Research Article

Journal of Clinical Obstetrics and Gynecology Research

Preemptive Analgesic Effect Of Intravenous Diclofenac In Women That Underwent Abdominal Hysterectomy Under General Anesthesia In A Limited Resource Settings: An Observational Cohort Study.

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Received Date : November 17, 2024
Accepted Date : November 18, 2024
Published Date : December 30, 2024

ABSTRACT

Background: A significant proportion of patients suffer moderate to severe pain after surgery despite wide pain management protocols. This study evaluated the effectiveness of diclofenac as a preemptive analgesic for postoperative pain management in patients that underwent abdominal hysterectomy under general anesthesia.

Methods: A prospective cohort study was conducted on 86 ASA I and II women aged >18 years old and undergoing abdominal hysterectomy from March to August 2020 Tertiary Hospital, Ethiopia. The participants were recruited into this prospective observational cohort study. Study participants were grouped as group D (who took preemptive IV diclofenac 75mg) and group C (who did not or control) based on whether or not IV diclofenac was given 30 minutes to one hour prior to the surgical incision. The pain severity, total analgesic consumption, first analgesic request time, and incidence of nausea and vomiting within 24 hours postoperatively were compared between the two groups. Student's t-test and Mann-Whitney U test were used for analyzing numeric data. Categorical variables between the groups were analyzed using the chi-square test. P-values <0.05 were considered statistically significant.

Results: Median pain score in the early postoperative period (in the 2nd, 4th, and 8thhr) was significantly lower in the diclofenac group (0.007, 0.004, 0.001, 0.261, and 0.796 respectively). The mean first analgesic request time between the groups was not significantly different (p>0.05). Total postoperative analgesic consumption was significantly lower in the diclofenac group (p=0.0006). The occurrence of nausea and vomiting was comparable between the two groups (p>0.05).

Conclusion and Recommendation: Preemptive diclofenac significantly reduced postoperative pain severity and total analgesic consumption and associated with fewer side effects in women undergoing abdominal hysterectomy. We recommend all anesthesia providers to use 75 mg IV diclofenac 30 min to 1 hour prior to surgical incision to minimize postoperative pain severity.

Keywords: *Abdominal hysterectomy, diclofenac, postoperative pain, preemptive analgesia, general anesthesia.*

INTRODUCTION

Pain is defined as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". Postoperative pain is the acute pain that is induced by surgical trauma and gradually decreases when the tissue starts healing [1]. Several degrees of postsurgical pain are expected after most surgical procedures to variable extent among individuals undergoing similar surgery. Current data shows that abdominal surgery accounts for the highest surgical volume (35.7%) and the incidence of postoperative pain after abdominal surgery was very high (91.4%). Moreover, about 80% of patients were undertreated and complained as they experienced severe pain with a mean pain intensity of 6.72±1.44 when measured on a 10-point numeric rating scale [2, 3].

Postoperative pain is experienced by nearly all patients undergoing surgical procedures as it is a predictable part of the surgical recovery process. Inadequately managed pain would have significant clinical, psychological, and economic implications. Evidence suggests that more than 50% of surgical patients reported inadequate postoperative pain relief that might end up in a negative effect on the quality of life and various organ systems [4-7].

Inadequately managed postoperative pain might also lead to thromboembolic complications, prolonged hospital stay, return to the hospital after discharge, reduced quality of life,

and may progress to chronic pain. Practices of acute pain management over the last 30 years have demonstrated that effective pain relief can be achieved with a multitude of drugs (NSAIDs, opioids, and nerve blocks)[8, 9]. However, opioid analgesia remains the gold standard technique for long periods, but its usage is not free of side effects, I.e., nausea, vomiting, bowel dysfunction, sedation, respiratory depression, and long-term physical dependence [4, 10].

Preemptive analgesia has become one of the most promising strategies for pain management. However, the precise definition of preemptive analgesia remained controversial, the explanatory concept behind it indicates that an analgesic intervention begins before the noxious stimulus arises which has beneficial effects in reducing postoperative pain and the occurrence of postoperative pain. [11]

A range of drugs with their antipain effects were studied to have their preemptive analgesic effect, however, NSAIDs had been suggested by scholars. Diclofenac sodium was a nonsteroidal drug with an opioid-sparing effect, good preemptive analgesic effect, fewer side effects, easy availability, and administration [12, 14]. This study aimed to evaluate the effectiveness of preemptive diclofenac for postoperative pain management in patients undergoing abdominal hysterectomy surgery at Tikur Anbessa specialized hospital.

