ORIGINAL ARTICLE

Effect of Analagesic Dose of Ketamine on Intraoperative Propofol Requirement and Postoperative Pain Relief After Diagnostic Gynaecological Laparoscopy

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ABSTRACT

Background: Analgesic dose of ketamine given at induction reduces usage of propofol intraoperatively and requirement of opioid analgesic drugs postoperatively.

Patients and Methods: Hundred patients were randomly allocated to two equal groups: saline or ketamine. It was a double blind study. Patients in both groups received premedication with midazolam and induction with propofol. Patients in ketamine group received 0.25 mg/kg ketamine at induction while the other group received saline. Anaesthesia was maintained with propofol infusion @ 6 mg/kg/min in both groups and additional boluses of propofol were used to deepen anaesthesia when required. Total amount of propofol used was noted at the end of procedure. Total amount of analgesic drug tramadol was also noted in the postoperative area at the time of discharge of patient.

Results: Amount of propofol used in patients of ketamine group was significantly lesser than the saline group. There was no difference in the analgesic requirements in the postoperative ward.

Conclusion: Ketamine in analgesic doses given at induction reduced the intraoperative propofol usage but had no effect on postoperative pain and analgesic requirement.

Key words: Propofol; Ketamine; Postoperative pain.

INTRODUCTION

Anaesthesia is defined as “an altered physiological state characterized by reversible loss of consciousness, analgesia of the entire body, amnesia, and some degree of muscle relaxation[1]”. These components of anaesthesia are routinely met with during most of the surgical procedures with the exception of muscle relaxation as agents used for induction and maintenance of anaesthesia cause some degree of muscle relaxation and complete paralysis is not always required. Propofol is an anaesthetic agent that causes sedation and hypnosis but no analgesia; it is widely used in day case surgery due to its properties of quick recovery and less hangover[2-5]. Adjuncts may be required to provide analgesia as its use as sole anaesthetic may require unacceptable depth of anaesthesia. When used with analgesic agents, its requirement should theoretically decrease since the response to painful stimuli is reduced. Ketamine is an anaesthetic agent which also possesses analgesic properties at a smaller dose[6-9]; its anaesthetic dose is associated with undesirable side effects. When used in low doses, it provides good analgesia, minimal sedation and lesser side effects but no anaesthesia. It may be inferred that if these two agents are combined, anaesthesia can be maintained with lesser doses of propofol and possibly better recovery profile and lesser side effects. Therefore, we undertook this study to determine the effect of ketamine in reducing the dose of propofol during short gynaecological procedures.

PATIENTS AND METHODS

The study was conducted over period of 6 months. After getting approval of from institutional review board and informed consent, 100 patients of ASA 1 and 2, were divided in two equal groups. Patients with psychiatric illness or drug allergy were excluded from the study.

Patients were randomly divided into two equal groups to receive either the study drug (group K) or saline as placebo (group S). Non-probability, convenience sampling was used.

Demographic details of every patient were recorded on the history sheet. Diagnosis of infertility was confirmed by history. The study nurse filled a 5 ml syringe with either 0.25mg per kg ketamine diluted to a volume of 5 ml or the same volume of normal saline. Observer and the patient both were blinded.

Every patient received premedication with intravenous Midazolam (0.05 mg per kg) before shifting to operation theatre. After applying standard monitors, anaesthesia was induced with

propofol (2.0 mg/kg) followed by propofol infusion at a rate of 6 mg per kg per min by syringe pump. Ventilation was assisted by a bag and mask using 100 percent oxygen. Patients in ketamine group received 5 ml prefilled ketamine syringe and others received 5 ml saline. Additional boluses of 10 mg propofol were given for maintenance of anaesthesia as required. Propofol infusion was stopped once the laparoscopic cannula was removed.

VARIABLES MEASURED

The primary outcome was total consumption of propofol intraoperative and tramadol postoperatively.

Other variable measured were duration of surgery, duration of anaesthesia, heart rate, blood pressure and oxygen saturation, PONV and discharge time.

STATISTICAL ANALYSIS

The data (total dose of propofol used, total amount of tramadol used in postoperative ward and mean pain score) was analysed using Statistical Package of Social Sciences (SPSS). Numerical variables are represented in terms of mean and standard deviation. Qualitative variables are represented as frequencies and percentages.

