

Comparing the Efficacy of Intravenous Acetaminophen and Intravenous Meperidine in Pain Relief After Outpatient Urological Surgery

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Background: Pain relief after surgery is an essential component of postoperative care.

Objectives: The purpose of this study was to compare the efficacy of intravenous acetaminophen and intravenous meperidine in pain relief after outpatient urological surgery.

Patients and Methods: In a prospective, randomized, double-blind clinical trial, 100 outpatients of urological surgery were studied in two groups of acetaminophen (A) and meperidine (M). Patients in group A received 1g of acetaminophen in 100 mL saline within 15 minutes and patients in group M received a single intravenous injection of meperidine 0.5 mg/kg, 15 minutes prior to the end of operation. Postoperative pain was recorded using visual analog scale (VAS). Vital signs, nausea, vomiting, dizziness and respiratory depressions were compared between the two groups.

Results: Pain severity in patients treated with intravenous acetaminophen six hours after the operation within one-hour interval was significantly lower than meperidine group ($P < 0.0001$). Ninety patients in the meperidine group and five patients in the acetaminophen group required additional doses of analgesics. Nausea was significantly lower in acetaminophen group than meperidine group.

Conclusions: Intravenous acetaminophen reduced pain following outpatient urological surgery more significantly than meperidine.

Keywords: Postoperative Pain; Acetaminophen; Meperidine; Outpatient Surgery

1. Background

Postoperative pain management has undergone extensive developments during the past decade as one of the most important challenges facing physicians. Postoperative pain is one of the classic and routine indications of systemic analgesics administration (1). Pain relief has always been in the center of attention for physicians from the beginning of medical history (2). Different analgesic approaches including IV opioids (3), corticosteroids (4), local anesthetics (5, 6), regional blocks (7), neuraxial analgesia (8) and infiltration (9) have been introduced to reduce postoperative pain. Effective control of postoperative pain is an essential component of postoperative care (10). Nowadays, outpatient surgical procedures are increasing, which necessitates an appropriate postoperative pain management. Unsuccessful control of postoperative pain is one of the main causes of prolonged hospitalization or rehospitalization after outpatient surgery. Ineffective postoperative pain management could cause many acute (adverse physiological responses) and chronic (delayed recovery and chronic pain) adverse effects (11). Analgesic techniques include systemic and regional ap-

proaches. Opioids, nonopioids such as NSAIDs, ketamine, and acetaminophen are some systemic analgesia medications. Opioids are considered as initial therapy in patients with moderate to severe pain (12) and mainly act through μ -receptors in the CNS (11). These are not always tolerated well by patients and associated with dose-dependent adverse effects (12) including nausea, vomiting, ileus, sedation, respiratory depression and prolonged discharge (13). Meperidine is a synthetic opioid derived from phenyl pyridine used in moderate to severe pain management. It is widely used since its introduction in 1930 due to its low-cost (14). Meperidine is primarily a μ -receptor agonist used orally or parenterally. Meperidine has a 2.5-4-hour plasma half-life and a narrow therapeutic index. It is metabolized by the liver extensively. Reported adverse effects of meperidine include drowsiness, dizziness, light-headedness, nausea, and vomiting. In a recent study, meperidine adverse effects (dizziness, anxiety, nervousness, hallucinations, twitch and seizures) were reported in 14% of patients (14). Meperidine also triggers the release of histamine more than other drugs.

Acetaminophen is known as a safe and effective medication to relieve pain and reducing fever in a wide range of patients (15). Acetaminophen is a central oxygenase inhibitor and one of the safest and most effective drugs in the treatment of mild to moderate pain (16). Intravenous acetaminophen may be administered as a single dose or repeated doses. The maximum single dose (one gram) can be administered as infusion and repeated every six hours to a maximum dosage of 4 grams daily. Therapeutic dosage (maximum 4000 mg daily) is rarely associated with hepatotoxicity (17). Intravenous acetaminophen has a peak effect of 4 to 6 hours (18, 19). Onset of analgesia effect occurs within 5 to 10 minutes of administration (20, 21).

2. Objectives

The aim of the present study was to compare the effects of intravenous acetaminophen and intravenous meperidine in outpatients of urological surgery.

