Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 3 Number 2, May - August 2016
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.3216.7

A Comparative Study of Ketamine and Propofol Versus Fentanyl and Propofol in Total Intravenous Anaesthesia for Short Surgical Procudures

Ramakrishna Reddy Mudiganti*, Aditya Pradeep Reddy B., Dasta Giri Reddy P.*****

Abstract

Background: Total Intravenous Anaesthesia using various drug combinations to produce adequate sedation and analgesia with rapid recovery for short surgical procedures is known for more than two decades. *AIM:* To compare the haemodynamic responses intra operatively and time to recovery in patients receiving Propofol-Ketamine and Propofol-Fentanyl in short surgical procedures. **Design:** Randomised controlled study. **Material and Method:** The study included 100 patients randomly selected into 2 Groups of 50 each.

Group 1: received Propofol 1.5mg/kg and Ketamine 1mg/kg (PK group)

Group 2: received Propofol 1.5mg/kg and Fentanyl 1 mcg/kg (PF group). **Statistical Analysis:** Using Chi-Square Test, Student t-test (paired and unpaired). **Results and Coclusion:** From the present study we concluded that both Propofol-Ketmine and Propofol-Fentanyl are equally safe and effective in Total Intra Venous Anaesthesia for patients undergoing short surgical procedures. Propofol-Ketamine combination has better haemodynamic stability than Propofol-Fentanyl combination.

Keywords: Not Provided

Introduction

Total Intra venous Anaesthesia is a technique of General Anaesthesia using a combination of agents given solely by IV route in the absence of all inhalational agents and Nitrous Oxide.

Propofol (2-6 di-isopropyl phenol) is a newer IV anaesthetic agent. It has already achieved considerable popularity for induction and maintenance of anaesthesia for short duration surgeries. *Propofol* has got favourable pharmacokinetic profile. It is suitable for infusion because of rapid decline in blood concentration. The decline in *Propofol* concentration following a bolus dose or following termination of an infusion can be described by 3 compartmenta open model. The first phase is rapid distribution (t1/2 alpha 2-8min) followed by rapid elimination (t1/2 beta 30-70min) and terminal long and slow elimination half life (4 to 23.5 hrs). *Propofol* is 96-99% protein bound. It has high clearance rate 1.5-2.2L/min. *Propofol* is rapidly metabolized in the liver by conjugation. *Propofol* rapid metabolism and high clearance rate explains the faster and clearheaded recovery after its use and makes it an ideal drug for use in day case surgery.

Propofol effect on Central Nervous System includes dose dependant sedation and hypnosis. It decreases cerebral blood flow by 26-51% due to cerebral vasoconstriction. It also reduces CMRO2 (Cerebral Metabolic requirement for oxygen) by 30% and reduces Intra Cranial Pressure by 30%. *Propofol* is associated with various neuroexcitatory events including convulsions, myoclonus and tremors, involuntary movements and dystonic posturing during induction of anaesthesia.

Propofol effect on Cardio Vascular system includes: decrease in mean arterial pressure, cardiac output and systemic vascular resistance. *Propofol* depresses the baroreceptor reflex control of heart rate. *Propofol* is a respiratory depressant, reduces both tidal volume and respiratory rate. Airway reflexes are depressed making it more advantageous to insert laryngeal mask. Apart form these major effects, it has anti-emetic effect and antipruritic effect, anti oxident effect.

Ketamine is a water soluble IV anaesthetic agent belongs to Phencyclidine group. It is the only

Author's Affiliation:
*Associate Professor, ** Senior Resident, *** Professor, Dept. of Anaesthesia, Mediciti Institute of Medical Sciences, Ghanpur, RR District, Telangana.

Corresponding Author:
Ramakrishna Reddy Mudiganti, Associate Professor, Dept. of Anaesthesia, Mediciti Institute of Medical Sciences, Ghanpur, Rr District, Telangana 501401.
E-mail: drrk_2003@yahoo.com

IV anaesthetic agent which has hypnotic, analgesic and amnestic properties and cheaper. *Ketamine* has high lipid solubility and low protein binding and extensive distribution. It has short elimination half-life of 2-3 hours due to high clearance (mean 1.4L/min). *Ketamine* is metabolized by hepatic microsomal enzymes.

Ketamine effect on Central Nervous system includes: Dissociative anaesthesia (disassociates the thalamus from the limbic cortex). It resembles a cataleptic state in which eyes remain open with a slow nystagmic gaze, but patient is not oriented to surroundings. *Ketamine* produces amnesia and intense analgesia. *Ketamine* increases cerebral oxygen consumption, cerebral blood flow and intracranial pressure. It is known to produce emergence reactions.

