Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(3); 318-324

Original Research Article

Effect of Intra-operative Ketamine on Post- operative Catheter Related Bladder Discomfort in Abdominal Surgeries: A Randomized Double Blind Interventional Controlled Study

Gaurav Sharma¹, Mayuresh Hanchnal², Rakesh Kalappa³

¹Associate Professor, Department of Pain and Palliative Medicine, SMS Medical College and Hospital, Jaipur

²Resident Doctor, Department of Anesthesiology, SMS Medical College, Jaipur, Rajasthan.

³Assistant Professor, Department of Anesthesiology, MVJ medical college, Bengaluru Received: 11-01-2023 / Revised: 18-02-2023 / Accepted: 21-03-2023

Corresponding author: Dr. Mayuresh Hanchnal

Conflict of interest: Nil

Abstract:

Background: Urinary catheter insertion peri-operatively may result in feeling of elevated urinary urgency, frequency and discomfort at supra-pubic region collectively these symptoms are referred as Catheter related bladder discomfort (CRBD). We evaluate the effect of intra operative ketamine in prevention of CRBD after elective abdominal surgeries in the post-operative period.

Methods: Ninety patients undergoing elective abdominal surgery were randomized into two equal groups of 45 subjects each. Group A received IV normal saline and group B received 0.5mg/kg IV ketamine after induction of anesthesia, but before urinary catheterization. The study compared incidence and severity of CRBD, Visual analogue scale (VAS) score and presence of side effects related to ketamine up to 12hr (hour) in the post-operative period.

Results: The Incidence of CRBD in post-operative period was significantly lower in group B (ketamine) compared to group A (p-value <0.01). Reduction in severity of CRBD was noted at 0hr and 1hr in group B. The mean VAS score at incision site was significantly lower (P<0.05) in group B as compared to group A at 0, 1 and 2 hour period. No statistically significant difference was noted in number of cases who showed side effects between the two groups.

Conclusion: Intra-operative 0.5 mg/kg of IV ketamine before urinary catheterization can reduce incidence and severity of CRBD as well as provide prolonged post-operative analgesia without significant side effects during the post-operative period.

Keywords: Laparoscopy, cholecystectomy, cholelithiasis, preoperative, sonography etc.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Urinary catheterization is one of the most common procedures performed in indoor patient settings, wards and operation theatre to measure the accurate urine output. Around 15% to 25% of patients admitted to the hospital undergo urinary catheterization [1].

Urinary catheter insertion peri-operatively may result in feeling of elevated urinary urgency, frequency and discomfort at supra-pubic region which can continue through the post-operative period. Collectively these symptoms have been

Sharma G et al. International Journal of Current Pharmaceutical Review and Research

referred to as Catheter related bladder discomfort (CRBD)[2, 3].

The incidence of CRBD has been reported to be around 47% and as can reach up to to 91% as observed in various studies, the incidence and severity of CRBD is highest among men, most probably due to the length & sigmoid curve of the urethra [4,5] . After several studies two independent factors which increased the risk of CRBD were the size of the urinary catheter (Foley's catheter larger than 18Fr) and male gender [6].

The occurrence of CRBD is extremely distressing for the patients, as it is resistant to conventional opioid therapy. This may result in increased incidence of postoperative complications which include surgical incision dehiscence, bleeding, circulatory system instability, arrhythmia, and increased severity of coronary artery disease [7].

As CRBD is observed in most of the patients with indwelling urinary catheter in indoor settings, wards and peri-operatively, it is necessary to investigate more into management of CRBD to improve quality of life of the patient, decrease patient discomfort and complications during hospital stay.

The mechanism of CRBD is found to be similar to that of overactive bladder, which is caused by involuntary contractions of the bladder smooth muscles mediated by stimulation of vesical muscarinic receptors [8].

Pre-operative treatment with antimuscarinic drugs like oxybutynin, tolteridone and gabapentin have been reported to reduce the incidence and severity of CRBD [9, 10].