RESULTS

There were one hundred patients included in the study and there was no difference regarding age and weight of the patients in both groups. Two patients were not followed properly and excluded from the study as their proformas were not filled properly. Mean age of the patients in saline group was 29 years and that of ketamine group was 28.8 years. Mean weight of the patients was almost similar as well. This has been shown in following tables:

Table 1: Comparison of the mean age of the patients between two study groups

Study groups	N	Mean age in years	Std. Deviation
Saline	49	29.00	5.0
Ketamine	49	28.80	5.6
Statistical Analysis t value= 0.18 P value two tailed = 0.85 (>0.05) There was no significant difference of mean age of the patients between two study groups			

Table 2: Comparison of the mean weight of the patients under study

Study groups	N	Mean weight in Kg	Std. Deviation
Saline	49	65.04	13.3
Ketamine	49	64.37	11.7
Statistical Analysis t value= 0.27 P value two tailed = 0.79 (>0.05) There was no significant difference of mean weight between two study groups			

Table 3: Comparison of the mean total dose of propofol between two study groups

Study groups	N	Mean dose of propofol in mg	Std. Deviation
Saline	49	301	76
Ketamine	49	242	81
Statistical Analysis t value= 3.69 P value two tailed = 0.001 (<0.05) Mean total dose of propofol was significantly higher in patient given saline as compared to ketamine			

Table 4: Comparison of the mean duration of procedure between two study groups

Study groups	N	Mean duraration of procedure in minutes	Std. Deviation
saline	49	14.40	5.3
ketamine	49	13.89	5.9
Statistical Analysis t value= 0.49 P value two tailed = 0.621 (>0.05) There was no significant difference of duration of procedure between two study groups			

Table 5: Comparison of the mean time of recovery between two study groups

Study groups	N	Mean time of recovery	Std. Deviation
Saline	49	8	3
Ketamine	49	8	4
Statistical Analysis t value= 0.198 P value two tailed = 0.843 (>0.05) There was no significant difference of mean time of recovery between two study groups			

Table 6: Comparison of the mean total dose of tramadol between two study groups

Study groups	N	Mean dose of tramadol in mg	Std. Deviation
saline	49	108	27
ketamine	49	107	32
Statistical Analysis t value= 0.154 P value two tailed = 0.878 (>0.05) There was no significant difference of mean dose of tramadol between two study groups			

Table 7: Comparison of the mean pain score between the two groups

Study groups	N	Mean pain score	Std. Deviation
Saline	49	5.11	0.81
Ketamine	49	4.80	0.90
Statistical Analysis t value= 1.77 P value two tailed = 0.08 (<0.1) Mean pain score was significantly higher with saline at P value 0.1 but not significant at P value 0.05 as compared to Ketamine			

These results have been summarized in the following table:

Table 8

Mean Variable	Ketamine group	Saline group	P value
Age	28.8	29	0.85
Weight	64.3	65	0.79
Duration of procedure	13.9	14.4	0.621
Total dose of propofol	242	301	0.001
Time of recovery	8	8	0.84
Total dose of tramadol	107	108	0.87
Mean pain score	4.80	5.11	0.08

Both groups had the same induction dose of propofol but when their total consumption of propofol was calculated at the end of the procedure, it turned out to be more in case of saline group. The difference reached to the statistical significance as shown in the following table:

Another important variable that could influence the use of propofol was the duration of the procedure as long procedures will require more doses of anaesthetic agent. When compared for duration of procedure, it was found that there was no significant difference between the two groups. The results are shown below:

The duration of procedure and the use of anaesthetic agent also affect the time of recovery. As shown above, duration of procedure did not differ significantly in two groups. However, the dose of propofol was significantly less among the patients in ketamine group. This could be the factor affecting the recovery time in patients of ketamine group but my study showed no significant difference in recovery times between the two groups.

The explanation of this fact is that more dose of propofol in saline group was not associated with pain relief at recovery and patients started to move earlier and opened their eyes. But in case of ketamine group, patients had lesser pain at recovery due to analgesic effects of ketamine and they recovered slowly despite the fact that they received lesser doses of propofol.

Both study groups were given tramadol boluses for pain relief in the post operative area and it was found that there was no significant difference regarding tramadol use between the two groups. The following table illustrates the fact:

Pain scores between the two group also failed to reach the statistical significance though patients in ketamine group seemed to have less pain postoperatively.