Ketamine increases arterial blood pressure, heart rate and cardiac output due to central stimulation of sympathetic nervous system. Respiration is not depressed by ketamine except in large doses and usually mildly stimulated. It increases salivary and tracheobronchial secretions.

Neither *Propofol* nor *Ketamine* are suitable as sole anaesthetic agents. The most common adjuvant is opiod analgesic to provide complete anaesthesia.

Fentanyl is used extensively nowadays in TIVA. It is hundred times more potent than morphine and as a part of balanced anaesthesia. It relieves pain, reduces somatic, autonomic response to airway manipulation, and provides haemodynamic stability with less respiratory depression.

Hence this study of two drug regimens were compared.

AIM

To compare the haemodynamic responses intra operatively and time to recovery in patients receiving *Propofol-Ketamine* and *Propofol-Fentanyl* in short surgical procedures.

Objectives

To Compare

- Haemodynamic stability
- Respiratory depression
- Emergence Phenomenon
- Time for spontaneous Eye Opening
- Post Operative Nausea and Vomiting

Patients and Methods

This prospective randomised study was conducted in Mediciti Institute of Medical Sciences, Ghanpur after approval by ethics committee from December 2012 to June 2014.

Inclusion Criteria

Age between 18-60years

ASA Grade 1 & 2

Short surgical procedures like:

Dilatation and Curettage

Suction and Evacuation

Incision & Drainage

Wound debridement

Circumcision

Closed reduction in Orthopaedic procedures.

Exclusion Criteria

Patient refusal

Allergy and Known Hypersensitivity to drugs

Contraindication to either *Propofol* or *Ketamine*

ASA physical status 3 and above

Age <18yrs and >60years

Anticipated difficult intubation

Pregnant and Lactating mothers

The Patients are randomly selected into 2 Groups of 50 each.

Group 1: *Propofol* 1.5mg/kg and *Ketamine* 1mg/kg (PK group)

Group 2: *Propofol* 1.5mg/kg and *Fentanyl* 1 mcg/kg (PF group)

Intermittent bolus doses were given when there was patient movement to surgical stimulus.

These are *Prpofol* 0.5mg/kg and *Ketamine* 0.5mg/kg in PK group, Propofol 0.5mg/kg and Fentanyl 0.5mcg/kg in PF group.

All patients were premedicated with Inj. Midazolam 1mg and Glycopyrrolate 0.2mg and Ranitidine 50mg IV before shifting to operating theatre. Standard Monitors like Pulse Oximeter, NIBP, ECG were attached to the paient.

Oxygen 5Lt/min was given throughout the procedure. Blood pressure, Heart Rate, Oxygen saturation were recorded at base level, at the time of induction and every 3 minutes thereafter.

Time for spontaneous eye opening, response of the patient to commands after surgery were recorded. Need for rescue analgesics was noted. Other parameters observed were nausea and vomiting, emergence reactions like hallucinations. Ramsay sedation score was also compared between the two groups. A total of 100 patients of either sex were participated in the study. Statistical data was analysed with stata 13.1 using: Chi-Square Test, Student t-test (paired and unpaired), P value of <0.05 was taken as significant and >0.055 was taken as not significant.

Table 1: Ramsay scale for the assessment of the level of sedation

Level of Activity	Points
Patient anxious, agitated or restless	1
Patient cooperative, oriented and tranquil	2
Patient responding only to verbal commands	3
Patient with brisk response to light glabella tap or loud auditory stimulus	4
Patient with sluggish response to light glabella tap or loud auditory stimulus	5
Patient with no response to light glabella tap or loud auditory stimulus	6

Table 1: Age distribution of the patients

Age (in yrs)	No. of patients	
	Group -PK(N=50)	Group PF (N=50)
18-30	20(40%)	17(34%)
31-40	21(42%)	18(36%)
41-50	8(16%)	14(28)
51-60	1(2%)	1(2)

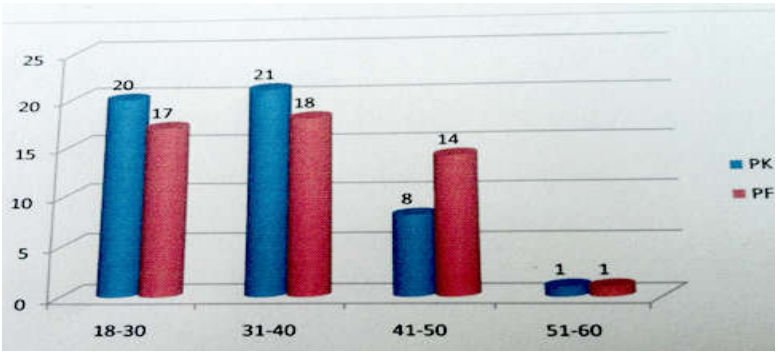

Fig. 1: Age wise distribution of patients

Age wise distribution was similar in two groups. Majority of the patients belonged to the age group 31-40 years.

