

Comparative study of ketamine, thiopentone and ketamine-thiopentone combination for short surgical procedures.

¹Dr Geeta Ahlawat, Professor, Deptt. of Anaesthesia, Pt. BDS PGIMS, Rohtak, Haryana.

²Dr Vikas Saroha, Chief Surgeon, Hirdaya Nilayam Hospital, Rohtak, Haryana.

³Dr Kirti kamal, Professor, Deptt. of Anaesthesia, Pt. BDS PGIMS Rohtak, Haryana.

⁴Dr Rajmala Jaiswal, Sr. Professor, Deptt. of Anaesthesia, Pt. BDS PGIMS Rohtak, Haryana.

⁵Dr. Mangal Ahlawat, Asistt. Professor, Deptt. of Anaesthesia, Pt. BDS PGIMS, Rohtak, Haryana.

Corresponding Author: Dr. Mangal Ahlawat, Asistt. Professor, Deptt. of Anaesthesia, Pt. BDS PGIMS, Rohtak, Haryana.

Citation this Article: Dr Geeta Ahlawat, Dr Vikas Saroha, Dr Kirti kamal, Dr Rajmala Jaiswal, Dr. Mangal Ahlawat, “Comparative study of ketamine, thiopentone and ketamine-thiopentone combination for short surgical procedures”, IJMSIR- February - 2020, Vol – 5, Issue -1, P. No. 95 – 103.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Since the introduction of intra venous anaesthesia, there has been a constant search for a safe intra venous anaesthetic technique, ketamine appears to be good candiadate. Inspite of several advantages that ketamine has to offer as a sole anaesthetic agent in minor surgical procedures, side effects(sympathomimetic effects, hallucination) associated with its use limits its utility. To reduce these side effects, combination of ketamine with various drugs have been tried. So we tried to evaluate and compare ketamine, pentothal, and combination of both drugs for short surgical procedures.

Material and methods: A randomized prospective study was conducted on 75 patients of either sex, ranging from 2 to 70 years of age, ASA physical status class I or II, posted for minor surgeries. All the patients were pre-medicated with inj. Atropine 0.01 mg/kg and inj.diazepam 0.1 mg/kg intra venously. All patients were randomized into 3 groups of 25 patients each. For

group A: Inj. ketamine 2mg/kg, group B: inj. Pentothal 5mg/kg, group C: inj. Ketamine 0.5mg/kg plus inj.Pentothal 2.5% 4mg/kg.

Results: In group A and C, no respiratory depression was found, where as in group B, one case(4%) showed respiratory depression and one case(4%) showed bronchospasm.

In our study 16% cases in Group B required supplementation with O₂, N₂O and 12% with O₂, N₂O and halothane, while in Group A, 8% required O₂, N₂O and 4% required O₂, N₂O, halothane. Whereas in Group C only one case(4%) required supplementation, that too where only O₂, N₂O could suffice.

Conclusion: From this study it is concluded that ketamine and pentothal combination provides satisfactory, safe and economical total intravenous general anaesthesia for minor surgical procedures.

Keywords: Thiopentone, General-anaesthesia, ketamine plus thiopental, minor surgeries.

Introduction

Anesthesiology is growing and progressing at an unprecedented pace. Since the introduction of intra venous anaesthesia, there has been a constant search for a safe intra venous anaesthetic technique having a potent analgesic effect; and which can thus provide good operative conditions with least disturbances in the body physiology.