3. Patients and Methods

A prospective, randomized, double-blind clinical trial was conducted on 100 male subjects aged 18-62 years scheduled for outpatient urological surgeries (inguinal hernia, hydrocele and varicocele) with physical status of ASA I and II in Imam Reza hospital, Tabriz, Iran. After obtaining an approval from the university regional ethics committee, the study was registered at the clinical trial site (code IRCT 201206094005 N5). Patients were divided into two groups of acetaminophen (A) and meperidine (M). Patients with gastrointestinal discomfort (nausea and vomiting and ulcers), dizziness, liver or kidney failure, history of alcohol abuse, drug addiction, or mental disorders were excluded from the study. Premedication of general anesthesia in all patients was performed using fentanyl 1 µg/kg and midazolam 0.01 mg/kg. Induction was performed with propofol 2.5 mg/kg and atracurium 0.5 mg/kg. Anesthesia was maintained with gas mixture containing oxygen and N₂O (50%-50%) and isoflurane (1-1.5%). At the end of operation, patients were divided into two groups with 50 individual in each using Randlist software (datinf gmbh tübingen, Germany). Fifteen minutes before the end of operation, one gram of acetaminophen (Combino Pharm SL, Sant Joan Despi, Spain) was solved in 100 mL saline and administered within 15 minutes in patients of group A and a single intravenous injection of meperidine (Caspian Tamin, Rasht, Iran) 0.5 mg/kg was injected in patients of group M. Postoperative pain was recorded and compared between the two groups using visual analog scale (VAS). Vital signs, nausea, vomiting, dizziness, and respiratory depression were recorded. Patients were divided into two groups of acetaminophen (A) and meperidine (M) based on the last digit of their medical record numbers. All stages of anesthesia were performed by an anesthesiologist unaware (blinded) of grouping and patient assignment. Inal et al. study was used to determine the sample size of the present study

(22). Considering $\alpha = 0.05$, 80% power, and half unit difference in pain relief, a sample size of 84 patients was estimated and increased to 100 for increasing the credibility of the study. Descriptive methods (frequency, percentage, mean $\pm$ SD), Chi-square test (X²) and mean differences were used for comparison and statistical analyses. All statistical analyses were performed using SPSS 17 software (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered significant in all cases. Postoperative pain was evaluated using visual analog scale (VAS). Vital signs (blood pressure, respiratory rate, heart rate and oxygen saturation) were recorded hourly until 6 hours after the operation. Score of zero was considered as no pain and 10 as the most severe pain ever experienced. If patient had a severe pain (VAS over 5), meperidine 0.5mg/kg intravenous bolus was injected. Requirement of an additional dose and frequency of administration was registered. Furthermore, the most common adverse effects of medications, such as nausea, vomiting, dizziness, respiratory depression were recorded.

4. Results

There was no statistically significant difference between the two groups regarding the type of surgery, age, weight, ASA class, and duration of operation (Table 1). The pain severity one hour after the operation was 4.2 ± 1.39 in acetaminophen group and 3.14 ± 1.69 in meperidine group. Two hours after, it was 2.28 ± 1.40 in acetaminophen group and 3.24 ± 1.39 in meperidine group. Three hours after, it was 2.66 ± 1.32 in acetaminophen group and 3.78 ± 1.33 in meperidine group, 4 hours after, 3.08 ± 1.31 in acetaminophen group and 4.34 ± 1.21 in meperidine group, 5 hours after, 3.58 ± 1.49 in acetaminophen group and 4.30 ± 1.25 in meperidine group and finally 6 hours after, 3.60 ± 1.51 in acetaminophen group and 4.06 ± 1.02 in meperidine group. The overall mean pain intensity during the first six hours after the operation, with an hour interval, was significantly lower in patients treated with intravenous acetaminophen than those in meperidine group ($P < 0.0001$) (Table 2). In five patients treated with intravenous acetaminophen, additional doses of analgesics were required. Whereas, in patients treated with meperidine, 16 patients required an additional single dosage, but two additional doses were needed in three patients. The need for additional doses of analgesics in patients treated with meperidine was significantly higher than acetaminophen group ($P = 0.001$). Seven patients of acetaminophen group and 17 patients of meperidine were treated for postoperative nausea. Nausea incidence rate in patients treated with meperidine was significantly higher than acetaminophen group ($P = 0.019$). Four and eight patients of acetaminophen and meperidine groups experienced postoperative vomiting, respectively. There was no significant difference in the incidence of vomiting in the two groups ($P = 0.218$). Only four patients treated with meperidine had dizziness after the operation.