Table 2: Sex distribution of patients

No. of patients	Female	Male
Group PK (N=50)	42(84%)	8(16%)
Group PF (N=50)	39(78%)	11(22%)

Gender Wise Distribution

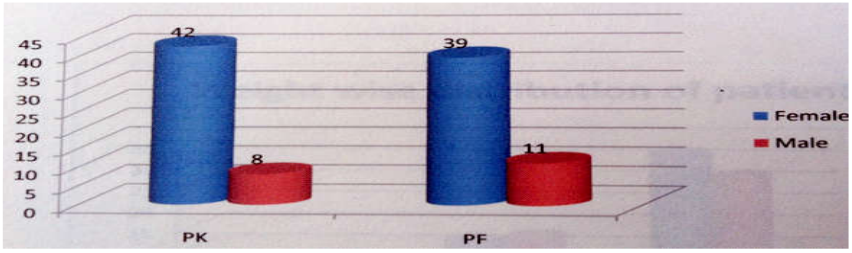

Fig. 2:

The majority of the patients were females 84% (PK group) and 78%(PF group) because most of the surgeries were gynaecological procedures.

Table 3: Weight wise distribution of patients

Weight in kgs	Group		P value
	Group PK (N=50)	Group PF (N=50)	
Mean(SD)	57.94±5.57	60.26±11.59	0.2051

The mean weight of both the groups was comparable.

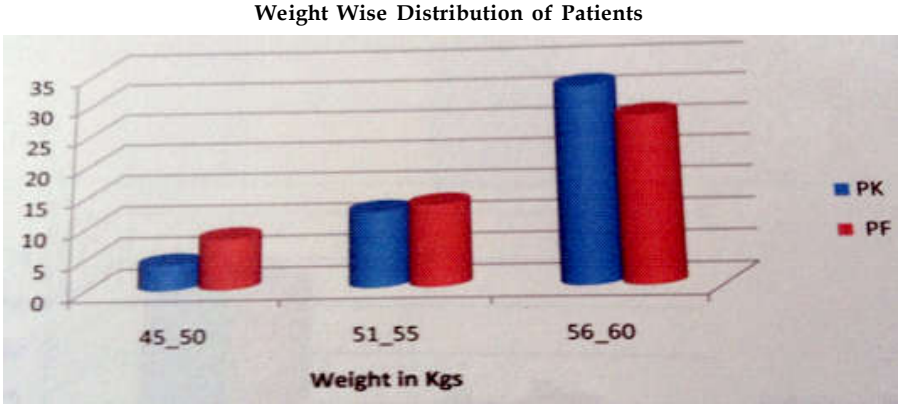

Fig. 3: Weight wise distribution of patients

Table 4: Comparison of mean age and weight between the groups

	Group – PK (n=50)		Group – PF (n=50)		*p* value	Result
	Mean	Std. deviation	Mean	Std. deviation		
Weight (KGS)	57.94	5.57	60.26	11.59	0.2051	Not sig.
Age (years)	33	8.92	35	9.41	0.2781	Not sig.

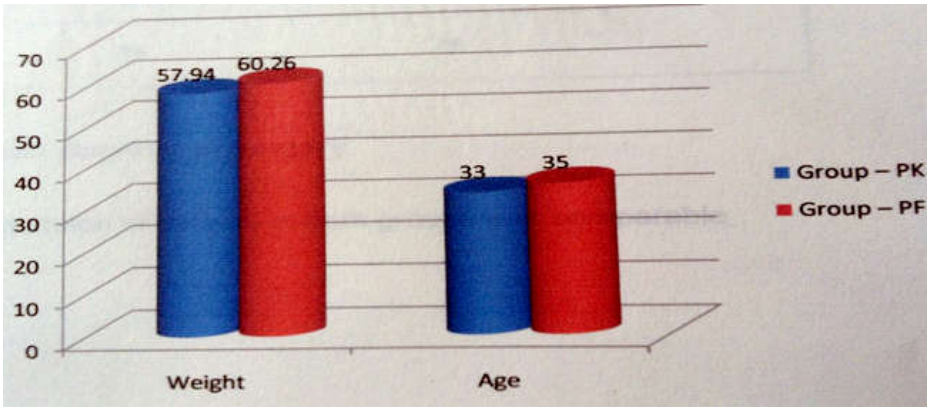

Fig. 4: Comparison of mean age and weight

'p' value: <0.05 – significant. The mean age and weight values in both groups were comparable each other statistically('p' value >0.05).

