Open Access

Original Article

Optimum Perioperative Analges ia in Radical Nephrectomy, Multimodel Approach with Nalbuphine and Ketamine

Maqsood Ahmad, Fatima Wajahat*, Amna Wajahat**

Department of Anaesthesia, Combined Military Hospital Okara/National University of Medical Sciences (NUMS) Pakistan, *Department of Anaesthesia, Al Nafees Medical College, Islamabad Pakistan, Fazaia Medical College, Islamabad Pakistan

ABSTRACT

Objective: to find perioperative analgesic effectiveness of low dose Ketamine in radical nephrectomy operations and comparing its anodyne potency with Nalbuphine Hcl (Nalbin).

Study Design: Quasi-experimental study.

Place and Duration of Study: Armed forces institute of urology from Sep 2016 to June 2019.

Methodology: The 60 randomly selected surgical patients for radical nephrectomy were divided into two groups in a random manner. The Anaesthetic technique used in both groups (K and N) was standard along with 10 mg injection Nalbin given to both groups at induction. Group-K (n=30) patients had IV Ketamine bolus 0.3 mg /kg followed by 0.1 mg/kg/h infusion at induction till completion of surgery. Group-N (n=30) received a similar volume of saline in bolus as well as an infusion. The pain score (VAS) at different intervals and total Nalbin consumed in 12 hours were recorded for each group. Patient satisfaction and complications were recorded during this period.

Results: The effective intraoperative analgesia was achieved with an infusion of low dose Ketamine which continued till completion of surgery as seen in group K which has reduced Nalbin requirement 8.8± 3.5 mg (Group N 25±5 mg). There was a statistically significant reduction in overall pain scores and Nalbin demand (P≤0.05) in the Ketamine group (p≤0.00, 0.036, 0.286, 0.257, 0.253 respectively). Patient satisfaction was better in the Ketamine group but few patients in this group had delayed recovery.

Conclusion: Intraoperative low-dose Ketamine infusion provides good postoperative analgesia while reducing the need for opioid analgesics, which must be considered for better management of postoperative analgesia.

Keywords: Ketamine, Nephrectomy, Nalbuphine, Visual analogue scale.

How to Cite This Article: *Ahmad M, Wajahat F, Wajahat A. Optimum Perioperative Analges ia in Radical Nephrectomy, Multimodel Approach with Nalbuphine and Ketamine. Pak Armed Forces Med J 2023; 73(Suppl-1): S89-92. DOI: https://doi.org/10.51253/pafmj.v73iSUPPL-1.4654*

INTRODUCTION

Drug of choice for radical surgeries are opioids but with side effects.[1] Their use mask complex stress response related to surgery which disturbs the normal balance of different vital functions of the body. However large doses of opioids can incur postoperative recovery side effects like respiratory depression, nausea, and emesis which are hard to manage sometimes.[2] Despite all limitations, they are an integral part of perioperative care. Fewer choices of opioids are available in our hospitals providing either poor quality of analgesia or more than necessary side effects. To get maximum analgesic effects out of these opioids while decreasing total dose, Ketamine (an N-methyl-D-aspartate (NMDA) receptor antagonist) having excellent analgesic activity and opioid-sparing effect even at sub-anesthetic doses was used. [3]

Ketamine use prevents many side effects associated with opioids.[4] In low doses, it has much potential for decreasing the dose of opioids in pain conditions.[5] The documented mechanisms of analgesic action are through NMDA receptor antagonism, opioid receptor agonism, local anesthetic action, sigma receptor interaction, cholinergic effects, monoamine effects, and supraspinal mechanisms. [6-9]. Considering all this, we tested the beneficial effects of Ketamine in low doses in radical nephrectomy with fewer side effects.

