

Utilization and Evaluation of Analgesics in Post Gynecologic Operations: A Cross- Sectional Study

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Abstract

Background: This study evaluated the current practices of opioid and non-opioid analgesic administration for postoperative pain management in gynecological surgeries, aiming to optimize pain relief while minimizing side effects.

Methods: A cross-sectional, prospective Drug Utilization Evaluation (DUE) study was conducted at Al-Zahra Hospital, Tabriz, Iran. Medical records of 100 patients undergoing gynecological surgery were reviewed over five months. Data on prescribed analgesics, pain scores, and adherence to APS2016 and ERAS2016 guidelines were collected and analyzed statistically.

Results: Meperidine (pethidine) and diclofenac were the most frequently prescribed analgesics. The average patient pain score was 2.48 units. A combination of meperidine, diclofenac, and acetaminophen was identified as the most effective regimen for pain control. Prescribed regimens demonstrated 41.4±27.3% theoretical and 60.60 ± 28.77% practical compliance with APS2016 and ERAS2016 guidelines. While achieving the primary objective of pain relief with minimal side effects, compliance with established guidelines could be further improved through educational interventions.

Conclusion: Optimizing analgesic regimens for postoperative pain management requires careful consideration of individual patient needs, including the benefits of opioid analgesics in achieving greater pain reduction. Adherence to evidence-based guidelines and ongoing educational programs for healthcare professionals are crucial for ensuring optimal pain relief with minimal side effects.

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Introduction

There has been little improvement in post-surgical analgesia during the past 20 years, despite the increased awareness and clinical advances in pain management. In many cases, patients continue to experience considerable pain after surgery (1-3). A growing emphasis on performance-based reimbursement and public participation in healthcare data will make it more challenging for healthcare professionals to achieve adequate analgesia post-surgery. The most common therapeutic problem in hospitals is postoperative pain. As a result, it can lead to reduced breathing and

cough suppression, pulmonary secretion retention, and pneumonia as well as delayed gastric and bowel function, thus prolonging the recovery process. While there is no compelling evidence, reducing postoperative pain may increase patients' comfort and reduce their hospital stay (4-6). However, even when doctors and nurses acknowledged moderate to severe pain, the stated aim was to partially reduce pain, but not to eliminate it completely. The high failure rate of analgesic therapy is clearly influenced by patient attitudes and convictions (7, 8). The United States has adopted enhanced recovery after surgery (ERAS) protocols to improve patient recovery (9). To limit opioid

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consumption during hospital care, enhanced recovery after surgery protocols includes multimodal analgesia (10, 11). This includes medications administered preoperatively, intraoperatively, and immediately following surgery to target different pain pathways. These efforts aim to reduce the negative effects of opioids (sedation, nausea, vomiting, ileus, respiratory depression, and pruritus), which can impair the patient's recovery. Unfortunately, many ERAS protocols neglect to post-discharge patient care, which leads to an over prescription of opioid pain medications for patients at home (12-14). The use of multiple, or "balanced," analgesic techniques is becoming increasingly popular to prevent pain after surgery, such methods include local anesthetics, ketamine, acetaminophen, and nonsteroidal anti-inflammatory drugs (10, 11, 15). The main topic of this research is pain relief in gynecological surgeries, which includes the following: (I) Vaginal hysterectomy; (II) Open general gynecologic surgery; (III) Caesarean section; (IV) Laparoscopic and oncology surgery. Researchers can manipulate pain severity data using a variety of instruments that convert internal painful experiences into a number (7, 8, 16). A Visual Analog Scale (VAS), Numeric Rating Scale (NRS), and Verbal Rating Scale (VRS) are all commonly used. VAS is a horizontal or vertical line, most commonly 10 cm long, marked at its extremes with "no pain" and "worst pain imaginable." Moreover, an NRS provides numbers from 0 to 10 (often 0-20 or 0-100) to represent levels of pain severity, from none to "the most intense pain imaginable." For postoperative analgesia, opiates are commonly administered systemically or neuraxial (7, 9). Thromboembolic events are more likely to occur in patients after cesarean delivery, which is also associated with immobility from insufficient pain management and excessive sedation caused by opioids. In addition, the analgesic of choice should be minimally absorbed through breast milk, have little to no effect on neonates, and should not interfere with the care of the newborn or discharge from the hospital. The more pain relief provided, the better the postoperative outcomes, whereas unrelieved postoperative pain could result in heightened pain responses and chronic pain, whose incidence after cesarean delivery is unknown and currently investigated (15, 17, 18). Based on their chemical structure, opioids can be categorized into three main groups: 1) morphine-like agents including hydromorphone and morphine; 2) Meperidine-like agents such as fentanyl, remifentanyl, and meperidine; and 3) diphenyl heptanes, including methadone (14, 19). Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), specifically ibuprofen, are both effective and analgesic. Low postoperative VAS scores, extubating times, and opioid consumption were examples of these