Table 5: Mean duration of surgery

Group	Mean duration of surgery	P value
PK	25.84 ± 1.76 min	0.4782
PF	26.1 ± 1.89 min	

Mean duration of surgery in both the groups was comparable.

Table 6: Comparision of Heart Rate between the two groups

Group	PK		PF		P value
	AVG	SD	AVG	SD	PK VS PF
Before induction	86.38	8.10	84.98	9.60	0.432
After induction	89.08	8.30	81.72	9.74	0.000
3 min	93.86	7.96	77.38	9.47	0.000
6 min	97.1	5.57	70.14	7.70	0.000
9 min	95.42	7.36	67.86	11.93	0.000
12 min	89.42	4.87	73.5	6.74	0.000
15 min	85.96	3.57	76.86	7.36	0.000
18 min	82.64	3.14	80.98	6.42	0.104
21 min	82.1	4.56	81.52	7.58	0.644
24 min	81.42	4.81	81.04	6.91	0.750
27 min	82.1	4.72	81.52	7.55	0.646
30 min	81.42	4.58	81.16	6.95	0.826

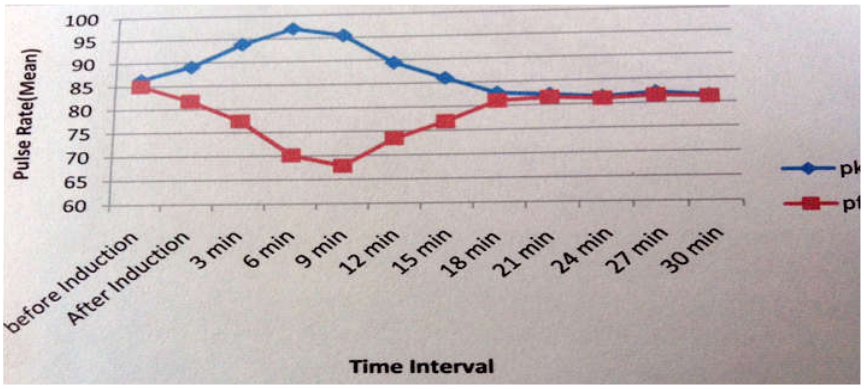

Fig. 5: Comparison of heart rate between the two groups

There was an increase in Heart rate after induction in PK group, whereas heart rate decreased after induction in PFgroup. At 30 min heart rate in both the groups was comparable.

Table 7: Comparision of Systolic Blood Pressure between the two groups

Group	SBP in mmHg				
	PK group		PF group		P value
	AVG	SD	AVG	SD	PK vs PF
Before induction	126.48	5.40	123.52	9.20	0.053
After induction	128.52	5.58	121.88	9.21	0.000
3 min	130.02	4.52	114.24	9.72	0.000
6 min	134.52	4.26	106.76	8.48	0.000
9 min	135.76	5.67	107.2	9.84	0.000
12 min	133.22	7.44	113.38	9.46	0.000
15 min	130.12	6.33	117.1	9.06	0.000
18 min	125.82	5.89	123.02	8.94	0.067
21 min	125.56	5.93	122.7	9.41	0.072
24 min	123.3	5.84	122.36	8.30	0.514
27 min	125.62	5.50	122.62	9.34	0.053
30 min	122.98	5.62	121.64	8.80	0.366

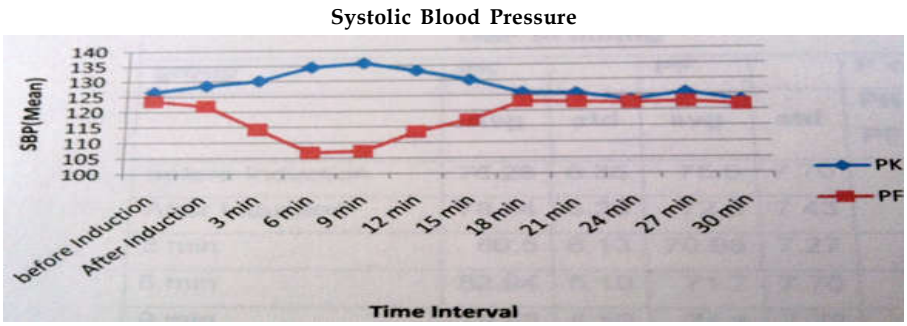

Fig. 6: Comparison of systolic blood pressure between two groups

There is statistically significant difference in systolic blood pressure between the two groups. In PK group there was an increase in SBP 3 min after induction, whereas in PF group SBP decreased.