METHODOLOGY

The quasi-experimental study was started at Armed Forces Institute of Urology Rawalpindi, from Sep 2016 to June 2019. Following approval from the Hospital Ethics Committee (Uro-Adm-Trg1/IRB/2020/108), written informed consent was obtained from 60 patients, aged 30 to 60 years of both genders belonging to American society of Anesthesiologist physical status 1,2 and 3. The sample size was calculated with the help of the "WHO STEPS sample calculator" and studied done on the subject.[10].. The mean of sample size of different studies on the subject were 40 (12 to 100). These radical nephrectomy

Correspondence: Dr Maqsood Ahmad, Department of Anaesthesia, Combined Military Hospital Okara Pakistan

Received: 29 Jul 2020; revision received: 22 Jul 2020; accepted: 28 Jul 2020

patients were randomly divided into two groups. The patients having an addiction, prolonged drug dependence for pain, and a history of allergy to analgesic drugs were excluded. Similarly the pregnant women and high-risk patients with multiple coexisting diseases falling in ASA 3, 4 were not included. The patients were educated preoperatively about visual analog scale (VAS consisting of a100-mm line with 0 equaling "no pain" and 100 equaling "worst possible pain").

The patients were divided randomly into two groups of 30 patients each and injection Nalbin 10 mg was given to all patients at induction. Patients in Group K were administered Ketamine bolus 0.3 mg/kg followed by infusion of 0.1 mg/kg/h and Group N patients were given similar normal saline infusions. Infusions of Ketamine or normal saline were started after induction with an SK-600II infusion pump (Biotec Pakistan), following bolus doses but decidedly before skin incision. The same infusion rates of saline or Ketamine were continued intra-operatively until wound closure.

Randomization of patients was done by the computer while no researcher involved in the study knew about the group of patients. Drugs were prepared by a person not involved in the study. On the morning of surgery, another anesthetist prepared drugs and collected initial data. Both Ketamine (Ketamine 0.5mg/ml) and normal saline were prepared in 50 ml syringes with the same marking.

After 6 hours of NPO (nil per os), standard monitoring was done with Mindray monitor during surgery time. Infusions of Ringers Lactate were started with 18 G cannula and induction was done with boluses of propofol (2 mg/kg) and Nalbin (10 mg) for each patient followed by Inj Atracurium besylate (0.5 mg/kg) for intubation. Close circuit anesthesia with a mixture of oxygen and isoflurane was started. At the end of the operation, neostigmine (2.5mg) and atropine (0.5mg) were used for neuromuscular blockade reversal and extubation was done after complete recovery of reflexes.

VAS pain scores were recorded for patients in the recovery area starting at 0, 2, 4, 6, and 12 h postoperatively. Nalbin 5 mg bolus was used for additional analgesia when required if the VAS score was more than 50.

Thus total Nalbin given to both groups was noted for 12 h. After 12 hours, we used paracetamol IV for pain control. All side effects like postoperative nausea, vomiting, respiratory depression (respiratory rate <10/min), confusion at recovery, and any delays in recovery were entered. Metoclopramide IV 10 mg was used for nausea and vomiting. Patient satisfaction was noticed on a three-point scale (satisfied, neutral, and dissatisfied) at 12 h postoperatively. The results were analyzed using SPSS 16 software (IBM Corporation). During the planning stage of the study, the sample size was calculated with the help of a power analysis. The power of study was 80% and the significance interval 5% was selected with descriptive data presented in Mean±SD and percentages. Statistical significance was calculated on the Student's t-test ($p \leq 0.05$).

RESULTS

The demographic data of the patients is presented in the Table-I.

Table-I: Descriptive statistics (n=60)

Variables	Group N (n=30)	Group K (n=30)
Gender		
Male	27	24
Female	3	6
Age in years	49±10	46±12
Weight (Kg)	50±15	55±12
Operation time	170±20	190±15

For initial 2 hours, the statistical signi-ficance was seen concerning hemodynamic variables in group N and group K (4.56±1.38 vs. 3.16±1.01 and 5.26±.74 vs. 4.8±.75 respectively) but no difference was seen after this time (4.7±1.02 vs. 4.66±1.24, 6.5±1.3 vs. 6.1±1.39, 7.4±.96 vs. 7.06±1.04). It is apparent from Table-II that there is less VAS score in Ketamine group with $p \leq 0.05$ (p-values ≤0.00, 0.036 for the first 2 hours, and patients had less pain. After the first 4 hours, the difference of

Table-II: Pain Assessment Score (VAS) two Groups(n=60)

Groups		Visual Analogue Scale 0 Hour	Visual Analogue Scale 2 Hour	Visual Analogue Scale 4 Hour	Visual Analogue Scale 6 Hour	Visual Analogue Scale 12 Hour
Group N	Mean±SD	4.56±1.38	5.26±.74	4.7±1.02	6.5±1.3	7.4±.96
Group K	Mean±SD	3.16±1.01	4.8±.75	4.66±1.24	6.1±1.39	7.06±1.04
p-value		<0.01	<0.036	0.286	0.257	0.253

VAS between two groups is not significant as seen in Table-II (p≤0.286, 0.257, 0.253 at 4, 6, and 12 hours).