effects (12, 20, 21). In addition to being safe and cost-effective, acetaminophen (also known as paracetamol) provides significant analgesic effects when administered in analgesic dosages. Even though both parenteral and rectal acetaminophen has analgesic effects in the postoperative period, an NSAID in conjunction with acetaminophen is superior. Also, a variety of non-opioid pharmacologic agents for use during the perioperative period, such as adenosine, droperidol, magnesium, neostigmine, and gabapentin, are believed to reduce pain (6, 9, 16). There are several nonpharmacologic "electroanalgesic" techniques that are beneficial in the management of acute postoperative pain, including transcutaneous electrical nerve stimulation (TENS), acupuncture-like transcutaneous electrical nerve stimulation, and percutaneous neuromodulation therapy (4, 9, 16). Studies conducted between 1987 and 2002, coupled with subsequent meta-analyses in 2012, revealed that the general population undergoing surgical procedures often lacked adequate pain relief (6, 8, 9, 16, 19). and the emergence of new methods to reduce pain requires more insightful re-examination. To describe the type of medication used and its compliance with the APS 2016 and ERAS 2016 guidelines and to answer the basic question of whether these analgesics have been able to relieve the patient's pain or not, using the Drug Assessment Pattern (DUE) (Drug Utilization Evaluation) was used. An evaluation of drug utilization aims to identify individuals who adhered to guidelines and target this population for interventions to improve clinical outcomes (22-24). By preventing flares that result in costly interventions, these strategies will enhance both the quality of care and the value of the healthcare system. The main outcome of this study is to rationalize the administration of opioids along with other analgesics to control pain after gynecological surgery based on the APS2016 and ERAS2016 guidelines.

Methods

The study is a DUE (Drug Utilization Evaluation) study that is cross-sectional and prospective. This study has been designed to explain the rational use of analgesics in patients who underwent any type of surgery in Al-Zahra Hospital in Tabriz at four major wards (surgery, gynecology, ICU, oncology) from September to January 2020 and received postoperative analgesics. Due to emerging covid 19 the study limited to minimum patient needed for significance of analytic test that is 100. The collected information can be divided into three categories: First, the demographic information included all personal information including age, height, weight, cause of hospitalization, type of operation, history of underlying disease, date of hospitalization, date of operation, date of data collection, duration of

hospitalization. The second part included information on various drugs other than analgesics. Information such as type of drug, prescribed dose, intervals of administration and period of use, and route of use were recorded. In the third section, we discuss analgesics and the assessment of pain relief. The researcher collected data on pain levels before and after taking the drug to assess the amount of pain, pain level assessed with NRS 5 (15). For analgesic drugs, information was collected regarding the types, the prescribed doses, the intervals of administration, the period of use, as well as the method of consumption. The study was approved by the ethics committee of Tabriz University of Medical Sciences with the ethical code IR.TBZMED.REC.1398.1108.