Ketamine administration intra-operatively as well as in the post-operative period is found to be an effective modality for reduction in incidence and severity of CRBD [11]. Ketamine is a centrally acting non opioid analgesic agent. Ketamine inhibits muscarinic signaling which explains its anti-cholinergic clinical effects, this action of ketamine can be used as a treatment modality in CRBD, although there is relative paucity of literature regarding role of ketamine given in intraoperative period in prevention as well as reducing the severity of CRBD.

With this aim, we conducted a randomized, controlled interventional trial to evaluate the effect of ketamine on incidence as well as severity of CRBD after elective abdominal surgeries.

Materials and Methods

The study was conducted as a prospective randomized, double blinded, interventional controlled trial in patients undergoing elective abdominal surgery at general surgery operation theatre-2, S.M.S. medical college and hospital, Jaipur after obtaining clearance from Office of Ethics Committee ,SMS medical college and hospital, Jaipur with approval number No.738/MC/EC/2020.

A sample size of 45 subjects in each group was calculated (Using the incidence rate of CRBD at 1hour) [8] at confidence interval of 95% and power of 80% to verify the expected difference in incidence of CRBD during the post-operative by at least 30% in both the groups. Patients were randomized by opaque sealed envelope method into two equal groups and were double blinded.

Patients belonging to either sex, aged 20-40 weighing 50-80kg vears. and ASA(American Society of Anesthesiologists Physical Status Scale) grade 1 and 2 were included. Patients urological undergoing surgeries or requiring intervention were excluded from the study. After taking informed written consent and confirming overnight fasting, patients received pre-medication with Inj.Ranitidine (1mg/kg),Inj.Metoclopromide (0.15 mg/kg),Inj.Glycopyrrolate (5mcg/kg),Inj.Midazolam (0.01 mg/kg)and Inj.Fentanyl (2mcg/kg). After pre-

International Journal of Current Pharmaceutical Review and Research

oxygenation with 100% O2 for 5minutes induction was done with Inj.Propofol (2mg/kg) and Inj.Atracurium (0.5mg/kg). Direct laryngoscopy was done and endotracheal tube of appropriate size was placed. Anesthesia was maintained using sevoflurane, Inj.Atracurium (0.1mg/kg) and Inj.Paracetomol (15mg/kg).

Group B patients received ketamine (0.5mg/kg diluted with normal saline to make total volume of 2ml) 3 minutes after intubation, whereas the group A patients received 2ml of normal saline. Urinary catheterization was performed with 16 Fr. Foley's catheter 90 seconds after injection of ketamine or normal saline. Oil based gel 2% lignocaine was used to lubricate and catheterization was done 3 minutes after lubrication. Balloon was inflated with 10ml of normal saline and the catheter was left free to drainage. Intra- operative vitals monitoring was performed using noninvasive blood pressure cuff, pulse oximetry, respiratory rate, five lead ECG and end tidal carbon dioxide monitor. At the end of the surgery, all patients had neuromuscular blockade reversed by a mixture of Inj.Neostigmine (0.07 mg/kg) and Inj.Glycopyrrolate (0.01mg/kg) to normalize their muscle force. Finally, they were extubated in the operating room and transferred to the post anesthesia care unit (PACU) for recovery.

The study compared incidence and severity of CRBD(based on CRBD scale as none , mild, moderate and severe) [11],Visual analogue scale(VAS) score at incision site and local site, presence of side effects like sedation(by Ramsay sedation scale), postoperative nausea and vomiting(PONV) , hallucinations, respiratory depression and diplopia on arrival in PACU as 0hr, 2hr,4hr,6hr and 12hrs post-operatively.