DISCUSSION

The objective of this study was to determine the effect of analgesic dose of ketamine on requirement of propofol during short gynaecological procedures. Patients in both groups were similar regarding their demographic details. The results have demonstrated a significant reduction in the dose of propofol in patients receiving a low dose of ketamine before the surgical stimulus (P <0.001. 95% confidence interval). Our results confirmed the work by Aouad MT[10] who used ketamine and propofol for procedural sedation and analgesia in paediatric population. He found that a combination of propofol and ketamine reduced the propofol required to maintain anaesthesia. Messenger DW[11] used ketamine in subdissociative doses in conjunction with propofol and found that it was as effective as fentanyl, which was a newer opioid. Analgesic dose of ketamine did not provide anaesthesia but it reduced propofol dose used by reducing the patient movements during painful stimuli due to its analgesic property. Its use in combination with propofol has resulted in hemodynamic stability and fewer side effects.

Low doses of ketamine when used at induction may affect the postoperative requirement of analgesic agents by neuromodulation of pain. This preemptive effect of ketamine has not been substantianed. Ketamine failed to show a preemptive effect when used as sole analgesic or in a single dose in the previous studies. We studied this effect of ketamine using tramadol as postoperative analgesic. Results of our study also showed that preemptive effect of ketamine was not significant (P=0.878; 95% CI). This result correlates with the previous data. Concept of preemptive effect of ketamine was rejected by the work of Beck K[7] in children undergoing urological surgery. Betra YK and colleagues[8] reached the same conclusion after their study in children undergoing tonsillectomy. The study of Dix P[12] in children undergoing appendectomy also showed that ketamine had no opioid sparing effects rather it caused hallucinations which limited its use. These results are contradictory to many studies which favour preemptive effect of ketamine but it may be because of the fact that most of those studies used multimodal approach towards pain control or ketamine was used in boluses and infusion form as well. However, all patients in ketamine group generally had better pain control in recovery period in my study though it could not reach statistical significance. If we increase the level of significance from 0.05 to 0.1, then our results become statistically significant.

CONCLUSION

This study showed that low dose of ketamine provided intraoperative analgesia and reduced the dose of propofol required to maintain anaesthesia. However, it had no effect on postoperative analgesic requirements.

REFERENCES

1. Morgan G E, Mikhail M S and Murray M J. Inhalation Anesthetics. In: clinical Anaesthesiology.4th ed. United states of America: McGraw-Hills 2006;161
2. Kaki A M and Al Marakbi W. Post-herniorrhapy infiltration of tramadol versus bupivacaine for postoperative pain relief: a randomized study. Ann Saudi Med. 2008 May-Jun;28(3):165-8.
3. Kargi E, et al. Tramadol as a local anaesthetic in tendon repair surgery of the hand. J Int Med Res. 2008 Sep-Oct;36(5):971-8.
4. Altunkaya H, et al. The postoperative analgesic effect of tramadol when used as subcutaneous local anesthetic. Anesth Analg. 2004 Nov;99(5):1461-4
5. Hashmi Z A, Bashir G, and Shah S A. Tramadol hydrochloride in postoperative analgesia:Clinical comparison with diclofenac sodium. Gomal Journal of Medical Sciences July–Dec., 2004, Vol. 2, No. 2
6. Adams HA, Brausch M, Schmitz CS, Meyer MC and Hecker H. Analgesic dosage with S-ketamine/propofol vs ketamine/midazolam: sedation, stress response and hemodynamics. A contolled study of surgical intensive care patients. Anasthesiol Intensivmed Notfallmed Schmerzther. 2001 Jul;36(7):417-24.
7. Eugene S, Miguel R and John E. Preemptive Ketamine Decreases Postoperative Narcotic Requirements in Patients Undergoing Abdominal Surgery. Anesth Analg 1997;84:1086-90
8. Becke K, et al. Intraoperative low-dose S-ketamine has no preventive effects on postoperative pain and morphine consumption after major urological surgery in children. Paediatr Anaesth. 2005 Jun;15(6):484-90.
9. Dix P, Martindale S and Stoddart P A. Double-blind randomized placebo-controlled trial of the effect of ketamine on postoperative morphine consumption in children following appendicectomy. Paediatr Anaesth 2003; 13: 422-6
10. Priestley SJ, Taylor J, McAdam CM and Francis P. Ketamine sedation for the children in the emergency department. Emerg Med (Fremantle), 2001 Mar;13(1):82-90.
11. Elia N and Tramer MR. Ketamine and postoperative pain—a quantitative systematic review of randomized trials. Pain. 2005 Jan;113(1-2):61-70
12. Wong CS, et al. Ketamine potentiates analgesic effect of morphine in postoperative epidural pain control. Reg Anesth. 1996 Nov-Dec;21(6):508-13