Ketamine gives profound somatic analgesia, clear airway, without chin support and intact laryngeal and pharyngeal reflexes.¹ It provides stability to the cardiovascular and respiratory systems, with the absence of adverse effects on liver and kidney.^{2,3} In spite of several advantages that ketamine has to offer as a sole anaesthetic agent in minor surgical procedures, its tendency to produce tachycardia, hypertension and associated high incidences of unpleasant emergence phenomenon (psychomotor and psychomimetic effects) limits the utility of this otherwise excellent anaesthetic and potent analgesic agent, very near to an ideal intra venous agent.⁴

Thiopentone also proves to be a good induction agent with less chances of producing tachycardia and hypertension, so it can be given in old patients, but does not provide the intra-operative and post-operative analgesia. Its use demands a constant vigil on airway and requires supplementation with nitrous oxide and volatile anaesthetic agents.⁵

Regarding combination of ketamine and thiopentone in balanced anaesthetic technique, it has been suggested that it protects the brain from metabolic stimulatory effects of ketamine and therefore blocks dreams and hallucinations produced by ketamine. Similarly hypotensive action of thiopentone blunts the cardiostimulatory effects of ketamine.

To reduce these side effects, combination of ketamine with various drugs have been tried. These include droperidol, thiopentone, benzodiazepines as diazepam, lorazepam and midazolam. By using ketamine and thiopentone in total intra venous anaesthetic technique we can provide safe and cheap alternative to conventional method of giving anaesthesia for short surgical procedures. So i tried to evaluate and compare ketamine, pentothal, and ketamine plus pentothal in short surgical procedures.^{9,10,11.}

Material and methods

Study design: A randomized prospective study was conducted in the Department of Anaesthesia, Sheth V.S General Hospital, K.M. school of PGMER Ahmadabad, after approval from Institutional Ethical Committee.

Study period: December 1999 to December 2001

Study subjects: A total of 75 patients were grouped into three groups (25 of each) using sealed envelope containing code numbers of three groups.

1. Group A : Inj. ketamine 2mg/kg was given i.v after 5 min. of pre-medication
2. Group B : inj. Pentothal 5mg/kg was given i.v after 5 min. of pre-medication
3. Group C : inj. Ketamine 0.5mg/kg was given i.v after 5 min. of pre-medication plus inj. Pentothal 2.5% (4mg/kg) .

Inclusion criteria

- Age between 20–70 years of either sex
- ASA physical status class I or II
- Body Mass Index < 30
- Short surgical procedures i.e.(incision and drainage of abscesses, closed reduction of fracture upper limb, dilatation and curettage, circumcision, urethral dilatation, cystoscopy, orthopaedic procedures)
- Lasting up to 20-25 minutes.

Exclusion criteria

- ASA class III and IV
- Patients who received any analgesic or narcotic in the preceding 48 hours
- BMI > 30
- Anticipated difficult airway
- Morbid obesity

A detailed pre-anaesthetic evaluation including history, a thorough general, systemic examination and all relevant investigations were done for all the patients. All patients were kept fasting for at least 6 hours prior to anaesthesia. Preoperative baseline heart rate, blood pressure, respiratory rate, SpO₂ was recorded. A peripheral intravenous line was established. All the patients were pre-medicated with inj. Atropine 0.01 mg/kg and inj. diazepam 0.1 mg/kg intra venously. For group A: Inj. ketamine 2mg/kg was given i.v after 5 min. of pre-medication, for group B: inj. Pentothal 5mg/kg was given i.v after 5 min. of pre-medication, for group C: inj. Ketamine 0.5mg/kg was given i.v after 5 min. of pre-medication plus inj. Pentothal 2.5% (4mg/kg) was given i.v slowly after 1 min. of inj. Ketamine. Intra-operatively patients were spontaneously breathing atmospheric air and oxygen supplementation via Bain’s circuit was given to some patients who required inhalational anaesthetic supplementation. Dose of pentothal was calculated in each patient. Pulse rate and blood pressure were recorded in each patient at 5 min interval for 15 minutes. All patients were watched for airway obstruction by provocative test. It was applied with the patient in supine position, the head and neck were first passively flexed and patient closely observed for signs of airway obstruction. Patient’s head was then allowed to resume the extended position with lips closed, nostrils occluded and patient’s response noted. All the

patients were monitored during operative and post-operative period for any complication and duration of analgesia.

