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A Comparative Evaluation of Propofol-Ketamine and Propofol-Fentanyl As T.I.V.A Techniques In Terms Of Haemodynamic Variables And Recovery Characteristics In Minor Surgeries.

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Abstract: *T.I.V.A can be an effective alternative to inhalation anaesthesia.This study was conducted to compare the two T.I.V.A techniques Propofol-Ketamine and Propofol-Fentanyl in terms of haemodynamic variables and recovery characteristics in minor surgeries.*

Materials and Methods*: 100 patients undergoing short surgical procedures less than 30 minutes, of ASA grade I and II, 20 to 50 years of age were randomized into two groups.*
Group A *– Patients received Injection ketamine 0.5 mg/kg followed by I/V propofol 1% .*
Group B *-Patients received Injection fentanyl 1.5 microgram/kg I/V followed by I/V propofol 1% . Monitoring for HR, SBP, DBP, RR ,SpO_2 was done and recovery was also assessed. The results were tabulated and analyzed statistically with student unpaired 't'test and Chi square test. P value(<0.05) was considered significant.*

Results: *In Propofol-fentanyl group there was a significant fall in pulse rate and blood pressure at 1 minute of induction compared to propofol- ketamine group but post operatively they returned to baseline values in both the groups.There was more fall in SpO_2 in propofol-fentanyl group but the recovery was better in this group.*

Conclusions: *Both Propofol-ketamine and Propofol-fentanyl are comparable to each other as T.I.V.A techniques in minor surgeries.*

Keywords*: T.I.V.A(Total Intravenous Anaesthesia), propofol, ketamine, fentanyl.*

I. Introduction

Total intravenous anaesthesia (TIVA) is a combination of hypnotic agents, analgesic drugs and muscle relaxants, excluding simultaneous administration of any inhaled drugs [1].Therefore it can be an effective alternative to inhalational anaesthesia[2] and for ambulatory surgery when the speed and completeness of recovery are important[3].Drugs used for TIVA should have quick onset, smooth induction,easy maintenance , quick recovery and minimal side effects.Propofol (diisopropyl phenol) is a 1%oil in water emulsion formulation containing 10% soybean oil; 1.2% egg lecithin and 2.25%glycerol. It is commonly used in outpatient anaesthesia for its rapid and smooth onset of action, short recovery period and minimal per operative side effects[4]. Ketamine a phencyclidine derivative is a powerful analgesic even in doses insufficient to induce anaesthesia[5]. Continous infusion of ketamine and propofol allows T.I.V.A. with profound analgesia and spontaneous ventilation[6]. Fentanyl belongs to the opioid group of drugs, and relieves pain, reduces somatic and autonomic responses to airway manipulation.Propofol when combined with an opioid can provide balanced anaesthesia[7] and fentanyl also reduces the intra operative requirement of propofol[8]. Thus drugs like propofol, ketamine and fentanyl are used in various combinations for TIVA as these combinations provides complete and balanced anaesthesia.Hence this study was undertaken to study and compare the two TIVA techniques i.e propofol- ketamine and propofol- fentanyl in minor surgeries in terms of haemodynamic variables and recovery characteristics.

II. Material And Methods

The study was conducted in the Department of Anaesthesiology and Critical Care,Mohan Dai Oswal Cancer Treatment and Research Foundation,Ludhiana after approval by the Academic Council on 100 patients undergoing short surgical procedures less than 30 minutes, of ASA grade I and II between 20 to 50 years of age with average weight and height. The following patients were excluded from the study: those with a history of drug or egg allergy, pregnant females, patients on MAO inhibitors and history of jaundice.

