificantly, but significantly decreased postoperative pain in both recovery and ward settings compared to a placebo. The quality of improvement in recovery was also significantly better in the duloxetine group.

YaDeau et al[14] and Gilron et al[15] have demonstrated the effectiveness of using antidepressants as adjunct drugs in multimodal analgesia approaches. Their studies have shown that integrating antidepressants into pain management protocols can lead to positive outcomes in terms of managing postoperative pain and facilitating recovery in patients. This suggests that antidepressants can play a valuable role in enhancing the efficacy of multimodal analgesia strategies, potentially offering patients better pain relief and improved overall recovery outcomes following surgical procedures.

Attia et al[16] conducted a review on DLX, a second-line antidepressant, as an adjuvant drug for analgesia, suggesting it as a promising choice, consistent with findings from other studies. The proposed mechanism involves the inhibition of spinal noradrenaline and serotonin reuptake, leading to pain inhibition through SNRIs[17].

Castro-Alves et al[18] demonstrated the efficacy of DLX in a comparable number of cases to ours during the same surgical procedure, affirming that perioperative DLX administration improves the quality of recovery, consistent with our findings. Additionally, Heyer et al[19] observed reduced postoperative pain and enhanced quality of recovery with DLX administration, mirroring our own observations.

In a recent study, we did not observe any notable differences in vital signs between two groups under investigation. Unfortunately, there are no other comparable studies available for direct comparison[20]. However, it's worth noting that a study conducted by Haelst et al[21] a few years ago found a correlation between the use of SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors) and shorter episodes of intraoperative hypotension. This suggests that there may be some impact of SNRI use on blood pressure regulation during surgery, although further research is needed to fully understand the implications of this finding.

5. CONCLUSION

DLX, a drug commonly used in multimodal anesthesia, has been found to significantly improve postoperative pain management and enhance the quality of recovery in patients undergoing abdominal hysterectomy.

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