

TO STUDY AND COMPARE HAEMODYNAMIC AND RESPIRATORY CHANGES WITH TOTAL INTRAVENOUS ANESTHESIA USING KETAMINE-PROPOFOL AND FENTANYL-PROPOFOL FOR SHORT SURGICAL PROCEDURES

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Abstract:

Ketone - Propofol combination produces rapid anesthesia with stable haemodynamics & respiratory stability. Awakening from anesthesia, recovery of intellectual & cognitive functions is faster in Ketamine - propofol group along with better post anesthesia recovery (Aldrete Kraulik). Incidence or side effects like emergence delirium are associated with Ketamine. Incidence of nausea, vomiting is higher in fentanyl group with significantly low post operative pain.

Both Fentanyl & Ketamine are good analgesics for total intravenous anesthesia in combination with propofol. Ketamine - propofol combination is having better cardio-respiratory stability & recovery profile than fentanyl propofol group in short surgical procedure and day care surgery.

Keywords: Haemo dynamics Ketamine, propofol fentanyl.

Introduction:

Day care surgical procedures are those elective minor or intermediate surgeries performed under local, regional or general anesthesia.

Recent advances in anesthesia & surgical techniques combined with cost containment concerns, have made day care surgeries increasingly popular.¹ Day care anesthesia has dual goals of rapidly and safely establishing satisfactory procedural condition and ensuring rapid, predictable recovery with minimum post operative sequelae. With the introduction of modern shorter acting anesthetics and sophisticated monitors, it became easy to ensure titration of anesthetic agents. Inhalation agents² including N₂O cause pollution of operation theatre and impose hazards to the health of theatre personnel including the anesthesiologist himself. The scavenging

used to remove waste gases, regional anesthesia, another effective alternative, avoids all hazards associated with general (both intravenous & inhalation anesthesia) and tracheal intubation. But it demands high degree of technical excellence and are safe & effective in experienced hands only.

Intravenous anaesthetic agents provide rapid and smooth induction over last couple of decades. The growth in knowledge of pharmacokinetics and pharmacodynamics of intravenous anaesthetic agents has resulted in better understanding of relationship between drug dose, blood concentration & effect.^{3,4}

Various intravenous agents have been tried for short surgical procedures.

Thiopentone was introduced in 1935 and has been used extensively but its use as an infusion or in repeated doses is associated

with profound cardio respiratory depression^{5,6} and delayed recovery^{7,8} ketamine was introduced in 1970 and was used to induce as well as for maintenance.⁹ But its use was associated with sympathetic activation^{9,10} and psycho mimetic effects.¹¹

Propofol as a result of its favourable pharmacokinetics and pharmacodynamics¹²⁻¹⁴ has become an ideal agent for induction & maintenance of anaesthesia for short surgical procedures along with hypnotic and sedative properties. Propofol has got unique mood elevating and anti emetic property. Induction with propofol is rapid and smoother. However propofol has got disadvantage like pain on injection^{15,16} & lack of analgesic property.

In day care anesthesia for short surgical procedures choice of agent should be such that, it should minimally affect induction time, maintenance & recovery profile of main induction & maintenance agent if total intravenous anaesthesia is planned.

Amongst opioid newer potent short acting drugs like fentanyl.¹⁷ Sufentanil are agents of choice for anesthesia with propofol with adequate analgesia and rapid recovery also ketamine in subanesthetic doses¹⁸ is known to produce minimum cardio- respiratory depression while providing intense analgesia. Combination of ketamine with propofol and midazolam can minimize its cardiovascular stimulating & psycho mimetic effect¹⁹.

In present study we have planned total intravenous anesthesia with propofol as main induction and maintenance agent along with ketamine^{20,21} or fentanyl as supplementary analgesic.

We have compared the effect of these two combinations in terms of cardiovascular (haemodynamic) stability, respiratory changes, requirement of anaesthetic agents, recovery profile & side effects.

Aims & Objectives:

- (i) To study & compare changes in heart rate, blood pressure, respiratory rate & oxygen saturation.
- (ii) To study & compare recovery time, cardio respiratory status in recovery room by Aldrete score & side effects.

Material & Methods:

This study to compare haemodynamics and respiratory changes with total intravenous anesthesia using ketamine-propofol and fentanyl-propofol for day care short surgical procedure was conducted in the department of anaesthesiology, Bombay hospital Indore on 50 patients 48 females and 2 males between age group of 18-60 years with ASA grade I & II. It was prospective interventional & observational study. Patients were divided in 2 groups, each group consists of 25 patients.