Statistical Analysis: Statistical analysis was performed by the SPSS program for windows, version 17.0 (SPSS, Chicago, Illinois). Continuous variables (age, weight, height, pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate, SpO₂, route of administration, dose of drug, duration of 1st dose(in minutes), total no. of doses given, supplementation, duration of anaesthesia, duration of surgery, awareness, total dose of thiopentone and ketamine and combination of ketamine and thiopentone were recorded. All the data was compiled and analysed by arithmetic mean and percentage.

Results: A total of 75 patients who underwent short surgical procedures lasting up to 25 minutes were enrolled for the study and were randomly divided into three groups. The demographic profiles of the patients in the three groups were comparable with regards to age and gender (Table-1).

Table 1: Demographic data of our study

Groups	Age (in years)			Sex	
	< 20 years	20- 40 years	>40 years	Male	Female
A	10	10	5	15	10
B	4	13	8	11	14
C	3	12	10	13	12

Table – 1 showing demographic data of our study. Majority of cases enrolled were between the age group of 20 -40 years. Majority of cases selected were male as compared to female. The distribution of minor surgical procedures done in all groups can be summed up as short gynaecological procedures (24 cases), orthopaedic procedures-(13 cases) and incision and drainage were 11 cases (table- 2).

Table 2: Distribution of minor surgical procedures

Serial no.	Procedures	Group- A	Group- B	Group- C
1.	Incision and drainage	5	2	4
2.	Gyanecological procedures	4	11	9
3.	Orthopaedic procedures	7	2	4
4.	Suturing	1	-	-
5.	Debridement and scrapping	4	2	2
6.	STG	2	-	-
7.	Circumcision	2	-	-
8.	Lord’s dilatation	-	4	2
9.	Urethral dilatation	-	2	2
10.	Cystoscopy	-	2	2
	Total	25	25	25

Table 2: Shows various surgical procedures conducted in this study. This table shows short gynaecological procedures – 24 cases, orthopaedic procedures-13 and incision and drainage – 11 cases were done in total.

In Group A: 52% cases have increase in pulse rate more than 15 beats /min, in Group B it is 60 % whereas in

Table 3 Hemodynamic parameters

Group	Changes in Pulse Rate					Changes in Blood Pressure(mm of Hg)				
	NO Change	Decreased 0-15/min	Decreased more than 15/min	Increased 0-15/min	Increased more than 15/min	No Change	Decreased upto 20	Decreased more than 20	Increased upto 20	Increased more than 20
A	-	-	-	12	13	-	-	-	18	7
%	-	-	-	48	52	-	-	-	72	28
B	-	-	-	10	15	4	17	4	-	-
%	-	-	-	40	60	16	68	16	-	-
C	5	9	-	10	1	5	7	-	12	1
%	20	36	-	40	4	20	28	-	48	4

Group C it is seen only in 4% of the cases. In Group A: all cases show increase in blood pressure, whereas in group B, all shows decrease in blood pressure; while in Group C, 20 % show no change in blood pressure, while in 80% of cases only minor changes in blood pressure was observed (table-3).

Table 3: showing hemodynamic parameters of patients. It shows that in group A- 52 % patients have increase in pulse rate more than 15 / min, in group B-it is 60 %, where as in group-C it is only in 4%of the cases. This table also shows increase in blood pressure (B.P) i.e in group-A all cases show increase in B.P, whereas in group-B, all cases shows decrease in B.P; while in group-C, 20% show no change, while 80% show only minor changes in B.P.

The duration of induction dose was more than 10 minutes in all cases of Group C (100%) as compared to other groups (table).Majority of the surgeries chosen were planned .The duration of operative procedures were between 5 -15 minutes in majority of cases. In Group A (68%), B(100%),C(76%) respectively (table-4).

Table 4: Duration of surgical procedure and duration of induction dose.