Table 8: Comparision of diastolic blood pressure between the two groups

Group	Diastolic Blood Pressure in mmHg PK AVG	PK STD	PF AVG	PF STD	P value PK VS PF
Before induction	76.28	6.35	75.6	7.70	0.631
After induction	78.84	6.29	72.9	7.43	0.000
3 min	80.5	6.13	70.98	7.27	0.000
6 min	82.94	5.10	71.7	7.70	0.000
9 min	79.58	6.52	74.4	7.72	0.000
12 min	77.16	6.49	74.56	7.84	0.074
15 min	76.18	6.52	74.78	7.78	0.332
18 min	76.02	6.47	74.5	8.12	0.303
21 min	75.1	5.83	74.58	7.90	0.709
24 min	76.14	6.53	74.76	8.00	0.347
27 min	75.86	6.47	74.94	7.64	0.517
30 min	76.1	6.54	75.52	7.87	0.689

There is statistically significant difference between the two groups.

Diastolic Blood Pressure

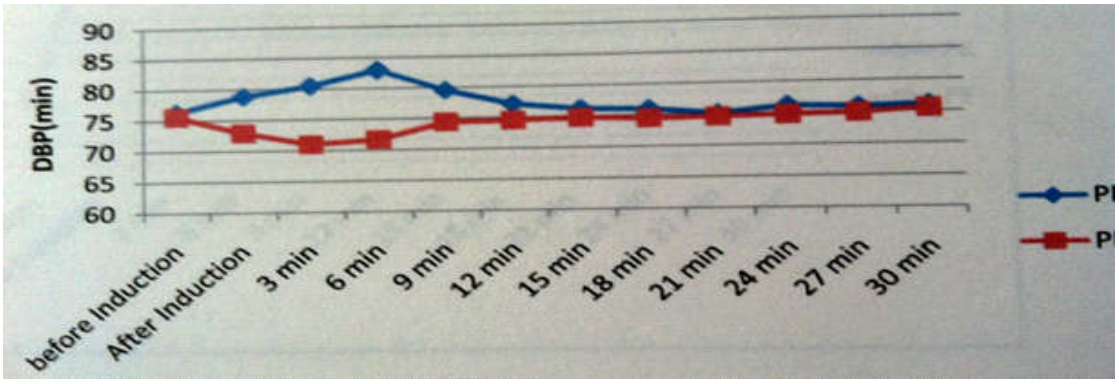

Fig. 7: Comparison of Diastolic blood pressure between two groups

In PK group DBP increased 3 min after induction. In PF group DBP decreased 3 min after induction.

Table 9: Comparison of Oxygen saturation between the two groups

Group	Oxygen saturation in % PK Avg	PK Std	PF Avg	PF Std	P value PK vs PF
Before induction	97.56	1.417	97.66	0.94	0.678
After induction	99.28	0.454	99.34	0.48	0.521
3 min	99.28	0.454	99.32	0.47	0.666
6 min	99.44	0.501	99.32	0.47	0.220
9 min	99.34	0.479	99.32	0.47	0.834
12 min	99.34	0.479	99.36	0.48	0.836
15 min	99.4	0.495	99.34	0.48	0.539
18 min	99.44	0.501	99.46	0.50	0.843
21 min	99.28	0.454	99.32	0.47	0.666
24 min	99.26	0.443	99.3	0.46	0.660
27 min	99.3	0.463	99.32	0.47	0.831
30 min	99.28	0.454	99.34	0.48	0.521