Grouping -

Group I- (N=25): Ketamine 5 mg/Kg with propofol induction & maintenance.

Group 2- (N=25): Fentanyl 2 µg/ with propofol for induction and maintenance.

Inclusion criteria:

All patients of ASA grade I & II and age group of 18-60 years require 20-40 pf surgical intervention were included in study.

Exclusion criteria:

Patients having medical co-morbidity like hypertension, diabetes mellitus, liver disease, psychiatric disorder, convulsion & asthma etc were excluded from study.

Methodology:

Patients were kept nil by mouth for 6 hours prior to surgery. Weight was recorded. Cardio vascular, respiratory & CNS parameters were examined clinically. All the patients were having normal preoperative investigations.

Anesthesia Technique:-

Vital parameters were recorded using Niden-koheden multi parameter monitor. An intravenous line & bivalve was secured & a drop of Ringer's lactate solution was started.

An ATOM or a Claris Infusion set was kept ready by assembling on it a 50 ml medisafe and a 100 ml extension tube, both changed with 1% propofol.

All the patients were premeditated with Inj. Glyco pyrrolate 0-2 mg IV, Inj Ranitidine 50 mg., Inj midzolam 1mg IV. 5 minutes after premedication vital parameters were recorded & then patients were induced with Inj. ketamine 0.5mg/kg (Group-I) I.V. or Inj. fentanyl 2 ug/kg, Inj propofol 2mg/kg over 30 seconds (1ml/3second).

Vital parameters were recorded at 1 minute after loss of eyelash reflex.

Loading dose of propofol was immediately followed by infusion of propofol by infusion pump 0.9 ml/kg/hr. (9 mg/kg/hr.) through 2nd port of bivalve recorded every 5 minutes.

Number of active movements done by patient 10 mg fentanyl (group-2) or 5 mg of ketamine (group-I) was administered along with 10 mg of Inj propofol as an additional (supplementary/top up) dose. Number of such top up & Active movements also recorded.

Patients were oxygenated and assisted ventilation were given with Bain's circuit when oxygen saturation was below 95% or in case of apnoea. The infusion of propofol

was stopped immediately at the end of surgery.

Time period of immediate recovery viz., awakening of patient from stoppage of propofol, infusion up to eye opening of patient, spontaneously or on verbal command was recorded & then patient shifted to recovery room.

Monitoring of parameters every 5 minutes was continued up to 30 minutes in recovery room stay. Following parameters were also noted in recovery room, Aldrete and Kraulik score²² which consist of:-

- Respiratory rate.
- Movements (Power in all extensities).
- O₂ saturation, colour of Skin.
- Systolic & diastolic blood pressure.
- Consciousness of patients whether spontaneous (0) or on verbal command (1) or Painful stimulus (2).
- Orientation in time, place & person
- Digit span scale- time required for patient to count digits from 0 to 9 without mistake (75 sec.) was noted.
- Episodes of nausea & vomiting.
- Post operative pain using verbal pain scale. Patients were then shifted to ward from recovery room & were discharged in the same evening after 12 hours.
- Emergence delirium.

Observations & Results

Table No. 1
Comparison of mean verbal command time (seconds) between the two study groups (N=50)

Parameter	Ketamine Group (Mean±SD) (n=25)	Fentanyl Group (Mean±SD) (n=25)	't' Value, df	P value
Verbal command time	526.20 ± 114.76	711.96 ± 101.27	-6.068, df=48	0.000*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Table No. 2
Comparison of time, place and person orientation time (seconds) between the two study groups (N=50)

Parameter	Ketamine Group (Mean±SD) (n=25)	Fentanyl Group (Mean±SD) (n=25)	't' Value, df	P value
Orientation time	662.40 ± 154.90	935.20 ± 85.10	-7.72, df=48	0.000*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Table No. 3
Comparison of verbal pain scale in the two study groups

(N=50)

Verbal Pain scale		Study Groups		Total
		Ketamine Group	Fentanyl Group	
No pain	N	10	20	30
	%	40.0%	80.0%	60.0%
Mild pain	N	14	5	19
	%	56.0%	20.0%	38.0%
Moderate pain	N	1	0	1
	%	4.0%	0.0%	2.0%
Total	N	25	25	50
	%	100.0%	100.0%	100.0%

$\chi^2=8.59$, $df=2$, P value = 0.014, significant

Table No. 4
Comparison of Aldrete-Kraulik Score at different points of time between the two study groups

(N=50)