Group	Induction dose maximum effect (Minutes)						Duration of Surgery (Min)					
	0-5	6-10	11-15	16-20	21-25	>25	0-5	6-10	11-15	16-20	21-25	>25
A	-	1	10	14	-	-	-	4	13	4	4	-
%	-	4	40	56	-	-	-	16	52	16	16	-
B	-	5	10	-	-	-	-	20	5	-	-	-
%	-	60	40	-	-	-	-	80	20	-	-	-
C	-	-	17	7	1	-	-	12	7	6	-	-
%	-	-	68	28	4	-	-	48	28	24	-	-

Table- 4: shows duration of surgery(in mins) and duration of induction dose. This table shows that duration of induction dose was more than 10 minutes in all cases of Group C (100%) as compared to other groups. The duration of operative procedures were between -15 minutes in majority of cases. In Group A (68%), B(100%(76%) respectively. In Group A, 2 cases(8%) showed excessive secretions, in Group B : 1

case(4%) showed respiratory depression and 1 case(4%) showed bronchospasm, while in Group C, no adverse reactions were seen per-operatively. In Group A (ketamine), shows more dreams and hallucinations. Group (pentothal) B, shows more nausea, vomiting and respiratory depression while in Group C (pentothal+ketamine), complications were very less (4% i.e only one case) (table-5).

Table – 5 Adverse reaction and various complications in peri-operative period .

Group	Adverse Reaction intra-operative							Post-operative complication				
	Excessive secretion	Apnoea	Resp. Depression	Bronchospasm	Laryngospasm	Rigidity	Involuntary Movements	Nausea	Vomiting	Resp. Depression	Dreams	Hallucinations
A	2	-	-	-	-	-	-	-	-	-	1	2
%	8	-	-	-	-	-	-	-	-	-	4	8
B	-	-	1	1	-	-	-	1	1	1	-	-
%	-	-	4	4	-	-	-	4	4	4	-	-
C	-	-	-	-	-	-	-	1	-	-	-	-
%	-	-	-	-	-	-	-	4	-	-	-	-

Table 5: shows adverse reaction that occurred during intra-operative period and post-operative complications.

There was no case of intraoperative awareness. Post-operative analgesia was good in all Group A patients, none in Group B, whereas only two (8%) patient of Group C complained of pain at operative site. Patients in Group A and B required supplementation with O₂+N₂O+Halothane repetitive doses which increased cost ten fold. Therefore Group C proves to cheapest of all above. Therefore, In Group A: 100% cases showed increase in blood pressure with increase in pulse rate; all the patients had post-operative analgesia. Increase in

secretions was seen in 8% cases, while 12% showed emergence reaction. Supplementation of anesthesia with inhalational agents was needed in 12% of patients. In group B: 100% cases had shown decrease in blood pressure and increase in pulse rate, 8% cases showed respiratory complications intra operatively. 28% required supplementation with inhalational agents. No incidence of analgesia was found in postoperative visit. In group C: Minor changes in pulse rate and blood pressure was seen in 96% cases, and only 4% cases required supplementation with inhalational agents (oxygen and nitrous oxide only). Post operative analgesia was observed in 88% of cases (table- 6).

Table 6: Supplementation of anaesthesia required

Group	Supplementation of Anaesthesia			Intra-operative awareness	Post Operative Analgesia
	None	O ₂ + N ₂ O with mask	O ₂ + N ₂ O + Halothane with mask		
A	22	2	1	No	25
%	88	8	4	-	-
B	18	4	3	No	No
%	72	16	12	-	-
C	24	1	-	No	23
%	96	4	-	-	-

Table 6: showing number of patients requiring supplementation of anaesthesia, intra-operative awareness and post-operative analgesia in three groups. In Group C only one patient (4%) required supplementation with O₂ + N₂O as compared to group A where two patients (8%) required nitrous oxide and one patient (4%) required nitrous oxide + halothane supplementation. In Group B, where 4 cases (16%) required nitrous oxide in addition and in 3 cases (12%) nitrous oxide and halothane was required in addition to oxygen.

Discussion

Ketamine is an excellent anaesthetic, but its use in many developing countries is limited by relatively high cost and restricted availability. This study was This study was undertaken to assess a combined anaesthetic technique in which a small doses of ketamine and pentothal are used. Attention was concentrated on the adequacy of operating condition, affect on the hemodynamics, safety of the patients airway and effects of premedication.