METHODS AND MATERIALS

Study setting

The study was conducted at Tikur Anbessa Specialized Hospital which is among the highest-ranked public hospitals in Ethiopia and is located in the capital city, Addis Ababa. This manuscript was prepared and reported according to STROCSS 2021 guidelines [15] and registered with at http://www.researchregistry.com with unique identity number researchregistry8074.

Study design and period

A hospital-based observational prospective cohort study was conducted from March to August 2020.

Source population

All patients who were scheduled for elective gynecologic surgery at Tikur Anbessa specialized Hospital.

Study Population

All eligible patients underwent abdominal hysterectomy under general anesthesia during the study period.

Eligibility criteria

All adult ASA class I and II patients undergoing gynecologic surgery were included in the study. Whereas patients with a history of peptic ulcer disease, allergy to diclofenac, renal disease, hypertension, bleeding diathesis, patients in chronic pain, age<18, use of analgesics (morphine, diclofenac, tramadol...etc.) within 6 hours preoperatively, patients with nerve blocks in perioperative time, and patients with cognitive impairment were excluded from the study.

Study variables

Dependent variables

- Postoperative pain severity,
- time to first analgesic request,
- total analgesic consumption with in the first 24 hours , and
- The occurrence of nausea and vomiting with in the first 24 hours after surgery.

Independent variables

- Sociodemographic
- Intraoperative analgesics
- Exposure variable (diclofenac IV or not)

Sample size calculation and sampling procedures

The sample size was calculated based on the mean comparison of pain scores with equal sample sizes for two independent cohorts. We used the study conducted in India in 2016 to compute the sample sizes for our study since we could not find related studies in our country. The mean pain score of the above-mentioned study was 1.80 (±1.19) and 2.53 (±1.11) in the preemptive diclofenac and placebo group respectively in the first 24 postoperative hours [13].

The following assumptions were considered during the sample size determination: significance level at 5 %(α=0.05), and a power of the study (1-β) of 80%. The required sample size was calculated as:

$$n1 = n2 = \frac{\left(\delta 1^2 + \delta 2^2\right)\left(z\alpha/2 + z\beta\right)^2}{\left(\mu 1 + \mu 2\right)^2}$$

Where n1 =n2= the sample size in each of the groups.

μ1 = Sample mean in the exposure group.

μ2= Sample means in the nonexposed group.

μ1 - μ2 = the difference the investigator wishes to detect

$\delta 1^2$= Sample variance in the exposure group

$\delta 2^2$= Sample variance in the nonexposed group.

α =0.05, $Z_{\alpha/2}$= 1.96.

Power = 0.80, Z_{β}= 0.84.

$$n1 = \frac{\left(1.19^2 + 1.1^2\right)\left(1.96 + 0.84\right)^2}{\left(1.8 + 2.53\right)^2} = 39$$

since two equal samples assumed, n2=39.

Adding an attrition rate of 10% makes the total sample size of the study 86, with each group comprising 43 participants.

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Sampling procedures

A systematic random sampling technique was used to select the participants.

Data collection Procedures

Data was collected by two trained anesthetists and supervised by a senior anesthetist. Before starting the data collection, an explanation of the objectives of the study and how to report pain using the visual analog scale (VAS scale) was provided to the study participants. Informed consent was obtained verbally (since this study was just observational) from each participant. On the morning of the surgery, the data collectors instructed the participants on how to self-report their pain after surgery using the VAS scale. The majority of anesthetists in our clinical area used to practice diclofenac sodium 75 mg IV 30 min to one hour prior to (prophylaxis) starting surgical incision preoperatively for postoperative analgesic augmentation. However, some anesthetists do not use this technique and only order analgesics in the postoperative period. Thus, we used this practical discrepancy to group the study participants as group D (diclofenac IV given) and group C (diclofenac not given or control) while other pain management approaches were held similar in both groups.