All the statistical analysis of data was done with statistical programming software-SPSS (Statistical Package for the Social Science) version 21.0.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data was presented as mean and standard deviation using Student unpaired T test. Qualitative data was presented as numbers (percent) using Chi-Square test. A p-value of less than 0.05 was considered statistically significant in all the analysis. The study was registered under CTRI (Clinical Trails Registry-India) with registration number CTRI/2021/01/030506.

Results

Patients were randomized into two equal groups of 45 subjects. All patients were assessed upon arrival to the PACU. They were assessed at 0,1, 2, 4,6 and 12 hours presence and severity of CRBD, postoperative pain (using VAS score) and presence of side effects like sedation (using the Ramsay sedation scale), post- operative nausea and vomiting, hallucinations, respiratory depression and diplopia were recorded.

Demographic data	Group A	Group B	p-value*
Age (years)	33.36±7.63 (mean ±SD)	34.24±6.25 (mean ±SD)	0.645 (NS)
Sex (male/female)	30/15	35/10	0.347 (NS)
Weight (kg)	65.18±8.66 (mean ±SD)	67.84±9.03 (mean ±SD)	0.156 (NS)
ASA grade (1/2)	33/12	30/15	0.645 (NS)
Duration of surgery (minutes)	91.22±10.57 (mean ±SD)	90.47±13.80 (mean ±SD)	0.771 (NS)

Table 1: Demographic data

Data are presented as either number of patients or mean (SD).

p - value < 0.05 was considered statistically significant(S) in all the analysis.

*p – value >0.05 was considered statistically non-significant(NS) in all the analysis.

Table 1 shows demographic data among the study groups. The mean age of the patients

was 33.36 years in group A and 34.24 years in group B and the range was 20-40 years.

Sharma G et al.

International Journal of Current Pharmaceutical Review and Research

The mean weight of the patients was 65.18 kg in group A and 67.84 kg and the range was 50-80 kg. Both the groups were comparable in terms of ASA grade distribution and duration of surgery. There were no statistically significant differences (NS) in the demographic data among the study groups.

CRBD incidence	Group A	Group B	p-value
Number of patients developing CRBD	31	17	<0.001 (S)
Percentage of patients developing CRBD	68.8%	37.7%	<0.001 (S)

Table 2:	CRBD	incidence*
----------	------	------------

²Data are expressed as number of patients (%).

Table 2 shows incidence of CRBD between two groups. In present study the incidence of CRBD in group A was 68.8% and group B 37.7%. The incidence was significantly lower in group B compared to group A with p- value <0.001(S).



Figure 1: CRBD severity Data are expressed as number of patients.

Figure 1 shows severity of CRBD observed between two groups. Reduction in severity of CRBD was observed at 0hr and 1hr period in patients belonging to group B when compared to group A, as all group B patients experienced only mild form of CRBD. While in group A, patients also experienced moderate form of CRBD. At 2hr, 4hr, 6hr and 12hour, there was no significant difference between two groups in terms of severity of CRBD.

VAS at incision site	Group A		Group B		p -value
	Mean	SD	Mean	SD	_
0 hr	5.71	1.29	4.56	1.93	0.001 (S)
1 hr	1.64	0.57	2.11	0.71	0.0009 (S)
2 hr	1.49	0.51	1.93	0.39	0.001 (S)
4 hr	1.96	0.56	2.04	0.42	0.399 (NS)
6 hr	2.56	0.50	2.56	0.62	1.00 (NS)
12 hr	2.56	0.59	2.49	0.66	0.614 (NS)

Table 3: VAS score at incision site

Data are presented as mean (SD).

The mean VAS score at incision site was significantly lower (P<0.05) in group B as compared to group A at 0, 1 and 2 hour period. However no statistically difference regarding the same was noted at 4hr, 6hr and 12hr period between the groups.

Table 4. Side effects after intervention				
Side effects	Group A	Group B	p-value	
PONV	13	24	0.523 (NS)	
Sedation	0	0	-	
Respiratory depression	0	0	-	
Hallucination	0	0	-	
Diplopia	0	0	-	

Table 4: Side effects after intervention

Data are expressed as number of patients.