In our study, 75 cases were studied, which included the commonly conducted short surgical procedures of

various types, most of them being planned surgeries(table-2) and the duration being 5-15 minutes in majority of the cases (table-4). The patients included were all without any major systemic diseases (i.e ASA grade I and II) and were of age group 20- 40 years.

Premedication:

D.L cappel and J.G. Bovill showed that diazepam i.v in ketamine anaesthesia is effective in prevention of emergence delirium. Compared to diazepam, this incidence of emergence is more with midazolam, due to its short duration of action, and more over it proves to be more costly. In our study, all patients were premedicated with inj. Atropine 0.01 mg/kg and inj. Diazepam 0.1 mg/kg i.v 5 minutes before induction. Atropine is given to prevent vagal stimulation and to decrease salivary secretion. Increased secretions were found in 2 (8 %) cases of group A even after giving atropine as premedication.¹

Course of anaesthesia: In group A and C, no respiratory depression was found, where as in group B, 1 (4%) case showed respiratory depression and 1 case(4%) showed bronchospasm. Ketamine and bronchospasm: ability of ketamine to antagonize bronchospasm might be partly related to its vagolytic and direct smooth muscle relaxant effect but more importantly to its sympathomimetic properties.

Dr P.K Gupta and B.P. Sarkar had studied ketamine and ketamine-pentothal (thiopentone) combination and compared the systolic blood pressure rises. They showed that only 25% cases in combination group had rise in BP as compared to 75 % in ketamine alone. (similar study was also done by Liang and Liang).^{3,5}

Ozlem Ozkan Kuscu et al, had conducted a study using thiopental (4 mg kg⁻¹), ketamine and combination of ketamine & thiopental (1 mg kg⁻¹ and 4 mg kg⁻¹ respectively) during electroconvulsive

therapy(ECT) on Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Rating Scale (HAM-A) and haemodynamic variables in patients with resistant major depression. They concluded that anaesthesia induced with thiopental, ketamine and thiopental–ketamine combination did not produced any difference in ECT effects for patients with treatment-resistant depression. Ketamine at a dose of 1 mg kg⁻¹ given just before ECT did not enhance the antidepressant effect of ECT; however, anxiety scores were increased with ketamine application.¹³

In our study only 4% of cases had tachycardia in Group C as compared to 52% cases in Group A and 60% in Group B (table-III). The cardiostimulatory effects of ketamine is attenuated by pentothal in Group C while in Group B, the tachycardia may be compensatory due to fall in blood pressure (84% cases).

In Group C only 52% of cases showed raised blood pressure as compared to 100% cases in group A. This further shows attenuation of cardio-stimulatory effects of ketamine by pentothal and diazepam (table- 3).

Corssen and Domino had described a state of profound analgesia with ketamine anaesthesia. In our study 16% cases in Group B required supplementation with O₂, N₂O and 12% with O₂, N₂O and halothane, while in Group A, 8% required O₂ , N₂O and 4% required O₂, N₂O, halothane.

Whereas in Group C only 1 case (4%) required supplementation, that too where only O₂, N₂O could suffice(table-6).

This shows that ketamine in Group A provides adequate anaesthesia but not adequate depth; pentothal in Group B provides adequate depth but not adequate analgesia.

Whereas in Group C both are provided, thus reducing the need for supplementation with other inhalational agents like nitrous oxide + Halothane.

Review of Post-operative Period

J.K.Liburn and J.W.Dundee showed higher incidence of emergence reactions with ketamine anaesthesia.⁴

In our study in Group B and C none of the cases showed emergence reactions, whereas in group A 12% of the cases showed emergence reactions (table-5).

It has been suggested that pentothal protects the brain from metabolic stimulatory effects of ketamine and therefore blocks the dreams and hallucinations produced by ketamine.

In our study, the mean value of duration of 1st dose of intravenous pentothal was 10.32 min that of ketamine is 17.4 min whereas that of combination group is 13.9 min (table- 4).