Table 1. Demographic, Physical Status, and Type of Surgery in Acetaminophen (A) and Meperidine (M) Groups

	Group A	Group M	P Value
Age, y	35.64 ±11.70	34.64 ± 11.29	0.665
Weight, kg	69.70 ±11.33	69.86 ± 11.19	0.944
Operation duration, min	63.67 ±9.17	62.55 ± 11.23	0.589
Type of Operation			
Varicocele	31	32	
Hydrocele Inguinal	7	6	
Hernia	12	12	0.955
ASA Class			
I	43	43	1
II	7	7	

Table 2. Comparison of Postoperative Pain Severity Between the Two Groups Based on VAS

Pain severity	Group		P Value
	Acetaminophen	Meperidine	
After one hour	2.14 ± 1.39	3.14 ± 1.69	0.003
After two hours	2.28 ± 1.40	3.24 ± 1.39	0.002
After three hours	2.66 ± 1.32	3.78 ± 1.33	< 0.0001
After four hours	3.08 ± 1.31	4.34 ± 1.21	< 0.0001
After five hours	3.58 ± 1.49	4.30 ± 1.25	0.02
After six hours	3.60 ± 1.51	4.06 ± 1.02	0.193

Table 3. Incidence of Nausea and Vomiting, Dizziness, Respiratory Depression, and Need for Additional doses of Analgesics in the Two Groups

	Group A	Group M	P Value
Nausea	7	17	0.019
Vomiting	4	8	0.218
Dizziness	-	4	-
Respiratory depression	-	-	-
Additional doses of analgesics	5	15	0.001

There was no respiratory depression in any of the patients (Table 3). There was no statistically significant difference between the two groups regarding vital signs (systolic and diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation rate) after six hours after the operation.

5. Discussion

Relieving pain after surgery is an essential issue (23). Studies have shown that 30-40% of patients have moderate to severe pain after the operation. Emotional distress, pain caused by sensitive nerve ends is the result of a subjective or personal multifactorial phenomenon, which is influenced by physiological, cultural, social, and psychological factors (23). The current treatment strategies for

pain control during surgery are based on analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs). In addition, nonopioid drugs can be used. A study by Serinken et al. compared the effect of intravenous acetaminophen with intravenous morphine on pain management of patients with renal colic; they stated that acetaminophen is effective as well as morphine in reducing pain (24). Morgan et al. demonstrated significant decrease in pain following intravenous acetaminophen in patients with renal colic (25). Wininger et al. reported significant effects of intravenous acetaminophen on abdominal pain post-operatively (26). A study performed by Bektas et al. evaluated intravenous administration of acetaminophen and reported that it is effective and can decrease the need for narcotic analgesics, particularly morphine (27). Another study by Ergenoglu et al. demonstrated that intravenous