No statistically significant difference in number of cases who showed side effects in form of sedation, PONV, respiratory depression, hallucination and diplopia was observed.

Discussion

CRBD, defined as an urge to void or suprapubic discomfort is common in the patients who have an indwelling urinary catheter in postoperative period. CRBD shows symptoms similar to overactive bladder that is characterized by the urinary frequency, urgency with or without urge incontinence that negatively influence the patient's quality of life [5].

The incidence of CRBD has been reported to be around 47-91% [4, 5] after surgery in previously published literatures. In our study, we observed the incidence of CRBD was around 53.3%.We observed incidence of CRBD in post-operative period was significantly lower in group B (ketamine) compared to group A (normal saline) and reduction in severity of CRBD was noted up to 1hr post- operatively in group B compared to group A as all group B patients experienced only mild form of CRBD [Table 2]&[Figure 1]. These findings are in accordance with A. Agarwal et al (2006) [11] who observed reduction in incidence of CRBD at 2hr and 6hr in the postoperative period and reduced severity of CRBD at 1hr in the postoperative period in IV ketamine groups as compared to placebo group. Similarly Reza Shariat Moharari et al (2013) [8] reported reduction in incidence and severity of CRBD at the 0 hr and 1 hr visit (P < 0.001) in the ketamine group and concluded that pre-emptive administration of IV ketamine (0.5 mg/kg) can reduce incidence and severity of CRBD in the early postoperative period. Additionally we assessed the analgesic potency of ketamine.

Human urinary bladder exhibits heterogeneous populations of various muscarinic receptors with a predominance of M2 muscarinic receptor subtype and a minor population of the M3 receptor. Ketamine has been shown to interact with muscarinic acetylcholine receptors. It has muscarinic antagonist activity.

Sharma G et al.

Ketamine acts on muscarinic receptors and analgesic effect of ketamine might be additive or synergistic with its antimuscarinic activity in decreasing the severity of CRBD. At clinically relevant concentration of ketamine profoundly inhibits muscarinic receptor signaling. By inhibition of the cholinergic system, which supplies trigone of the urinary bladder ketamine reduces the contractile response of the bladder [12,13].

Additionally we observed mean VAS score at incision site was significantly lower (P < 0.05) in group B as compared to group A up to 2 hour period[Table 3]. Similarly Azim Honarmand et al (2011)[14] observed that intravenous ketamine given prior to surgery provides prolongation of analgesia even up to 24 hours post- operatively. Hence providing post-operative analgesia and reducing total opioid consumption. In our study we didn't observe any significant side effects between the two groups[Table 4}. This shows that addition of IV ketamine in dose of 0.5mg/kg as single dose intraoperatively is not associated with any significant adverse effects and has completely safe profile as observed by Simin Atashkhoyi et al (2013)[15].

Limitations

In our study, single dose of intra-operative 0.5mg/kg IV ketamine before urinary catheterization provided relief from CRBD up to 1hour in the post-operative period.

As this is a short period of time, to maximize the effect of ketamine to provide relief from CRBD for a longer duration of time, we may have to give multiple doses/ incremental doses of ketamine. But this assessment has to be based on further studies as very few literatures are available currently regarding use of gradual/phased dosing of ketamine. Hence more largescaled multi-centric. randomized. interventional controlled studies are required.

CRBD is extremely distressing for the patients with indwelling urinary catheters. The intensity of the discomfort experienced by the patient can start from a mild unpleasant feeling to a permanent painful severe form causing behavioral responses leading to increased risk of post-operative complications, poor quality of recovery and prolonged the hospital stay. we observed the incidence of CRBD was around 53.3%. In developing countries postoperative quality of life assessment and management have not had the necessary consideration since adequate data for the management are not available. Therefore patients still battle with CRBD and pain control leading to negative psychological and physiological outcomes for patients.