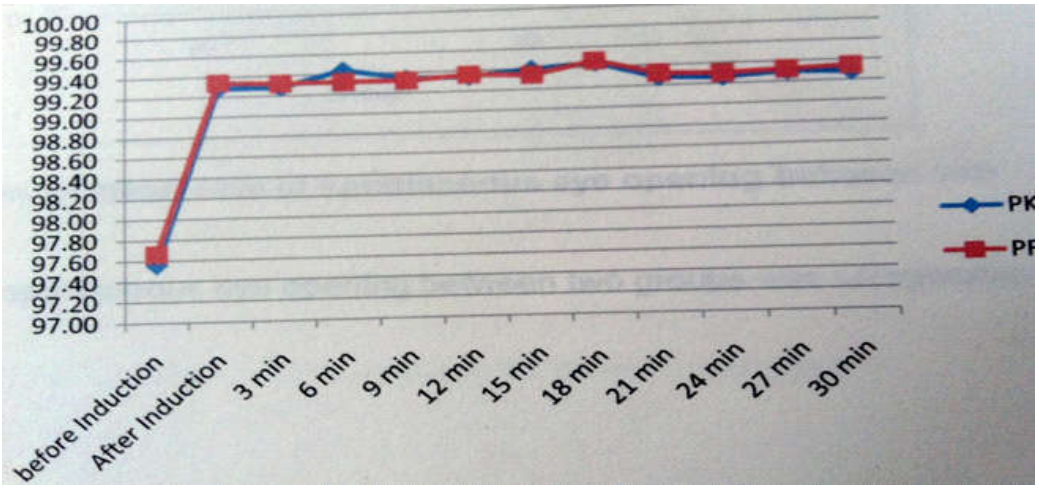

Fig. 8: comparison of oxygen saturation between two groups

Time for Spontaneous Eye Opening

Group	Mean time of Eye opening	P value
PK	6.42 ±1.3 min	<0.01
PF	3.64±1.2 min	

At the end of the surgery time for spontaneous eye opening is more in PK group. P value is significant.

Duration of Drowsiness

Group	Mean duration of drowsiness	P value
PK	12.72±1.61 min	>0.01
PF	7.42±1.32 min	

There is statistically significant difference in duration of drowsiness between the two groups.

Nausea and Vomiting

Group	No. of patients	P value
PK	6	0.74
PF	5	

The was slightly less incidence of post operative nausea and vomiting in PF group.

Emergence Reactions (Postop Delirium)

Group	No. of patients	P value
PK	3	>0.05
PF	0	

Postoprative delirium was noted in PK group.(in 3 cases)

Discussion

Total Intra Venous Anaesthesia has been a subject of interest for all the anaesthesiologists, as it avoids operating theatre pollution.

The availability of rapid and short acting sedatives, hypnotics,analgesics, muscle relaxants has refocused the attention on complete anaesthesia by IV route.The advent of continuous infusion system has made TIVA more popular and convenient.

In this study comparison was done between *Propofol* and *Ketamine* Vs *Propofol* and *Fentanyl* in terms of haemodynamic stability and postoperative recovery.

Patient Demographics

Weight: The mean weight of patients in PK group and PF group were 57.94+/-5.57 and 60.26+/-11.59. The two groups were statistically comparable.

(p>0.05) The mean weight of the patients in two groups of the present study correlates with that of study done by R Mahajan et al. Gender: In present study majority of patients were females as most of surgeries done were dilatation and curettage and suction curettage. Age: The mean age of the patients in two groups of the present study (PK group33+/-8.92, PF group 35+/-9.41) correlates with that of study done by R Mahajan et al.

Haemodynamic Parameters

Changes in Heart Rate

In the PK group there was an increase in the heart rate after induction in the present study and study by R Mahajan et al [1] , whereas there was no increase in the heart rate after induction in the study by Ranju Singh et al [2]. There was decrease in heart rate in PF group after induction in all the three studies. At 30 minutes all the three studies showed heart rate comparable to that of baseline value. Propofol does not change heart rate significantly. Ketamine increases heart rate due to increase in central sympathetic tone. Whereas Fentanyl can cause dose dependant decrease in heart rate. Bradycardia may occur due to central vagal nucleus stimulation.

Changes in Blood Pressure

The baseline systolic and diastolic blood pressure in both groups PK and PF in the present study and studies by R Mahajan et al, Ranju Singh et al were comparable. 3 minutes after induction in PK group there was significant rise in systolic blood pressure in Ranju Singh study, whereas in the present study only slight increase was observed. In PF group 3 minutes after induction significant decrease in systolic blood pressure in present study which is comparable to study by Ranju Singh et al. At 30 minutes systolic blood pressure was comparable in both groups in all three studies.

In the present study, diastolic blood pressure 3 minutes after induction in PK group slightly increased, in PF group a slightly decreased. However at 30 minutes diastolic blood pressure comparable in both the groups in all the studies.

The reason for the rise in Systolic and Diastolic blood pressure in PK group is Ketamine associated stimulation of cardiovascular system. In PFgroup fall in BP observed as Propofol decreases mean arterial pressure and cardiac index.