acetaminophen is useful to decrease pain in patients undergoing urological surgery (28). Maghsoudi et al. evaluated the effect of intravenous acetaminophen to reduce the need for narcotic analgesic in patients undergoing urological surgery, and reported its efficacy in pain reduction (29). Inal et al. study demonstrated that intravenous acetaminophen was more efficient than meperidine in postoperative pain management (22). Amrimalah et al. study on comparing the effects of intravenous acetaminophen and meperidine analgesic after cesarean section revealed significant analgesic effects of intravenous acetaminophen than meperidine; also, intravenous acetaminophen reduced total dosage of meperidine dramatically (30). Rahimzade et al. compared the effects of intravenous acetaminophen and ketamine in control of pain after hysterectomy and suggested that acetaminophen was more effective than ketamine in pain control (31). Yazdani et al. reported that intravenous acetaminophen was as effective as intravenous meperidine in acute pain control after maxillofacial surgery. Acetaminophen reduced the need for additional drug use. Nausea and vomiting between the two groups were not different statistically. Acetaminophen group had higher systolic blood pressure compared to meperidine group (32). In our study, the average severity of pain in the first six hours after the operation with a one-hour interval in patients treated with intravenous acetaminophen was significantly less than meperidine group; this indicates the optimal effect of intravenous acetaminophen to provide analgesia after the operation. Nausea in patients treated with acetaminophen was significantly less than meperidine group; there was no significant difference in the incidence of nausea, dizziness and respiratory depression between the two groups. Requirement for additional doses of analgesics in patients treated with intravenous acetaminophen was significantly lower than the meperidine group. Average pain intensity during the first six hours after the operation in patients treated with acetaminophen was significantly lower than the meperidine group. Furthermore, the need for additional doses of analgesics and nausea in patients treated with intravenous acetaminophen was significantly lower than the meperidine group.

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Authors' Contributions

Khosro Kolahdouzan and Mahmood Eydi designed the study; Hassan Mohammadipour Anvari and Reyhaneh Abri collected data and helped in the design of study; Morteza Ghajazadeh and Samad EJ Golzari provided the draft of the study and finalized the study.

References

- Rieck BS. Systemic pain therapy, evaluation from surgeon point of view. *Reg Cancer Treat*. 1990;122-5.
- Golzari SE, Khan ZH, Ghabili K, Hosseinzadeh H, Soleimanpour H, Azarfarin R, et al. Contributions of Medieval Islamic physicians to the history of tracheostomy. *Anesth Analg*. 2013;116(5):1123-32.
- Soleimanpour H, Hassanzadeh K, Vaezi H, Golzari SE, Esfandjani RM, Soleimanpour M. Effectiveness of intravenous lidocaine versus intravenous morphine for patients with renal colic in the emergency department. *BMC Urol*. 2012;12:13.
- Soleimanpour H, Ghafouri R, Taheraghdam A, Aghamohammadi D, Negargar S, Golzari SE, et al. Effectiveness of intravenous Dexamethasone versus Propofol for pain relief in the migraine headache: A prospective double blind randomized clinical trial. *BMC Neur*. 2012;12(1):114.
- Golzari SE, Soleimanpour H, Mahmoodpour A, Safari S, Ala A. Lidocaine and pain management in the emergency department: a review article. *Anesth Pain Med*. 2014;4(1).
- Golzari SE, Soleimanpour H, Rahmani F, ZamaniMehri N, Safari S, Heshmat Y, et al. Therapeutic Approaches for Renal Colic in the Emergency Department: A Review Article. *Anesthesiol Pain Medic*. 2014;3(3).
- Agamohamdi D, Hosseinzadeh H, Golzari S, Alizadeh A, Peirovfar A, Movassaghi R, et al. Preincisional ipsilateral stellate ganglion block for acute post-operative pain control in unilateral mastectomy. *Pak J Med Sci*. 2011;27(4):879-83.
- Naghipour B, Aghamohammadi D, Azarfarin R, Mirinazhad M, Bilehijani E, Abbasali D, et al. Dexamethasone added to bupivacaine prolongs duration of epidural analgesia. *Middle East J Anesthesiol*. 2013;22(1):53-7.
- Dahl J. Institutionalizing pain management: the post-operative pain management quality improvement project. *The J Pain*. 2003;4(7):361-71.
- Dahl JL, Gordon D, Ward S, Skemp M, Wochos S, Schurr M. Institutionalizing pain management: the Post-Operative Pain Management Quality Improvement Project. *J Pain*. 2003;4(7):361-71.
- Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. *Br J Anaesth*. 2014;112(6):991-1004.
- Eydi M, Golzari SE, Aghamohammadi D, Kolahdouzan K, Safari S, Ostadi Z. Postoperative Management of Shivering: A Comparison of Pethidine vs. Ketamine. *Anesth Pain Med*. 2014;4(2).
- Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudin SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery. *Anesthesiology*. 2005;102(4):822-31.
- Shipton E. Should New Zealand continue signing up to the Pethidine Protocol? *N Z Med J*. 2006;119(1230):U1875.
- Pasero C, Stannard D. The role of intravenous acetaminophen in acute pain management: a case-illustrated review. *Pain Manag Nurs*. 2012;13(2):107-24.
- Mackenzie R, Lockey DJ. Pre-hospital anaesthesia. *J R Army Med Corps*. 2001;147(3):322-34.
- Dejonckheere M, Desjeux L, Deneu S, Ewalenko P. Intravenous tramadol compared to propacetamol for postoperative analgesia following thyroidectomy. *Acta Anaesthesiol Belg*. 2001;52(1):29-33.
- Van Aken H, Thys L, Veekman L, Buerkle H. Assessing analgesia in single and repeated administrations of propacetamol for post-operative pain: comparison with morphine after dental surgery. *Anesth Analg*. 2004;98(1):159-65.
- Tigerstedt I, Leander P, Tammisto T. Postoperative analgesics for superficial surgery. Comparison of four analgesics. *Acta Anaesthesiol Scand*. 1981;25(6):543-7.
- Ali MA, Siddiqui S. Is intravenous paracetamol a useful adjunct for intraoperative pain? *The Health J*. 2012;3(1):13-5.
- Hyllested M, Jones S, Pedersen JL, Kehlet H. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management: a qualitative review. *Br J Anaesth*. 2002;88(2):199-214.
- Inal MT, Celik NS, Tuncay FS. IV Paracetamol infusion is better than IV meperidine infusion for postoperative analgesia after caesarean section.: ISPUB J of anesthesiology;.
- Alimian M, Pournajafian A, Kholdebarin A, Ghodraty M, Rokhtabnak F, Yazdkhasti P. Analgesic effects of paracetamol and mor-