Ito and Ichiyangi found that ketamine is an attractive drug for post-operative analgesia even with sub anaesthetic dose.²

Peltz B. and Sinclair D.M. showed marked reduction in intra operative awareness and enhanced post-operative analgesia with ketamine anaesthesia.⁷

In our study there was no evidence of analgesia in Group B and patients immediately complained of pain. Post-operative was excellent in Group A (100%) and good in group C (92%) (table-6).

David L. Reich showed that ketamine reduces the intra operative awareness.⁷

In our study there was no intra operative awareness seen in all groups (table-6).

COST:

Michael and Dobson showed that a technique of general anaesthesia using small doses of intravenous ketamine and pentothal provide satisfactory operative

conditions at little more than half the cost of using ketamine alone.⁸

In our study, the cost of anaesthesia in NP/kg/min for Group A is 1.2 NP/Kg/min and for Group B is 3.4 NP/Kg/min while that for Group C is 2.2 NP/Kg/min but the agents in Group A and B require supplementation with oxygen, nitrous oxide and halothane which increases the cost nearly tenfold. Therefore, Group C proves to be economical (cheapest) of all the three groups when compared.

Conclusion: From this study, it is concluded that, combination of thiopentone and ketamine (in doses 5 mg kg⁻¹ and 2 mg kg⁻¹ respectively) provide cardiovascular stability, safe airway without assistance, satisfactory operative condition, fewer cases require inhalation supplementation, minimal emergence phenomenon, good post-operative analgesia and it proves to be most economical. In nutshell, ketamine and thiopentone combination provides satisfactory, safe and economical total intravenous general anaesthesia for minor surgical procedures.

References

1. Coppel D L, Bovill JG, Dundee JW. The taming of ketamine. *Anaesth* 1973; 28: 293-96.
2. Ito, Yangi I. ketamine as an analgesic agent in subanaesthetic doses. *Curr Res Anaesth* 1974; 50: 452.
3. Liang H.S, Liang. Minimising emergence reaction phenomenon: subdissociative dose of ketamine in balanced anaesthesia and analgesia. *Curr Res Anesth Analg* 1975; 54: 312.
4. Lilburn JK, Dundee JW, Nani S.G, Fee JPH, Johnstone HML. Ketamine sequelae: Evaluation of the ability of various premedicants to attenuate its psychic actions. *Anaesth* 1978; 33: 307-11.

5. Gupta PK, Sarkar BP. Thiopentone and diazepam for prevention of undesirable side effects of ketamine. *Indian J Anaesth* 1989; 37: 12.
6. Peltz B, Sinclair DM. Induction agents for cesarean section. *Anaesth* 1973; 28: 37-42.
7. Reich DL, Silvey G. ketamine: an update on the first 25 years of clinical experience. *Can J of Anaesth* 1989; 36(2):186-97.
8. Dobson MB et al. Anaesthesia with ketamine and thiopentone combination for short surgical procedures with reference to anaesthesia in developing countries. *Anaesth* 1978; 33(3).
9. Sprung J, Shoewald PK, Schwartz LB. Cardiovascular collapse resulting from thiopentone induced histamine release. *Anesthesiology* 1997; 80: 1006-9.
10. Cheng KI, Tang CS. Anaesthesia for pediatric herniorrhaphy or hydrocelectomy. *J Formosan medi assoc (Taiwan)* 1998; 97.
11. Tamminga, Noordhoek. Ketamine anaesthesia with or without diazepam premedication for bone marrow punctures in children with acute lymphoblastic leukemia. *J Paediatr hemat and onco* 2000; 17.
12. Irifune, Sato, kamata. Evidence for GABA (A) receptor agonistic properties of ketamine. *Anaesth and Analg* 2000; 91.
13. Kuscu OO, Karacaer F, Biricik E, Gulec E, Tamam L, Gunes Y : Effect of ketamine, thiopental and ketamine- Thiopental combination during electroconvulsive therapy for depression. *Turk J Anaesthesiol Reanim* 2015; 43(5): 313-17.