Nalini KB et al [3], Riham Hasaneun, Wael-El-Syed [4] studies have shown that Propofol-Ketamine combination is superior to Propofol-Fentanyl in terms of haemodynamic stability and respiratory depression.

Ritu Goyal et al [5] concluded that Ketamine being a cardio stimulant drug is better than Fentanyl with respect to haemodynamic stability. The incidence of apnea and respiratory depression are less with Ketamine, but Fentanyl showed faster recovery. Studies by *Guit JB et al [6], Meyer and co-workers [7]* showed stable haemodynamics in both the groups.

Hernandez et al [8] compared 3 combinations in TIVA: Propofol-Ketamine, Propofol-Fentanyl, Midazolam-Ketamine. They concluded that PK group was haemodynamically stable with less respiratory depression. Propofol induced fall in blood pressure was noted in the study by *Berlic et al [9]* .

Sameer kumar Khutia et al [10] Erdenl A , Panuk AG [11] conducted studies in paediatric patients for short surgical procedures. They concluded that Propofol-Ketamine combination provides better sedation and analgesia and reduces the incidence of hypotension when compared to Propofol-Fentanyl.

Oxygen Saturation

Oxygen saturation of both groups before induction were 97.34+/-1.55 and 97.66+/-0.94 which were comparable.

Post Operative Parameters

Time for Spontaneous Eye Opening

In the present study there was significant difference in both PK and PF groups at the end of surgery which were 6.42+/-1.3 min and 3.64+/-1.2 min respectively, p value<0.001 which is significant. In study done R Mahajan et al both groups did not differ significantly in relation to spontaneous eye opening.

Duration of Drowsiness

In present study duration of drowsiness in both PK and PF groups were 12.72+/-1.61 min and 7.42+/-1.32 min, p value is <0.01 which is statistically significant. **S**ukhminder Singh and Sukhminder Bajwa [12] compared Propofol-Ketamine Vs Propofol-Fentanyl, and found recovery was better in Propofol-Fentanyl group. This correlates with our present study.

Ramsay Sedation Score

The mean Ramsay sedation score in PK group is lower than PF group during the procedure.

Mortero et al [13] Sincignano et al [14] found adequate sedation and anaesthesia with fewer side effects with Propofol-Ketamine combination.

Post Operative Nausea and Vomiting

In present study 5patients in PK group and 6 patients in PF group complained of nausea and vomiting, p value 0.74. Similar results were reported by R Mahajan et al. In study by Ranju Singh et al nausea and vomiting higher in PK group when compared to PF group where p value was significant(0.04).

Vallejo et al [15] compared Propofol-Ketamine and Propofol-Fentanyl for laparoscopic tubal ligation. They concluded nausea and vomiting are not less in PK group when compared to PF group.

Emergence Reactions (Postop Delirium)

In present study 3 patients had emergence ractions like postop delirium in PK group whereas none in PF group. In study by R Mahajan et al incidence of emergence reaction in PK group were high.

Benzodiazepines have proved more effective in preventing this phenomenon, Midazolam being more superior than Diazepam. (Cart Wright and Pingel 1984). Inclusion Thiopentone may decrease the incidence whereas Atropine or Droperidol may increase the emergence delirium.

Summary

The present clinical study '*A Comparative Study of Ketamine and Propofol Versus Fentanyl and Propofol in Total Intravenous Anaesthesia for Short Surgical Procudures*' was undertaken in Mediciti Institute of Medical Sciences, Ghanpur, RR District, Telangana.

Total of 100 patients of either sex aged between 18-65 years and ASA grade I & II undergoing short surgical procedures of less than half an hour were allocated into two groups of 50 each.

Group 1: *Propofol* 1.5mg/kg and *Ketamine 1*mg/kg (PK group)

Group 2: *Propofol* 1.5mg/kg and *Fentanyl* 1 mcg/kg (PF group)

Observations Made in this Study

Heart rate is statistically significant in both PK and PF groups upto 15 minutes. In PK group it returned to base line level at 15th minute.

Systolic blood pressure in both PK and PF group show significant difference upto 15min. At 18th minute systolic blood pressure in both groups returned to base line level.

Diastolic blood pressure in both PK and PF group showed significant difference statistically upto 9 min. In both groups it returned to base line level at 12 min.

There was no incidence of apnea or desaturation in both the groups.

Incidence of Post operative nausea and vomiting is more in PF group, although insignificant when compare to PK group.

Emergence reactions observed in PK group only. (3 patients).