- phine after elective laparotomy surgeries. *Anesth Pain Med.* 2014;**4**(2).
24. Serinken M, Eken C, Turkcuer I, Elicabuk H, Uyanik E, Schultz CH. Intravenous paracetamol versus morphine for renal colic in the emergency department: a randomised double-blind controlled trial. *Emerg Med J.* 2012;**29**(11):902-5.
25. Morgan S. Intravenous paracetamol in patients with renal colic. *Emerg Nurse.* 2011;**18**(9):22-5.
26. Wininger SJ, Miller H, Minkowitz HS, Royal MA, Ang RY, Breitmeyer JB, et al. A randomized, double-blind, placebo-controlled, multicenter, repeat-dose study of two intravenous acetaminophen dosing regimens for the treatment of pain after abdominal laparoscopic surgery. *Clin Ther.* 2010;**32**(14):2348-69.
27. Bektas F, Eken C, Karadeniz O, Goksu E, Cubuk M, Cete Y. Intravenous paracetamol or morphine for the treatment of renal colic: a randomized, placebo-controlled trial. *Ann Emerg Med.* 2009;**54**(4):568-74.
28. Ergenoglu P, Akin S, Yalcin Cok O, Eker E, Kuzgunbay B, Turunc T, et al. Effect of intraoperative paracetamol on catheter-related bladder discomfort: a prospective, randomized, double-blind study. *Curr Ther Res Clin Exp.* 2012;**73**(6):186-94.
29. Maghsoudi R, Tabatabai M, Radfar MH, Movasagi GH, Etemadian M, Shati M, et al. Opioid-Sparing Effect of Intravenous Paracetamol After Percutaneous Nephrolithotomy: A Double-Blind Randomized Controlled Trial. *Journal of Endourology.* 2014;**28**(1):23-7.
30. Amrimalah P, Alijanpour E, Zabihi A, Attarzadeh H, Shirkhani Z, Rezaee B, et al. Comparison of Analgesic Effect of Intravenous Paracetamol plus Meperidine and Meperidine alone on Post-operative Pain after Elective Cesarean. *J Applie Phys.* 2013;**4**(1):1-7.
31. 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.* 2013:15-24.
32. Yazdani J, Ghavimi MA, Hajmohammadi SM, Zarrintan S. Acute pain control by Pethidine versus intravenous acetaminophen in maxillofacial surgeries: a double blind randomized-controlled trial. *J Am Sci.* 2013;**9**(7):51-5.