Aldrete-Kraulik Score	Study Groups	N	Mean \pm SD	't' Value, df	P value
5 min	Ketamine group	25	9.68 \pm 0.48	8.82, df=48	0.000*
	Fentanyl group	25	8.24 \pm 0.66		
10 min	Ketamine group	25	9.80 \pm 0.41	9.17, df=48	0.000*
	Fentanyl group	25	8.40 \pm 0.65		
15 min	Ketamine group	25	9.88 \pm 0.33	8.20, df=48	0.000*
	Fentanyl group	25	8.76 \pm 0.60		
20 min	Ketamine group	25	9.96 \pm 0.20	4.77, df=48	0.000*
	Fentanyl group	25	9.44 \pm 0.51		
25 min	Ketamine group	25	10.00 \pm 0.00	2.14, df=48	0.043*
	Fentanyl group	25	9.84 \pm 0.37		

Table No. 5
Comparison of Mean Heart Rate at different points of time between the two study groups

(N=50)

Mean Heart Rate	Study Groups	N	Mean \pm SD	't' Value, df	P value
Pre-op	Ketamine group	25	87.0 \pm 9.3	1.50, df=48	0.140. NS
	Fentanyl group	25	83.7 \pm 6.0		
Intra-op 1 min	Ketamine group	25	91.5 \pm 8.4	0.853, df=48	0.398, NS
	Fentanyl group	25	89.0 \pm 12.2		
Intra-op 5 min	Ketamine group	25	93.3 \pm 8.6	-0.197, df=48	0.845, NS
	Fentanyl group	25	93.9 \pm 13.8		
Intra-op 10 min	Ketamine group	25	92.6 \pm 9.1	-1.646, df=48	0.106, NS
	Fentanyl group	25	97.6 \pm 12.0		
Intra-op 20 min	Ketamine group	25	90.5 \pm 8.2	-4.640, df=48	0.000*
	Fentanyl group	25	102.8 \pm 10.5		
Intra-op 30 min	Ketamine group	11	88.9 \pm 8.2	-2.399, df=22	0.025*
	Fentanyl group	13	98.8 \pm 11.4		
Intra-op 40 min	Ketamine group	2	86.0 \pm 2.8	-	-
	Fentanyl group	0	0.00 \pm 0.0		
Post-op 5 min	Ketamine group	25	86.5 \pm 5.8	-3.719, df=48	0.001*
	Fentanyl group	25	92.7 \pm 6.1		
Post-op 10 min	Ketamine group	20	86.0 \pm 5.9	-2.085, df=43	0.043*
	Fentanyl group	25	89.5 \pm 5.4		
Post-op 15 min	Ketamine group	1	78.0 \pm 0.0	-	-
	Fentanyl group	3	86.0 \pm 8.7		

* Statistically significant difference (P<0.05)

Table No. 6**Comparison of Mean Systolic Blood Pressure at different points of time between the two study groups (N=50)**

Systolic Blood Pressure	Study Groups	N	Mean \pm SD	't' Value, df	P value
Pre-op	Ketamine group	25	118.1 \pm 6.7	0.659, df=48	0.513, NS
	Fentanyl group	25	116.7 \pm 7.9		
Intra-op 1 min	Ketamine group	25	109.8 \pm 6.8	4.179, df=48	0.000*
	Fentanyl group	25	101.5 \pm 7.1		
Intra-op 5 min	Ketamine group	25	108.4 \pm 5.1	4.102, df=48	0.000*
	Fentanyl group	25	100.1 \pm 8.8		
Intra-op 10 min	Ketamine group	25	112.9 \pm 8.0	3.147, df=48	0.003*
	Fentanyl group	25	105.1 \pm 9.4		
Intra-op 20 min	Ketamine group	25	115.0 \pm 8.5	-0.232, df=48	0.818, NS
	Fentanyl group	25	115.8 \pm 13.0		
Intra-op 30 min	Ketamine group	11	118.2 \pm 10.2	-1.003, df=22	0.327, NS
	Fentanyl group	13	122.2 \pm 9.2		
Intra-op 40 min	Ketamine group	2	119.0 \pm 1.4	-	-
	Fentanyl group	0	0.00 \pm 0.0		
Post-op 5 min	Ketamine group	25	115.3 \pm 8.9	1.234, df=48	0.223, NS
	Fentanyl group	25	112.0 \pm 9.9		
Post-op 10 min	Ketamine group	20	113.8 \pm 7.8	1.725, df=43	0.092, NS
	Fentanyl group	25	109.7 \pm 8.1		
Post-op 15 min	Ketamine group	1	112.0 \pm 0.0	-	-
	Fentanyl group	3	108.7 \pm 5.0		

