Journal of Medicine, Physiology and Biophysics
ISSN 2422-8427 An International Peer-reviewed Journal
Vol.41, 2018


# EFFICACY OF INTRAVENOUS ACETAMINOPHEN VERSUS KETAMINE FOR POSTOPERATIVE PAIN AFTER ABDOMINAL HYSTERECTOMY

DR. ATIF NADEEM, MBBS

Department of Medicine,

Nishtar Hospital, Multan, Pakistan.

DR. MUHAMMAD ZAHID SHAHZAD, MBBS

Department of Medicine,

Nishtar Hospital, Multan, Pakistan.

DR. SHOAIB IQBAL, MBBS

Department of Medicine,

Nishtar Hospital, Multan, Pakistan.

**Abstract;**
**Objective;** To determine the efficacy of intravenous acetaminophen versus ketamine for postoperative pain after abdominal hysterectomy. **Material and Methods;** A total of 114 women undergoing abdominal hysterectomy were taken in this study. The study was conducted from June 2017 to May 2018 at department of Anesthesiology, Nishtar Hospital, Multan. **Results;** Our study comprised of 114 ladies undergoing abdominal hysterectomy, mean age of the study cases was 54.13 ± 6.89 years (with minimum age of the patients was 39 years while maximum age was 68 years). Majority of our study cases i.e. 92 (80.7 %) had parity more than 3 and American Society of Anesthesiology (ASA) score level 1 in 93 (81.6%). Sixty one (53.1%) belonged to rural areas, while mean duration of surgery was 72.80 ± 11.32 minutes. Mean BMI level in our study cases was noted to be 23.98 ±4.17 Kg/$m^2$ and obesity was present in 34 (29.8%) of our study cases. Efficacy was noted in 60 (52.6 %) of our study cases. Efficacy was 73.7% study cases in group A while 18 (31.6%) in group B (p=0.000). **Conclusion;** Our study results support the use of intravenous acetaminophen (IVA) for pain management in patients undergoing abdominal hysterectomy compared with ketamine. Intravenous acetaminophen is safe, reliable and effective for the pain management in postoperative abdominal hysterectomy patients which was associated with shorter hospital stay and cost effective for the suffering families. No adverse reactions were noted in this study with the use of intravenous acetaminophen.
**Keywords;** Intravenous acetaminophen, Ketamine, Abdominal Hysterectomy.

## Introduction:

Abdominal hysterectomy is one of the most common surgeries performed in gynecology. Abdominal hysterectomy is performed for malignant as well as benign indications such as uterine leiomyoma, persistent vaginal bleeding, or pelvic organ prolapse. Hysterectomy can be performed in several different approaches: vaginal, laparoscopic and open abdominal. The choice of surgical approach depends on the indication for surgery, the presence of previous abdominal or pelvic surgery, the patient's medical history and background illnesses, Body Mass Index, and the surgeon's expertise. The level of pain associated with hysterectomy as well as the length of the period of convalescence depends on the surgical approach. The open abdominal hysterectomy is considered a major surgery and is associated with a medium to high pain level.[1]

 

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage". Intense and prolonged pain transmission, as well as analgesic under medication, can increase surgical postsurgical / traumatic morbidity, delay recovery, and lead to development of chronic pain.[2]

Treatment of pain after abdominal hysterectomy begins with pre-emptive analgesia, starting with preparation and premedication for anesthesia, balanced anesthesia during the operation, and of course continued analgesia( repeated boluses or infusion) during the entire recovery period.[3] Pain management can take many forms, although systemic opioid analgesics and patient-controlled analgesia remain at the forefront of pain management, this class of medications is associated with multiple common adverse reactions (pruritus, nausea, vomiting, constipation, respiratory complications, urinary retention, and altered mentation).[4] Nonsteroidal anti-inflammatory drugs (NSAIDs), ketamine, acetaminophen, and local anesthetics have all been reported to reduce postoperative opioid consumption.[5]