Data Analysis

In order to comply with APS 2016 and ERAS 2016 (9, 16), patient information was analyzed with SPSS 26 software: Kolmogorov–Smirnov test and independent t-test were employed as statistical tests. In order to achieve accurate

drug compliance, these guidelines do not specify a fixed method of relieving pain, in reality, they give an overview of a set of recommendations for different situations, allowing them to make the right choice. To assess whether pain relief methods adhere to APS 2016 and ERAS 2016 guidelines, five recommendations from the entirety of APS 2016 and ERAS 2016 have been selected. These are as follows:

1. Multimodal method is used.
2. Morphine or another short-acting opioid has been used in the first line of treatment.
3. Acetaminophen has been used.
4. The combination of acetaminophen with NSAIDs has been used.
5. Electrical and mechanical stimulation methods have been used along with behavioral therapy.

Each of the above is worth one point, so it is obvious that the more methods and drugs used, the higher the score. (Table 1)

Table 1. Options for Components of Multimodal Therapy for Commonly Performed Surgeries

NONPHARMACO LOGIC Therapies	Cognitive modalities TENS	Cognitive modalities TENS	Cognitive modalities TENS	Cognitive modalities TENS	Cognitive modalities TENS	Cognitive modalities TENS	Cognitive modalities TENS
NEURAXIAL ANESTHETIC TECHNIQUES	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	Epidural with local anesthetic (with or without opioid), or intrathecal opioid	
REGIONAL ANESTHETIC TECHNIQUES	Paravertebral block	Transversus abdominis plane block	Site-specific regional anesthetic technique with local anesthetic	Site-specific regional anesthetic technique with local anesthetic		Transversus abdominal plane block	
LOCAL, INTRA-ARTICULAR OR TOPICAL TECHNIQUES*		Local anesthetic at incision i.v. lidocaine infusion	Intra-articular local anesthetic and/or opioid	Intra-articular local anesthetic and/or opioid	Local anesthetic at incision	Local anesthetic at incision	
SYSTEMIC PHARMACOLOGIC THERAPY	Opioids NSAIDs and/or acetaminophen Gabapentin or pregabalin i.v. ketamine	Opioids NSAIDs and/or acetaminophen Gabapentin or pregabalin i.v. ketamine i.v. lidocaine	Opioids NSAIDs and/or acetaminophen Gabapentin or pregabalin i.v. ketamine	Opioids NSAIDs and/or acetaminophen Gabapentin or pregabalin i.v. ketamine	Opioids Acetaminophen Gabapentin or pregabalin i.v. ketamine	Opioids NSAIDs and/or acetaminophen	Opioids Acetaminophen Gabapentin or pregabalin i.v. ketamine
TYPE OF SURGERY	Open laparotomy	Thoracotomy	Total hip replacement	Total knee replacement	Spinal fusion	Cesarean section	CABG

Results

100 patients who underwent surgery were evaluated in this study and the data they provided was categorized.

There was a mean age of 40.33± 13.94, a mean weight of

72.30± 11.81, and a mean height of 161.98± 8.02. After surgery, the average length of stay was 1.47 ± 1.34 days. 47 (47%) had an underlying disease and 53 (53%) had no history of underlying disease. Hypertension was the most common underlying disease observed in patients.

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Among the surgeries, hysterectomy was the most common operation. Including 24 % of all operations

Besides conventional medications, such as preoperative antibiotics, which were generally the same for everyone, patients with disease or a particular condition took other medicines.