* Statistically significant difference (P<0.05)

Table No. 7**Comparison of Mean Diastolic Blood Pressure at different points of time between the two study groups (N=50)**

Systolic Blood Pressure	Study Groups	N	Mean \pm SD	't' Value, df	P value
Pre-op	Ketamine group	25	78.7 \pm 5.2	1.607, df=48	0.115, NS
	Fentanyl group	25	76.2 \pm 5.9		
Intra-op 1 min	Ketamine group	25	74.0 \pm 6.4	3.870, df=48	0.000*
	Fentanyl group	25	67.5 \pm 5.4		
Intra-op 5 min	Ketamine group	25	75.4 \pm 7.0	5.810, df=48	0.000*
	Fentanyl group	25	64.8 \pm 5.9		
Intra-op 10 min	Ketamine group	25	76.0 \pm 5.1	3.668, df=48	0.001*
	Fentanyl group	25	69.7 \pm 6.9		
Intra-op 20 min	Ketamine group	25	76.3 \pm 6.3	0.443, df=48	0.660, NS
	Fentanyl group	25	75.4 \pm 8.8		
Intra-op 30 min	Ketamine group	11	76.9 \pm 7.0	-0.955, df=22	0.350, NS
	Fentanyl group	13	79.9 \pm 7.9		
Intra-op 40 min	Ketamine group	2	71.0 \pm 1.4	-	-
	Fentanyl group	0	0.00 \pm 0.0		
Post-op 5 min	Ketamine group	25	77.0 \pm 7.4	1.762, df=48	0.084, NS
	Fentanyl group	25	73.1 \pm 8.0		
Post-op 10 min	Ketamine group	20	75.5 \pm 6.7	2.734, df=43	0.009*
	Fentanyl group	25	69.8 \pm 7.3		
Post-op 15 min	Ketamine group	1	72.0 \pm 0.0	-	-
	Fentanyl group	3	73.3 \pm 5.0		

* Statistically significant difference (P<0.05)

Table No. 8
Comparison of Mean Respiratory Rate at different points of time between the two study groups (N=50)

Systolic Blood Pressure	Study Groups	N	Mean ± SD	't' Value, df	P value
Pre-op	Ketamine group	25	13.2 ± 1.3	0.779, df=48	0.440, NS
	Fentanyl group	25	12.9 ± 1.4		
Intra-op 1 min	Ketamine group	25	13.4 ± 5.0	2.265, df=41	0.029*
	Fentanyl group	18	9.8 ± 5.6		
Intra-op 5 min	Ketamine group	24	15.8 ± 5.4	1.258, df=39	0.216, NS
	Fentanyl group	17	13.4 ± 7.0		
Intra-op 10 min	Ketamine group	25	18.0 ± 5.1	0.481, df=43	0.633, NS
	Fentanyl group	20	17.3 ± 5.9		
Intra-op 20 min	Ketamine group	25	20.3 ± 2.3	-2.950, df=37.95	0.005*
	Fentanyl group	25	23.1 ± 4.1		
Intra-op 30 min	Ketamine group	11	19.8 ± 3.2	-1.132, df=22	0.270, NS
	Fentanyl group	13	21.2 ± 3.0		
Intra-op 40 min	Ketamine group	2	17.0 ± 1.4	-	-
	Fentanyl group	0	0.00 ± 0.0		
Post-op 5 min	Ketamine group	25	16.2 ± 1.8	-3.283, df=48	0.002*
	Fentanyl group	25	18.4 ± 2.8		
Post-op 10 min	Ketamine group	20	14.6 ± 1.5	-4.108, df=43	0.000*
	Fentanyl group	25	16.4 ± 1.6		
Post-op 15 min	Ketamine group	1	14.0 ± 0.0	-	-
	Fentanyl group	3	17.7 ± 1.5		

* Statistically significant difference (P<0.05)

Table No. 9
Comparison of Mean Oxygen Saturation at different points of time between the two study groups (N=50)