Although oral and rectal forms of acetaminophen have been in use for decades, intravenous (IV) acetaminophen has only recently become available. Despite its recent introduction, it has become a routine analgesic in operating rooms and inpatient wards. Its analgesic action has not been fully elucidated, but evidence suggests that it is mediated by both cannabinoid and serotonergic pathways in the central nervous system and, to a lesser degree, though peripheral anti-inflammatory effects.[6] Intravenous acetaminophen has been shown to have significant opioid-sparing effects for a multitude of surgical procedures, including abdominal hysterectomies.[7] Ketamine is N-methyl-*D*-aspartate (NMDA) receptor antagonist. Ketamine reduces the sensitivity of the central nervous system to painful stimuli.[8] Ketamine is generally accepted as an effective analgesic and has been used in obstetric and gynecological surgery for decades. Several systematic reviews have shown that subanaesthetic doses of ketamine. can reduce the intensity of postoperative pain and the consumption of opioids.[9] A recent study has reported that Visual analog scale score and the total analgesic use were both significantly less in the Acetaminophen group in comparison with the ketamine group.[10]Faiz HR and his associates has reported in a recent study that Visual analog scale scores were significantly lower in the IV acetaminophen (*P*=0.05), Visual analog scale score >3 was less in the IV acetaminophen group as compared with the ketamine group that is 50% versus 72.5% respectively.[11]

Internationally, many studies have been conducted comparing IV acetaminophen and ketamine for postoperative pain after abdominal hysterectomy. Different studies are showing different results. Some say IV acetaminophen is more effective for post operative pain and some studies favor ketamine as potent postoperative analgesia.

**Material and methods:**

Adult women with Planned abdominal hysterectomy having their age 25–70 years having American Society of Anesthesiologists (ASA) classification of 1 or 2 were included in this randomized controlled trial which was conducted by Department of Anesthesiology, Nishtar Hospital, Multan. Patients with H/o diabetes, Smokers, having severe hemorrhage (bleeding more than 1,500 ml during the surgery)( Blood was measured by using soaked gauzes, pads (weight = after use - before use) and blood clots which was weighed standardizing one milliliter blood to one gram) were excluded from our study. At study entry baseline demographics were recorded. Randomization was performed by Lottery method. It gave each potential participant a (usually equal) chance of being assigned to each group, 57 sample size for acetaminophen group while 57 sample size for ketamine group. Informed consent was taken. All patients were transferred to the operating room, standard ASA monitors was applied. Intubation was performed using 7 mm polyvinyl chloride endotracheal tubes. Anesthesia was maintained through the infusion of propofol at a rate of 100–120 μg/kg/min. The acetaminophen group (group A) received IV acetaminophen 15 mg/kg, and the ketamine group (Group B) received IV ketamine 0.15 mg/kg. Both medication solutions were prepared by the research pharmacist in 100 mL of normal saline and were administered by the anesthesia care team within a 15-minute time period. Duration of procedure was recorded. In the recovery room, an IV infusion pump (set to deliver a continuous infusion of fentanyl 30 μg per hour) was connected to each fully conscious patient. Patients were taught how to use Visual analog scale. Patients' levels of pain was assessed in the recovery room using a visual analog scale (VAS) 4 hours, 6 hours, 12 hours, and 24 hours after the surgery. Efficacy was finally assessed when Visual analog scale scores was < 3 at the end of 24 hours. Data was analyzed with statistical analysis program (SPSS version 21). Analysis was done to compare proportion of acetaminophen group and ketamine group. Chi-square test was applied to compare both groups in terms of efficacy taken $p \leq 0.05$ as significant.

 

**Results;**

Our study comprised of 114 ladies undergoing abdominal hysterectomy due to various underlying indications. Mean age of the study cases was 54.13 ± 6.89 years (with minimum age of the patients was 39 years while maximum age was 68 years). Mean age in group A was 54.77± 7.45 years while that of group B was 53.49 ± 6.27 years.

Majority of our study cases i.e. 92 (80.7 %) had parity more than 3 and American Society of Anesthesiology (ASA) score level 1 in 93 (81.6%) (Table No. 2 & 3). Sixty one (53.1%) belonged to rural areas, while mean duration of surgery was 72.80 ± 11.32 minutes. Minimum duration of the procedure was noted to be 55 minutes while maximum duration of surgery was 90 minutes. Mean duration of surgery in group A was 72.89 ± 11. 72 minutes while in group B was noted to be 72.70 ± 11. 01 minutes (p = 0.091). Our study results have indicated that majority of our study cases i.e. 84 (73.7 %) had duration of surgery more than 60 minutes. Mean BMI level in our study cases was noted to be 23.98 ±4.17 Kg/$m^2$ (with minimum BMI value was 20.5 while maximum level was 32 kg/$m^2$). Our study results have indicated that obesity was present in 34 (29.8%) of our study cases. Efficacy was noted in 60 (52.6 %) of our study cases. Efficacy was 73.7% study cases in group A while 18 (31.6%) in group B (p=0.000).