Conclusion

From the present study we concluded that both *Propofol-Ketmine* and *Propofol-Fentanyl* are equally safe and effective in Total Intra Venous Anaesthesia for patients undergoing short surgical procedures.

Though there was statistically significant difference in haemodynamic parameters when both groups compared, clinically there was not much difference. *Propofol-Ketamine* appears to be slightly better haemodynamic stability compared to *Propofol-Fentanyl*. Postoperative recovery was superior in *Propofol-Fentanyl* group. Postoperative nausea and vomiting was more in Propofol-Fentanyl group.

References

1. R Mahajan, N Swarnkar, A Ghosh, Comparison of Ketamine and Fentanyl with Propofol in total intravenous anaesthesia. A double blind randomised clinical trial. The internet Journal of Anaesthesiology. 2009; 23(2).
2. Ranju Singh, Mahmood Ghazanwy, Homay Vajifdar, A randomised controlled trial to compare Fentanyl-Propofol and Ketamine-Propofol combination for procedural sedation and analgesia in laparoscopic tubal ligation. Saudi Journal of Anaesthesia. Jan-Mar 2013 Jan-Mar; 7(1).
3. Nalini KB, Anusha Cherian, Yashwantha Kumar c, Comparison of Propofol and Ketamine versus Propofol and Fentanyl for Puerperal sterilisation, A randomised clinical trial. Journal of clinical and diagnostic research. 2014; 8(5): 01-04.
4. Riham Hasaneun, Wail-El- Syed. Ketamine /Propofol

versus Fentanyl/Propofol for sedating obese patients undergoing ERCP. Egyptian journal of anaesthesia. 2013; 29(3): 207-211.

5. Ritu Goyal, Manpreet Singh, Jai Prakash Sharma, Comparison of Ketamine with Fentanyl as coinduction in Propofol anaesthesia for short surgical procedures. International journal of critical illness and injury science. 2012 2; 1: 17-20.
6. Guit TBM, Koning HM, Coster ML. Ketamine and analgesia for total intravenous anaesthesia with Propofol. Anaesthesia. 1999; 46: 24-27.
7. Meyer M, Ochman O, Deonicke A, Angste JR, Suttam H. Influence of Propofol-Ketamine versus Propofol-Fentanyl anaesthesia in haemodynamics and analgesia. Anaesthesiology. 1990; 39: 609-616.
8. Hernandez C, Parramon F, Gracia, Vilaplona J. Comparative study of 3 techniques for total intravenous anaesthesia Midazolam-Ketamine, Propofol-Ketamine and Propofol-Fentanyl. Rev.esp anaesthesiology. 1999; 46: 154-8.
9. Berlic, Claeys MA, and Gepts E. Haemodynamic changes during induction and maintenance with Propofol. British Journal of Anaethesia. 1988; 60: 3-9.
10. Khutia SK, Mandal MC, Das S, Basu SR. Intravenous infusion of Ketamine-Propofol can be alternative to intravenous infusion of Propofol and Fentanyl for deep sedation and analgesia in paediatric patients undergoing short surgical procedures. Indian journal of anaesthesia. 2012 56; 2: 145-50.
11. Erden JA, Pamuk AG, Akinci SB, Koseoglu a, Ayepar U. Comparison of Propofol-Fentanyl with Propofol-Fentanyl and Ketamine combination in paediatric patients undergoing interventional radiological procedures. Journal of paediatric anaesthesia. 2009; 19(5): 500-6.
12. Sukhminder Jit Singh Bajwa, Sukhminder Kaur Bajwa and Jasbir Kaur. Comparison of two drug combinations in total intravenous anaesthesia, Propofol-Ketamine and Propofol-Fentanyl. Saudi journal of anaesthesia. 2010; 4(2): 72-79.
13. Mortero RF, Clark LD, Tolan MM, Metz RJ. The effect of small dose of Ketamine on Propofol sedation, respiration, postoperative mood perception, cognition and pain. Anaesthesia and Analgesia. 2001; 92: 1465-9.
14. Sincignano A, Bellato V, Cancillicr F, Faronic . Propofol-Ketamine versus Propofol-Fentanyl in short gynaecologic surgery. Minerva Anaesthesiology. 1990; 56: 61-6.
15. Vallejo MC, Romeo RC, Davies DJ, Ramanathan S. Propofol-Ketamine versus Propofol-Fentanyl for out patient laparoscopy, comparison of postoperative nausea, emesis,analgesia, recovery. Journal of clinical anaesthesia. 2002; 14(6): 426-431.