Our study concludes that administration of intra-operative 0.5 mg/kg of IV ketamine before urinary catheterization can reduce incidence and severity of CRBD as well as prolonged post-operative analgesia without significant side effects during the postoperative period helping to improve quality of life of the patient, decrease patient discomfort and complications in the perioperative period, wards and emergencies.

References

- 1. Kunin CM: Nosocomial urinary tract infections and the indwelling catheter: what is new and what is true? Chest [Comment Editorial. 2001; 120:10-2.
- Agarwal A, Raza M, Singhal V, et al.: The efficacy of tolterodine for prevention of catheter-related bladder discomfort: a prospective, randomized, placebo-controlled, double-blind study. Anesth Analg. 2005;101: 1065-7.
- Akca B, Aydogan-Eren E, Canbay O, et al.: Comparison of efficacy of prophylactic ketamine and dexmedetomidine on postoperative bladder catheter-related discomfort. Saudi Med J. 2016; 37:55-9.
- 4. Hu B, Li C, Pan M, et al.: Strategies for the prevention of catheter-related bladder discomfort: A PRISMA-

Conclusions

Sharma G et al.

compliant systematic review and metaanalysis of randomized controlled trials. Medicine. 2016; 95.

- 5. Hur M, Park SK, Yoon HK, et al.: Comparative effectiveness of interventions for managing postoperative catheter-related bladder discomfort: a systematic review and network meta-analysis. Journal of anesthesia. 2019; 33:197-208.
- 6. Binhas M, Motamed C, Hawajri N, et al.: Predictors of catheter-related bladder discomfort in the postanaesthesia care unit. Annales francaises d'anesthesie et de reanimation. [Clinical Trial. 2011; 30:122-5.
- 7. Bai Y, Wang X, Li X, et al.: Management of catheter-related bladder discomfort in patients who underwent elective surgery. J Endourol. 2015; 29:640-9.
- Shariat Moharari R, Lajevardi M, Khajavi M, Najafi A, Shariat Moharari G, Etezadi F: Effects of Intra- Operative Ketamine Administration on Postoperative Catheter-Related Bladder Discomfort: A Double-Blind Clinical Trial. Pain Practice. 2014; 14:146-50.
- Agarwal A, Dhirraj S, Singhal V, Kapoor R, Tandon M: Comparison of efficacy of oxybutynin and tolterodine for prevention of catheter-related bladder discomfort: a prospective, randomized, placebo-controlled, double-blind study. BrJ Anaesth. 2006; 96:377-380.

- 10. Agarwal A, Dhirraj S, Pawar S, Kapoor R, Gupta D, Singh PK: An evaluation of the efficacy of gabapentin for prevention of catheter-related bladder discomfort: a prospective, randomized, placebo-controlled, double- blind study. Anesth Analg. 2007;1454-1457.
- Agarwal A, Gupta D, Kumar M, Dhirraj S, Tandon M, Singh PK: Ketamine for treatment of catheter related bladder discomfort: a prospective, randomized, placebo controlled and double-blind study. Br J Anaesth. 2006; 96:587-589.
- 12. Wilson LE, Hatch DJ, Rehdsr K: Mechanism of the relaxant action on isolated porcine tracheal muscles. Br J Anaesth. 1993; 71:544-50.
- Durieux ME: Inhibition by ketamine of muscarinic acetylcholine receptor function. Anesth Analg. 1995; 81:57-62.
- 14. Honarmand A, Safavi M, Karaky H: Preincisional administration of intravenous or subcutaneous infiltration of low-dose ketamine suppresses postoperative pain after appendectomy. Journal of pain research. 2012; 5:1.
- 15. Atashkhoyi S, Negargar S, Hatami-Marandi P: Effects of the addition of low-dose ketamine to propofolfentanyl anaesthesia during diagnostic gynaecological laparoscopy. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2013; 1: 247-50.