Nalbin was given to 10 patients during the postoperative period to Ketamine group compared to group N which received additional analgesia in 30 patients. It is evident from Table-III that patients of Group K have reduced Nalbin requirement 8.8± 3.5 mg (Group N 25±5 mg).

TableIII: Post-Operative Analgesia (n=60)

Total Consumption of Nalbin		
Groups	**Total patients**	**Mean ±SD**
Group N	30	25.83±5.09
Group K	30	8.86±3.5
Total Patients	60	17.35±9.6

DISCUSSION

The surgical pain control has been the topic under discussion for a long time and various concepts were discussed for its mechanism. Preventive analgesia term is used when the administration of the analgesic drug has no relation with incision and has not received much popularity for postoperative pain management10. When drugs of different mechanisms of action are used to control pain then this approach is termed multi-model analgesia. The commonly used drugs for this purpose are variable, and few of them are opioids and NSAIDS (non-steroidal anti-inflammatory drugs). Anesthesia drugs like Ketamine, local anesthetics, and adjuncts like clonidine and anticonvulsants are also used for pain control.[11]

Ketamine in large doses can produce certain untoward side effects despite its strong analgesic action.[12] The effects of Ketamine in low doses are different from high doses which are used for anesthesia in certain conditions like a hypovolemic shock. Laskowski K, in his study, has used different doses of low dose Ketamine for intramuscular use and intravenous dose respectively (<2 mg/kg and <1 mg/kg). Moreover, a dose <20 µg/kg/min is also used continuously for the IV or epidural route. [13]

Most of the studies on post-operative pain control are carried out using a combination of morphine and fentanyl with low dose Ketamine and very few studies are available on Nalbin and Ketamine.A study by Yeom JH, on low dose Ketamine infusion with fentanyl, was carried out in spinal fusion surgery with statistically significant opioid-sparing effects but the results of the study are similar to our study using Nalbin 14. The significant reduction in total Nalbin dose consumption is found in the Ketamine group in a study by Parikh B and reduced pain scores which are similar to previous studies.[15] Alike results are also reported with perioperative Ketamine infusion in major abdominal and micro-discectomy surgery.[16] In these studies, the dose of opioids used for 12 h post-surgery was lower in the Ketamine receiving group, similar to early studies.[17,18] However, fewer studies have failed to elicit this synergistic effect which may be due to a low dose of opioids or the nature of surgical technique demanding more analgesia.[19] Nevertheless, Ketamine in low-dose remains useful for controlling post-operative pain with fewer side effects as proved by Suppa E in his study.[20] Higher doses of Ketamine were not used in our study because of its potential limitations like psychomimetic effects. The drug has its own limitations like it is sympathomimetic and contraindicated in many medical conditions. It has wide-ranging applications and to our interest is its perioperative opioid-sparing action in sub-anesthetic doses particularly in setups where opioids are in limited variety.

CONCLUSION

Multimodal analgesia approach combining low dose Ketamine with Nalbin is a beneficial option for patients undergoing major surgical procedures in underdeveloped countries with limited availability of novel opioids. We hope that current knowledge of the drug delivery system with the handiness of new opioids will help control perioperative pain in all major disciplines of surgical operations in the future.

Conflict of Interest: None.

Authors' Contribution

Following authors has made substantial contributions to the manuscript as under:

MA:, FW:, AW: Conception, study design, data acquisition, data analysis, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Author agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Xu W, Daneshmand S, Bazargani ST, Cai J, Miranda G, Schuckman AK, Djaladat H. Postoperative pain management after radical cystectomy: comparing traditional versus enhanced recovery protocol pathway. J Urol 2015; 194(5): 1209-1213.
2. Vadivelu N, K AM, Tran D, Kodumudi G, Legler A, Ayrian E. Options for postoperative pain management in neurosurgery. J Pain Res.2016 (10); 9: 37-47.
3. P Tsui, M Chu, Ketamine: an old drug revitalized in pain medicine. Br J Anaesth. Edu 2017; 17(3): 84-87. https:// doi.org/ 10.1093/bjaed/mkw034