Postoperative pain severity, total analgesic consumption, time to the first analgesic request, and the incidence of nausea and vomiting were compared at the 2nd, 4th, 8th, 12th, and 24th hour postoperatively in both groups.

Data Analysis and Interpretation

The data was analyzed using SPSS Version 22. Numeric data were described using the mean and standard deviation or median and interquartile range. Frequency and percentage were used to describe categorical variables. Numerical variables were analyzed using the student's t-test and Manny Whitney U test depending on the distribution of data. The results were displayed in tables. P-value <0.05 was considered statistically significant.

RESULTS

Sociodemographic and operative characteristics

Age, ASA, weight, induction agent, type and dose of analgesic drugs, duration of surgery and anesthesia, preoperative diagnosis/ indications for surgery, baseline MAP, and HR were compared between the two groups (**Table 1**).

Table 1. the demographic and intraoperative characteristics of women whom underwent abdominal hysterectomy surgery at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia.

Variables	Group D(n=43)	Group C(n=43)	P-Values
Age (year)	32.55±7.82	31.45±8.45	0.448
ASA I / II	29/16	27/18	0.664
Weight (Kg)	54.733±5.77	55.800±6.46	0.408
Induction agent			
Ketofol	28 (62.2%)	27 (60%)	0.996
Ketamine	11 (24.4%)	12(26.6%)	
Propofol	5(11.1%)	5(11.1%)	
Thiopentone	1 (2.2%)	1(2.2%)	
Intraoperative analgesic type			
Morphine	14 (31.1%)	16(35.6%)	0.655
Pethidine	31(68.9%)	29(64.4%)	
Intraoperative analgesic dose			
Morphine(mg)	1.24±2.11	1.74±2.47	0.302
Pethidine(mg)	37.78±26.43	33.22±26.93	0.418
Surgery duration (min)	81.60±25.19	80.70±22.89	0.868
Anesthesia duration(min)	95.85±26.68	94.20±23.97	0.772
Preoperative diagnosis (indications for surgery)			
Benign tumors	41(88.9%)	40(87.5%)	0.725
Neoplastic tumors	4(11.1%)	5(12.5%)	
Baseline MAP	90.10±10.95	89.42±10.79	0.778
Baseline HR	88.46±10.65	88.35±10.43	0.969

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Comparison of Postoperative Pain Severity

The median pain scores between the groups were compared at different time intervals and displayed below (**Table 2**).

Table 2. Comparison of postoperative pain severity among women whom underwent abdominal hysterectomy surgery at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia.

Variables	Group D (n=43)	Group C (n=43)	P -values
2nd post-operative hour	1(0-2)	2(1-3)	0.007
4thpost-operative hour	2(1-3)	3(2-4)	0.004
8th post-operative hour	2(1-3)	4(3-5)	0.001
12th post-operative hour	3(2-4)	3(2-4)	0.261
24th post-operative hour	3(2-4)	3(2-4)	0.796

Comparison of time to first analgesic request and total postoperative analgesic consumption

The mean duration of the first analgesic request and total postoperative analgesic consumption within the first 24 hours of surgery for both groups were compared and presented (**Table 3**).

Table 3. Comparison of the time to first analgesic request and total analgesic consumption over 24 hours among women whom underwent abdominal hysterectomy surgery at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia.

Variables	Group D(n=43)	Group C(n=43)	P-values
Time to first analgesic request (minutes)	186.60±35.19	174.45±24.88	.087
Total postoperative tramadol consumption within 24 hrs.(mg) Tramadol	153.75±44.41	174.44±50.57	.0350

The incidence of Nausea and Vomiting

The overall incidence of nausea and vomiting over 24 hours postoperatively was 37.5% and 15%, respectively. While nausea was observed in 32.5% of group D, it was reported as 42.5% in group C. (p=0.536). The incidence of vomiting over 24 hours was 12.5% and 17.5% in groups D and C, respectively. (p=0.531)