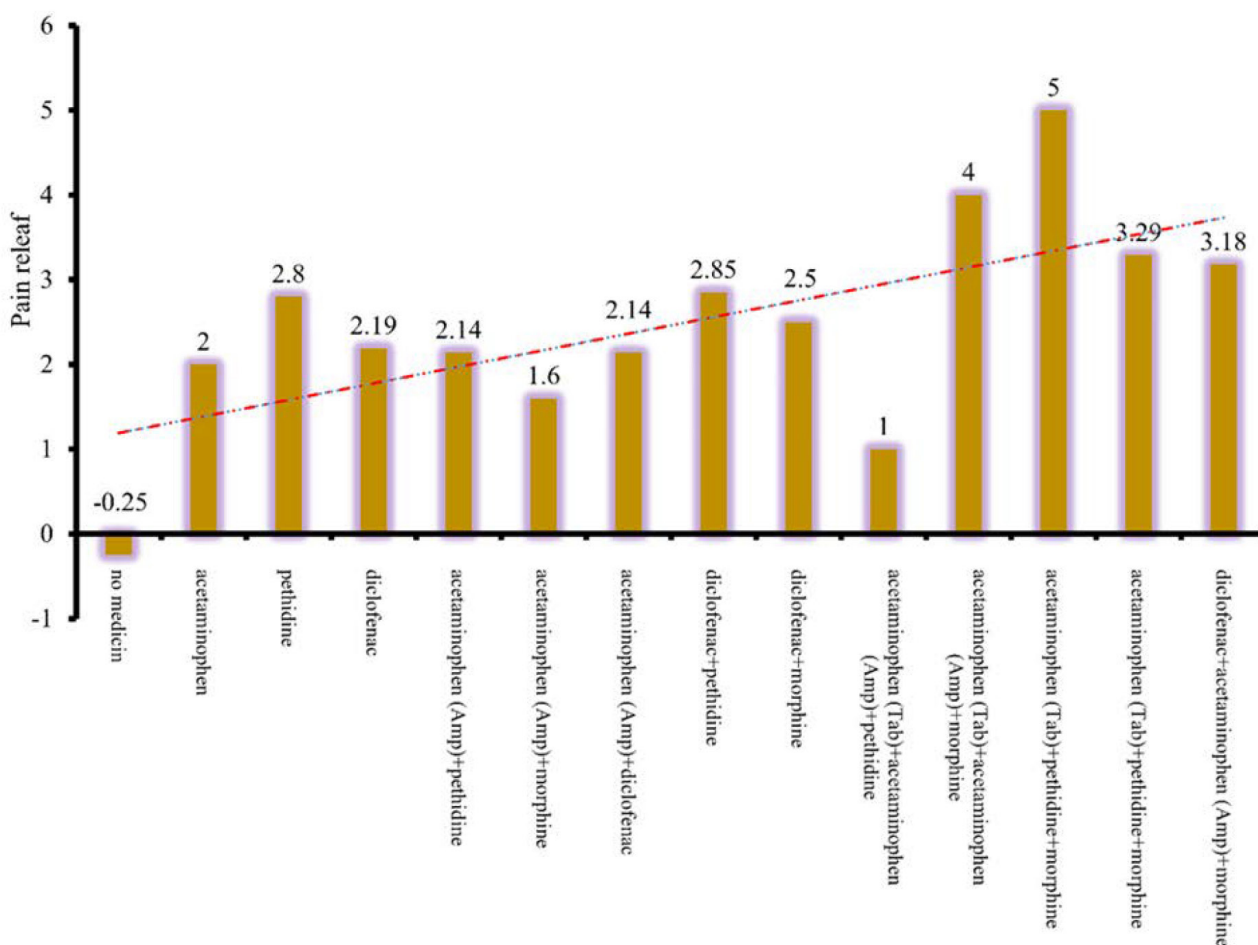
Generally, patients reported severe pain in scale of NRS 5 before taking painkillers (NRS ≥ 5), which is assumed normal after surgery. The frequency of pain levels can be seen as 61% of patients had a maximum pain level of 5 (average = 4.1 ± 1.34).

Analgesics significantly reduced the pain of patients by half after taking them. That drops pain level in scale of NRS 5 to average 2 ± 1.08

Patients received different combinations to provide pain relief, including diclofenac suppositories, 100 mg, morphine, 3 mg, meperidine (pethidine), 50 mg, and acetaminophen, 1000 mg, which are divided into three

categories: There are one type, two types and three types of analgesics. Based on the obtained statistics, a combination of 3 types of drugs was the most effective in reducing pain in patients. Acetaminophen ampoule, diclofenac suppository, and pethidine (meperidine) ampoule demonstrated the greatest reduction in pain among the 3 drug combinations due to their number of uses. Statistical testing showed no significant difference between the use of a combination of two drugs and the use of one drug with a p-value of 0.458. Therefore, two drugs are not more effective than one drug for relieving pain in a patient. Compared to a combination of two drugs, a combination of three drugs with a p-value of 0.025 significantly reduced the patient's pain. Also, In comparison with mono-drug compounds, the three-drug type has provided significantly more relief with a P value of 0.028. Statistically, the three medications in the combination most closely aligns with the APS 2016 and ERAS 2016 guidelines, demonstrating that following these guidelines can help relieve patients' pain (Fig.1).