Systolic Blood Pressure	Study Groups	N	Mean ± SD	't' Value, df	P value
Pre-op	Ketamine group	25	99.8 ± 0.4	-0.210, df=48	0.835, NS
	Fentanyl group	25	99.8 ± 0.3		
Intra-op 1 min	Ketamine group	25	98.2 ± 1.4	6.200, df=48	0.000*
	Fentanyl group	25	95.8 ± 1.3		
Intra-op 5 min	Ketamine group	25	97.8 ± 1.9	2.772, df=48	0.008*
	Fentanyl group	25	95.8 ± 2.9		
Intra-op 10 min	Ketamine group	25	97.8 ± 1.3	1.282, df=48	0.206, NS
	Fentanyl group	25	97.3 ± 1.7		
Intra-op 20 min	Ketamine group	25	98.1 ± 1.1	2.251, df=48	0.029*
	Fentanyl group	25	97.4 ± 1.3		
Intra-op 30 min	Ketamine group	11	98.5 ± 0.7	1.568, df=22	0.131, NS
	Fentanyl group	13	97.8 ± 1.3		
Intra-op 40 min	Ketamine group	2	99.5 ± 0.7	-	-
	Fentanyl group	0	0.00 ± 0.0		
Post-op 5 min	Ketamine group	25	98.9 ± 0.6	4.125, df=48	0.000*
	Fentanyl group	25	98.0 ± 1.0		
Post-op 10 min	Ketamine group	20	99.2 ± 0.4	3.779, df=43	0.001*
	Fentanyl group	25	98.6 ± 0.7		
Post-op 15 min	Ketamine group	1	99.0 ± 0.0	-	-
	Fentanyl group	3	98.7 ± 0.6		

* Statistically significant difference (P<0.05)

Discussion:

Day care surgery anaesthesia is new and established trend in field of anesthesia and can be accomplished by agent comprising of smooth induction, stable hemodynamics & respiratory rate & rapid good quality recovering with minimum adverse effects.

Present study revealed around evaluation of three intravenous anaesthetic agents Ketamine, fentanyl & propofol have all these qualities. Drugs Ketamine fentanyl and propofol, the former two drugs given in fixed doses followed by titrated doses of later.

Hence in present study we have evaluated & compared the effect of ketamine - propofol and fentanyl - propofol on different systems & out care of results.

All the patients were premedicated as given in methodology.

In recovery room parameters were noted in from of modified Aldrete & Kraulik score which comprises of as given in table 10.

According to Aldrete & Kralik²² total score of 8 or 9 was acceptable for discharge of patient from post anesthesia recovery room. In recovery room patients from both of our groups Ketamine (mean Aldrete score 10 +/- 005 SD) and fentanyl (mean aldrete score 9.84 +/- 0.07 SD) were fit for discharge from recovery room.

Change in heart rate: At 20 minutes after induction fentanyl group showed increase in heart rate (mean 102.8 +/- 10.5 SD) which was statistically significant (P=.00) compared to ketamine group (mean 90.5 +/- 8.2 S.D.)

Ghatak et al (2012)²³ in their study also found that heart rate were maintained in Ketamine than with Fentanyl group.

Charges in systolic & diastolic blood pressure:- Systolic & diastolic blood pressure followed similar trend. Ketamim group showed a very small decrease in blood pressure while Fentanyl group had a significant drop in blood pressure.

Changes in respiratory rate:- After induction respiratory rate remained stable in Ketamine group while Fentanyl group had a significant fall in respirator rate. In post operative early recovery period both groups had rate above the preoperative level & this increase was higher in Fentanyl

group. Akin et al (2005)²⁴ also found similar results.

Change in oxygen saturation:- After induction there was more fall in saturation in Fentanyl group in comparison to Ketamine group. Hosseinzadeh et al (2013)²⁵ also noted non significant changes in oxygen saturation in ketofol.

Time of awakening in our study is consistent with study of Hernandez et al (1999)²¹ & Nonaka et al (2000)³.

Thus all the parameters & result in our study are consistent and comparable with other studies.

Conclusion:

- (1) Both Fentanyl & ketamine are good anaesthetics for total intravenous anaesthesia in combination with Propofol.
- (2) Ketamine-propofol combination provides excellent haemodynamic & respiratory stability than fentanyl propofol.
- (3) Awakening from anaesthesia is faster with ketamine propofol than fentanyl propofol.
- (4) Recovery of intellectual & cognitive functions is also faster in ketamine propofol group along with better post anesthesia recovery (Aldrete Kraulik) score.
- (5) Incidence or side effects like emergence delirium is associated with ketamine while incidence of nausea & vomiting is higher in fentanyl group.
- (6) Post operative pain is significantly low in fentanyl propofol group.
- (7) Ketamine propofol combination is having better cardio-respiratory stability and recovery profile than fentanyl propofol in day care surgery.

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