**Discussion;**

Hysterectomy is the second-most-common gynecological surgery in the United States after cesarean section. Nearly 40% of American women undergo hysterectomy before the age of 60 years[12,13]. Of the various surgical approaches to hysterectomy (abdominal, vaginal, laparoscopic, or open), the open abdominal approach has been correlated with relatively greater postoperative pain [14,15].

Our study comprised of 114 ladies undergoing abdominal hysterectomy due to various underlying indications. Mean age of the study cases was 54.13 ± 6.89 years (with minimum age of the patients was 39 years while maximum age was 68 years). Mean age in group A was 54.77± 7.45 years while that of group B was 53.49 ± 6.27 years. A study conducted by Faiz et al [11] has reported mean age in acetaminophen group as 49.9±6.9 years while in Kitamine group to be 47.2±7.2 years which is close to our study results. A study conducted by Yelchin et al [16] reported mean age in acetaminophen group was 48.26 ± 5.66 years compared with that of Ketamine group was 47. 2 ± 5.5 years which is slightly lower than our study results. Bhatti et al [17] from Sukkhar also reported peak age of abdominal hysterectomies occurring in 35 – 60 years of age which is in compliance with that of our study results. Another study from Karachi by Iftikhar R et al [18] reported 47 years mean age of the patients undergoing abdominal hysterectomy which is close to our study results.

Different studies conducted in Pakistan have documented relationship with increasing parity and hysterectomy [17, 18], similar findings were noted in our study as well. Majority of our study cases i.e. 92 (80.7 %) had parity more than 3 and American Society of Anesthesiology (ASA) score level 1 in 93 (81.6%). A study conducted by Yelchin et al [16] documented similar findings.

Sixty one (53.1%) belonged to rural areas, while mean duration of surgery was 72.80 ± 11.32 minutes. Minimum duration of the procedure was noted to be 55 minutes while maximum duration of surgery was 90 minutes.

Mean duration of surgery in group A was 72.89 ± 11. 72 minutes while in group B was noted to be 72.70 ± 11. 01 minutes (p = 0.091). Our study results have indicated that majority of our study cases i.e. 84 (73.7 %) had duration of surgery more than 60 minutes. A study conducted by Yelchin et al [16] has reported mean duration of surgery in acetaminophen group to be 70.00 ± 13.41 minutes while in Ketamine group was 70.38 ± 13.26 minutes. These findings of Yelchin et al are similar to that of our study results.

Mean BMI level in our study cases was noted to be 23.98 ±4.17 Kg/$m^2$ (with minimum BMI value was 20.5 while maximum level was 32 kg/$m^2$). Our study results have indicated that obesity was present in 34 (29.8%) of our study cases. A study conducted by Faiz et al[11] has reported mean BMI value in women undergoing abdominal hysterectomy to be 24.5 ± 3 kg/$m^2$ which is similar to that of our study results.

Postoperative pain and its complications can be attenuated with an appropriate perioperative analgesic regimen. Insufficient pain control has been suggested to contribute to various short-term and long-term complications, including poor patient satisfaction, development of chronic pain syndromes, delayed postoperative rehabilitation and patient mobilization, atelectasis, deep vein thrombosis, pulmonary embolism,

 

psychological trauma, ischemia, and myocardial infarction. Conversely, adequate pain relief reduces patients' anxiety, morbidity, and duration of hospitalization, along with the associated costs of car. Efficacy was noted in 60 (52.6 %) of our study cases. Different studies have documented the efficacy of IV ketamine and acetaminophen in different abdominal surgery including hysterectomies [19]. In our study, efficacy was 73.7% study cases in group A treated with IV acetaminophen while 18 (31.6%) in group B treated with IV ketamine (p=0.000). Faiz HR and his associates has reported in a recent study that Visual analog scale scores were significantly lower in the IV acetaminophen (*P*=0.05), efficacy in the IV acetaminophen group as compared with the ketamine group was 50% versus 27.5% respectively.[11] Another study by Yelchin et al [16] documented that there was no significant difference between IV acetaminophen and Ketamine in patients undergoing abdominal hysterectomy.