Figure 1. The amount of pain reduction in drug combinations.

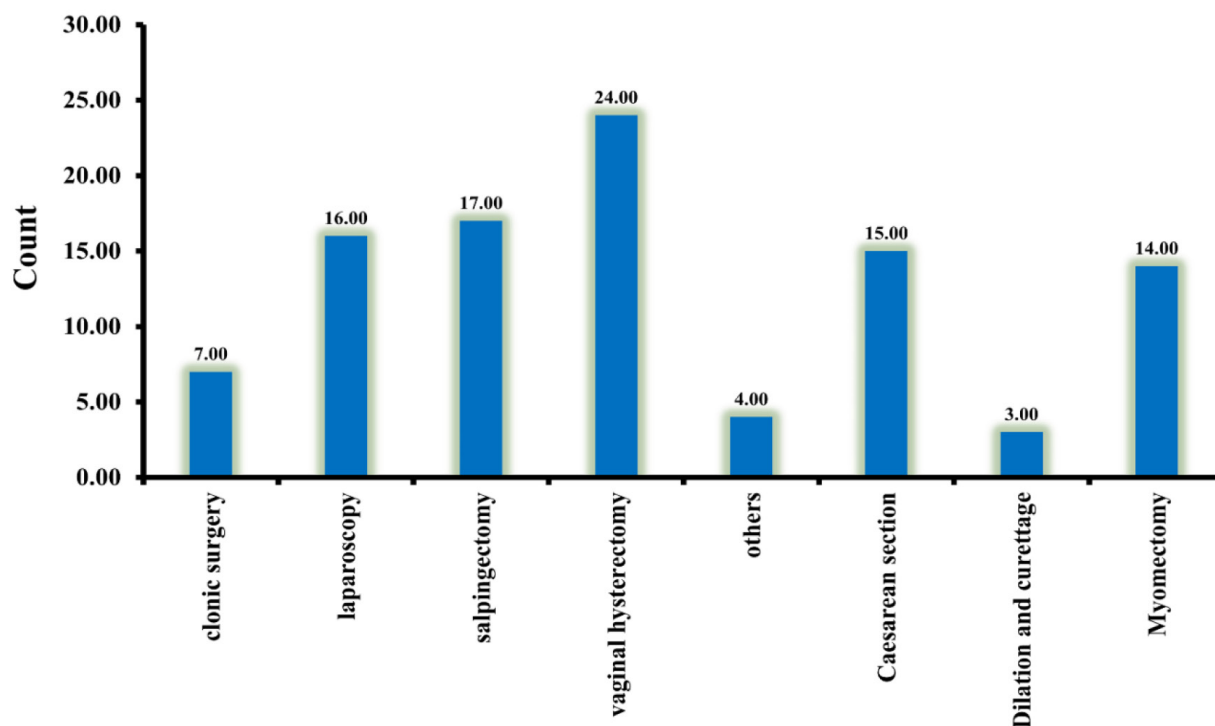


66% of cases have analgesic regime including narcotic analgesics while 34% of cases used analgesics except narcotic analgesics. Analgesic were significantly more effective in relieving

pain in versus regime without narcotic analgesics ($P = 0.018$).

By comparison, hysterectomy has led to the greatest reduction in pain following surgery (Figure 2).

Figure 2. Comparison of surgical procedures in pain reduction.



Oncology patients reported the most pain relief, while patients in gynecology experienced the lowest level of relief.

We compared the compliance with APS 2016 and ERAS 2016 guidelines when measuring pain management drug methods. According to the criteria, $41.4\% \pm 27.4\%$ of prescribed analgesics follow the recommendations of APS 2016 and ERAS 2016 guidelines. In addition, ketorolac and meperidine (pethidine) should not be used during cesarean surgery in certain case.