DISCUSSIONS

This study showed that a single preoperative dose of diclofenac sodium reduced the postoperative pain severity in the early postoperative hours and significantly reduced analgesic demand for 24hrs postoperatively in patients that underwent abdominal hysterectomy surgery. Our study revealed that preemptive diclofenac significantly reduced the median pain score in group D compared to group C at the 2nd, 4th, and 8th hours postoperatively (p= 0.007, 0.004, and 0.001 respectively). The result of this study is comparable with RCT conducted in Ethiopia which showed diclofenac had significantly reduced pain scores in the diclofenac group compared to the placebo group in the 4th, 6th, and 8th post-operative hours (p<0.05). The difference observed between the two studies in the 2nd hour is probably due to the difference in study design [16]. Our results were also supported by the findings of a study conducted in India which showed significantly lower pain scores in the 1st, 2nd, and 3rd postoperative hours(p<0.05). The likely explanation for this may be the usage of the same dose of diclofenac preemptively [17]. The result of this study is contrary to the result of RCT done in India which showed no significant difference in preoperative administration of diclofenac in the early postoperative hours(2nd and 4thhrs) between treatment and placebo groups(p>0.05). The likely explanation for this may be the difference in the route of administration of preoperative diclofenac (rectal suppository in their study) and the study population (conducted on the pediatric population) [18].

The total postoperative analgesic consumption was significantly lower in the diclofenac group (group D). The mean total postoperative diclofenac and tramadol consumption were 146.25±50.81mg and153.75±44.41mg in the diclofenac group (group D) and187.50±50.95mg and 174.44±50.57mg in the group C respectively (p<0.05). These results were in line with the study conducted in Ethiopia. The likely explanation may be the similarity between the study settings and the pain management practice [16]. The result of our study is also supported by the study done in Hungary which demonstrates that a single preoperative dose of diclofenac significantly reduced morphine consumption in five consecutive postoperative days in the treatment group when compared to the placebo group (p<0.05) [19].

The time to first analgesic request in our study showed a non-significant difference between the two groups. The mean duration in minutes for the first analgesic request was

186.60±35.19 and 174.45±24.88 for group D and Crespectively (p=0.087). This is contrary to the study done in Ethiopia that demonstrated a significant increase in the mean first analgesic request time in the preemptive diclofenac group compared to the placebo group. The probable reason for this may be due to differences in study design and the response of health caregivers to the patient's complaints [16].

Our result showed the overall incidence of nausea and vomiting in the first 24 hours is 37.5% and 15%, respectively. The proportion of patients who experienced nausea is 32.5% and 42.5% in Group D and C respectively (p=0.536). The proportion of patients who reported vomiting were 12.5% and 17.5% in group D and C, respectively (p=0.531). This finding is in line with a study conducted in Ethiopia that showed no significant difference in the incidence of nausea and vomiting [18]. Even though there is no statistical significance, a clinically better outcome has been observed in the diclofenac received group.

The strength and limitation of the study

Strength: this study was conducted on a homogenous population.

Limitations: it failed to assess the severity of pain at movement, lacks randomization and only considered single type of surgery.

The manuscript was derived from the original research conducted by the authors in 2020 [20].

CONCLUSION

The findings of this study showed that preemptive diclofenac sodium 75mg IV had significantly reduced pain severity, prolonged analgesic duration, and lower total postoperative analgesic consumption in gynecologic surgical patients while having fewer associated side effects. We recommend anesthesia providers use 75 mg of diclofenac sodium 30 minutes to one hour before surgical incision. Future studies with large sampled RCT will be recommended.

Acronyms

ASA: American society of anesthesiologists
HR: Heart rate
MAP: Mean Arterial pressure
VAS: visual analog scale
NSAIDs: non-steroidal anti-inflammatory drugs

Provenance and peer review

Not commissioned, externally peer-reviewed

Declarations

Competing interests: The authors do not have any competing interest to disclose

Ethics approval and consent to participate: Ethical clearance/ approval was obtained from Addis Ababa University College of health sciences IRB and verbal informed consent was obtained from the participants after explaining the study importance.

Consent for publication: Not applicable

Availability of data and materials: Data will be shared upon reasonable request from the corresponding author.

Funding: This study was funded by Addis Ababa University

Authors' contributions: Both authors contributed equally in this manuscript production

Acknowledgements: Special gratitude to those who had direct or indirect involvement in this study. We would like to thank data collectors and hospital employers for the facilitation of our study.

Author information (optional): not applicable

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