**Conclusion;**

Our study results support the use of intravenous acetaminophen (IVA) for pain management in patients undergoing abdominal hysterectomy compared with ketamine. Intravenous acetaminophen is safe, reliable and effective for the pain management in postoperative abdominal hysterectomy patients which was associated with shorter hospital stay and cost effective for the suffering families. No adverse reactions were noted in this study with the use of intravenous acetaminophen.

**References;**

1. Sutton C. Past, present, and future of hysterectomy. J Minim Invasive Gynecol. 2010;17(4):421-35.
2. Calderon M, Castorena G, Pasic E. Postoperative pain management after hysterectomy – a simple approach. Hysterectomy. 2012 Apr:269-82.
3. Arbel R, Stanleigh J, Ioscovich A. Pain management following abdominal hysterectomy: novel approaches and review of the literature. J Clin Gynecol Obstet. 2013;2(2):51-55.
4. Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka R, Sehgal N, et al. Opioid complications and side effects. Pain Physician. 2008;11(Suppl 2):S105–S120.
5. Tzortzopoulou A, McNicol ED, Cepeda MS, Francia MB, Farhat T, Schumann R. Single dose intravenous propacetamol or intravenous paracetamol for postoperative pain. Cochrane Database Syst Rev. 2011;(10):CD007126.
6. Mallet C, Daulhac L, Bonnefont J, Ledent C, Etienne M, Chapuy E, et al. Endocannabinoid and serotonergic systems are needed for acetaminophen-induced analgesia. Pain. 2008;139(1):190–200.
7. Moon YE, Lee YK, Lee J, Moon DE. The effects of preoperative intravenous acetaminophen in patients undergoing abdominal hysterectomy. Arch Gynecol Obstet. 2011;284(6):1455–60.
8. Petrenko AB, Yamakura T, Baba H, Shimoji K. The role of N-methyl-D-aspartate (NMDA) receptors in pain: a review. Anesth Analg. 2003;97(4):1108–16.
9. Bell RF, Dahl JB, Moore RA, Kalso E. Peri-operative ketamine for acute post-operative pain: a quantitative and qualitative systematic review (Cochrane review). Acta Anaesthesiologica Scandinavica. 2005;49:1405-28.
10. Rahimzadeh P, Imani F, Alimian M, Behzadi B, Faiz S. Comparison between ketamine and acetaminophen administered at the end of anesthesia for pain management after hysterectomy. JAP. 2013;4(1):15-24.
11. Faiz HR, Rahimzadeh P, Visnjevac O, Behzadi B, Ghodraty MR, Nader ND. Intravenous acetaminophen is superior to ketamine for postoperative pain after abdominal hysterectomy: results of a prospective, randomized, double-blind, multicenter clinical trial. J Pain Res. 2014 Jan 17;7:65-70.
12. Kongwattanakul K, Khampitak K. Comparison of laparoscopically assisted vaginal hysterectomy and abdominal hysterectomy: a randomized controlled trial. J Minim Invasive Gynecol. 2012;19(1):89–94.
13. Tzortzopoulou A, McNicol ED, Cepeda MS, Francia MB, Farhat T, Schumann R. Single dose intravenous propacetamol or intravenous paracetamol for postoperative pain. Cochrane Database Syst Rev. 2011;(10):CD007126
14. Nakamura K. Central circuitries for body temperature regulation and fever. Am J Physiol Regul Integr Comp Physiol. 2011;301(5):1207–28.
15. Moon YE, Lee YK, Lee J, Moon DE. The effects of preoperative intravenous acetaminophen in patients undergoing abdominal hysterectomy. Arch Gynecol Obstet. 2011;284(6):1455–60.
16. Yalcin N, Uzun ST, Reisli R, Borazan H, Otelcioglu S. A Comparison of Ketamine and Paracetamol for Preventing Remifentanil Induced Hyperalgesia in Patients Undergoing Total Abdominal Hysterectomy. Int J Med Sci 2012; 9(5):327-333.

 

17. Bhatti K, Lashari AA, Shaikh F. A clinico pathologic correlation of elective abdominal hysterectomy at teaching hospital Khairpur, Pakistan. Rawal Med J Apr - Jun 2013;38(2):143-6.
18. Iftikhar R. Outcome after total versus subtotal abdominal hysterectomy in benign uterine diseases J Surg Pak Sep 2007;12(3):102-5.
19. Laskowski K[1], Stirling A, McKay WP, Lim HJ. A systematic review of intravenous ketamine for postoperative analgesia. Can J Anaesth. 2011 Oct;58(10):911-23.