4. Mak P, Broadbear JH, Kolosov A, Goodchild CS. Long-term antihyperalgesic and opioid-sparing effects of 5-day Ketamine and morphine infusion ("burst Ketamine") in diabetic neuropathic rats. Pain Med 2015; 16(9): 1781-93.
5. Connolly SB, Prager JP, Harden RN. A systematic review of Ketamine for complex regional pain syndrome. Pain Med 2015; 16(5): 943-969.
6. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain 2011; 152(3): 82-15.
7. Laskowski, K, Stirling, A, McKay, WP, and Lim, HJ. A systematic review of intravenous Ketamine for postoperative analgesia. Can J Anaesth 2011(9); 58: 911–923
8. Barreveld AM, Correll DJ, Liu X, Max B, McGowan JA, Shovel L, Wasan AD, Nedeljkovic SS. Ketamine decreases postoperative pain scores in patients taking opioids for chronic pain: results of a prospective, randomized, double-blind study. Pain Med 2013; 14(6): 925-34.
9. Carstensen M, Møller AM. Adding Ketamine to morphine for intravenous patient-controlled analgesia for acute postoperative pain: a qualitative review of randomized trials. Br J Anaesth 2010; 104(4): 401-406.
10. Chen K, Wang J, Dai J, Luo A, Tian Y, Guan Z, Wang X. Anesthetic management of radical nephrectomy in patients with renal cell carcinoma involving renal vein or inferior vena cava. Tumori J 2019; 105(5): 411-416. https://doi.org/10.1177/0300891619839295
11. Rosero EJ, Joshi GP, Preemptive, preventive multimodel analgesia: what do they really mean? Plast Reconst Surg 2014 5(3); 134-2.
12. Tan M, Law LS, Gan TJ, Optimizing pain management to facilitate Enhanced Recovery After Surgery pathways. Can J Anaesth. 2015; 60(2): 203-18.
13. Andrew W, David M, Harish R. Intravenous sub-anesthetic Ketamine for perioperative analgesia. J Anaesthesiol Clin Pharmacol 2016; 32(2): 160-167.
14. Laskowski K, Stirling A, McKay WP, Lim HJ. A systematic review of intravenous Ketamine for postoperative analgesia. Can J Anaesth 2011; 58(11): 911–923.
15. Yeom JH, Chon MS, Jeon WJ. Peri-operative Ketamine with the ambulatory elastomeric infusion pump as an adjuvant to manage acute postoperative pain after spinal fusion in adults: A prospective randomized trial. Korean J Anesthesiol 2012; 63(1): 54–58.
16. Parikh B, Maliwad J, Shah VR. Preventive analgesia: Effect of a small dose of Ketamine on morphine requirement after renal surgery. J Anaesthesiol Clin Pharmacol 2011; 27(5): 485–4888
17. Hadi BA, Daas R, Zelkó R. A randomized, controlled trial of a clinical pharmacist intervention in microdiscectomy surgery - Low dose intravenous Ketamine as an adjunct to standard therapy. Saudi Pharm J 2013; 21(2): 169–75.
18. Kim SH, Kim SI, Ok SY, Park SY, Kim MG, Lee SJ, et al. Opioid sparing effect of low dose Ketamine in patients with intravenous patient-controlled analgesia using fentanyl after lumbar spinal fusion surgery. Korean J Anesthesiol 2013; 64(5): 524–528.
19. Cha MH, Eom JH, Lee YS, Kim WY, Park YC, Min SH, Kim JH. Beneficial effects of adding Ketamine to intravenous patient-controlled analgesia with fentanyl after the Nuss procedure in pediatric patients. Yonsei Med J 2012; 53(2): 427-432.
20. Riddell JM, Trummel JM, Onakpoya IJ. Low-dose Ketamine in painful orthopaedic surgery: a systematic review and meta-analysis. Br J Anaesth 2019; 123(3): 325-334.
21. Suppa E, Valente A, Catarci S, Zanfini BA, Draisci G. A study of low-dose S-Ketamine infusion as "preventive" pain treatment for cesarean section with spinal anesthesia: Benefits and side effects. Minerva Anestesiol 2012; 78(6): 774–81.