Discussion

In this study, we performed a DUE study to rationalize the use of opioids after surgery according to the APS 2016 and ERAS 2016 guidelines by considering different criteria, such as cost of medications, type of pain relief medications and opioid-sparing method has been performed. Hospitalizations were highest in the oncology ward with 46 patients, followed by the ICU ward and female ward with 26 and 28 patients, respectively. A hospital with an

oncology ward had the highest average pain reduction rate of 2.61 among all the wards. Additionally, ICU has a slight difference of 2.58. The only part rated lower for pain relief is gynecological surgery. A wide variety of surgeries are performed on patients. In terms of the number of operations, hysterectomies were the most common, followed by salpingectomies and laparoscopies. The highest amount of pain reduction compared to the number is related to vaginal hysterectomy. The best pain relief was obtained with a combination of three drugs. In this study, all protocols included diclofenac suppositories 100 mg, morphine 3 mg, meperidine (pethidine) 50 mg, and acetaminophen 1000 mg. Combinations of two drugs, three drugs, or just one drug have been prescribed, but the combination of two drugs is most commonly prescribed. Combining meperidine (pethidine) with diclofenac has the greatest number of uses. A combination of three drugs, acetaminophen, diclofenac, and meperidine (pethidine) provide the most pain relief for the number of uses. Also, taking more medications decreases the individual doses

required for each medication. It also means, reducing the side effects of the medications while achieving a greater analgesic effect with a synergistic effect of the medications. Prior to receiving analgesics, 61 patients (61%) reported the maximum level of pain, which is level 5 and the patients' mean total pain was 4.1. Among the three procedures, myomectomy, vaginal hysterectomy, and laparoscopy caused the most pain, respectively. Analgesics significantly reduced the pain of all patients and the average pain of patients shows 1.6 units. A total of 36 patients (equivalent to 36%) reported pain level 1, but only 7 patients (equivalent to 7%) reported pain level 4. There have never been reports of pain level 5 after taking painkillers. According to (9, 16, 25). Despite the availability of narcotic analgesia at the physician's order, 75.2% of the patients reported moderate to severe pain distress. According to Patient controlled-analgesia (PCA) with intravenous opioids leads to high satisfaction rates in the treatment of post-operative and cancer pain. Additionally, PCA with opioids is used to treat postoperative pain after cesarean delivery and labor pain in obstetric analgesia. In this study, people who used narcotic analgesics had significantly less pain than those who did not. However, none of the cases showed a reduction in narcotic dose by using several drugs. Nevertheless, they provided more pain relief than the drug alone (11, 15).

As a result of the present study, the use of multimodal methods could not reduce the opioid dosage. (It could have provided better pain relief) But for a variety of reasons, we cannot consider this information accurate:

- 1) Generally, patients in this study stay in the hospital for one day, and no further administration or dose adjustment is done in order to get a detailed analysis of the effects of the multimodal method.
- 2) Doctors have prescribed opioids alone at the same doses as they do when prescribing drugs together; in other words, they have not considered the principles of prescribing drugs together when prescribing opioids alone.

Although one of the aims of this study was to investigate the effects of using multimodal methods in reducing opioid doses. This study shows how increasing the total cost of analgesics leads to greater pain relief for the patient thus, the increase in the total price of drugs indicates the use of different types of analgesics. In addition, several analgesics further reduce the patient's pain. According to the use of opioid-sparing treatments can help to reduce postoperative pain, and this has had an actual economic impact. The interesting part of this study is that opioids in our country are not considered expensive drugs and are

among the cheapest drugs after the diclofenac suppository. In addition, Acetaminophen is more expensive than them, and Opioid Sparring methods may not always be more favorable than the drug itself. However, Opioid Sparring methods can still decrease side-effects costs. In terms of cost efficiency, diclofenac and meperidine (pethidine) had the best performance.

Conflict of interest

The authors declare that they have no conflict of interest in this work.

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