2.1 Pre Anaesthetic Check Up

A written informed consent from the patient was taken in the presence of his/her relatives. A thorough pre anaesthetic check up comprising of history, general physical examination and systemic examination of all the patients was conducted a day before surgery. All patients were given 0.25mg alprazolam orally a night before surgery and kept fasting for at least 6 hours prior to anaesthesia. Premedication was not given to any of them .Patients were randomly divided into two groups of 50 each. In the operation theatre I/V access was achieved and HR, BP, RR and SpO_2 were monitored. Patients were kept on spontaneous ventilation and 100% O_2 was given by mask when SpO_2 fell below 90%. **Group A** - Patients were given Injection glycopyrrolate 0.004mg/kg I/V followed by Injection ketamine 0.5 mg/kg I/V. After 2 minutes I/V propofol 1% was given at the rate of 40mg/10 seconds till the end point of induction (i.e. loss of consciousness and loss of eye lash reflex) . **Group B -** Patients were given Injection glycopyrrolate 0.004mg/kg I/V followed by Injection fentanyl 1.5 microgram/kg I/V. After 2 minutes I/V propofol 1% at the rate of 40mg/10 seconds was given till the end point of induction. Top up doses (25 mg) of propofol were given when the patient became light as evidenced by change in HR, B.P, lacrimation and limb movements.The Pulse Rate,Systolic and Diastolic Blood Presure, Respiratory Rate, SpO_2 were recorded before induction, 1 minute and 5 minute after induction, every 5 minute till the end of procedure and post operatively every 5 minutes till 15 minutes. Recovery from anaesthesia was assessed by **Modified Steward Score**, which has following three attributions.

Consciousness	**Points**
Fully awake, eyes open, conversive	4
Light asleep, eyes open intermittently	3
Eyes open on command or in response to name	2
Responding to ear pinching	1
Not responding	0
Airway	
Opening mouth +/- coughing on command	3
No voluntary cough but airway clear without support	2
Airway obstruction on neck flexion but clear without Support on extension	1
Airway obstruction without support	0
Activity	
Raising one arm on command	2
Non purposeful movement	1
Not moving	0

The score was calculated at 1, 3, 5, 10 &15 minutes postoperatively.

Post-operative period - Any complications,awareness during anaesthesia and the discharge time was recorded.

III. Analysis

All the results were tabulated and analyzed statistically with student unpaired 't' test and Chi-square test. The results were expressed as mean ± S.D. A p value < 0.05 was considered as statistically significant.

IV. Results

The **patients' characteristics i.e.** age, sex and weight were statistically similar in both the groups "Table I ". The **mean duration of surgery** was comparable in both the groups. It was 15.3±4.09 minutes in group A and 16.00±3.91 minutes in group B. "Table I". **Pre-induction** pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate and arterial saturation were comparable in both the groups with a statistically non significant difference between them ($p>0.05$).

The **pulse rate** increased intraoperatively in group A with the maximum rise at 10 minutes which was statistically non-significant ($p>0.005$) compared to preinduction value. In group B the pulse rate decreased with the maximum decrease at I minute post induction. The difference in pulse rate in both the groups was statistically significant ($p<0.05$).Post operatively in both the groups the pulse rate returned towards the preinduction value and the difference between them was statistically non-significant ($p>0.05$)"Table II".

The **systolic blood pressure** increased intraoperatively in group A and in group B there was a decrease and the maximum decrease was at 1 minute post induction. The difference between them was statistically significant up to10 minutes post induction.Postoperatively they gradually returned towards baseline and the difference between them was statistically non significant ($p>0.05$) "TableIII ".

The **diastolic blood pressure** increased intraoperatively in group A but it was statistically not significant($p>0.05$) compared to the baseline .While there was a fall in diastolic blood pressure in group B with the maximum decrease at 1 minute post induction. The fall in blood pressure till 10 minutes post induction was statistically significant ($p<0.05$) The difference between them was statistically significant ($p<0.05$) upto 15 minutes intraoperative. Post operatively the mean diastolic blood pressure gradually returned towards pre induction value"Table IV" in both the groups.

The **respiratory rate** increased intraoperatively in group A and the difference was statistically significant till 20 minutes post induction ($p<0.05$). The maximum increase was at 5 minutes post induction. In group B the respiratory rate decreased from the pre induction value and the decrease was statistically significant till 20 minutes post induction. The maximum decrease in respiratory rate was at 1 minute post induction in group B. Post operatively in both the group respiratory rate returned towards the pre induction value "TableV ".

Intraoperatively there was a fall **in SpO_2** in both the groups and the difference between them was statistically significant till 3 minutes post operatively ($p<0.05$). The decrease in group B was more than that in group A. In group A no patient while in group B 10 patients required O_2 supplementation by face mask when the SpO_2 fell below 90%. There was no significant change in SpO_2 (saturation) in the post operative period in both the groups "Table VI".

The **recovery profile** in both the groups was assessed by the number of patients' who attained modified Steward Coma Score of six at different time intervals. In group A no patient had score of six at one minute, 2 (4%) patients had 3 minutes, 8 (16%) had at 5minutes, 15 (30%) at 10 minutes and 25 (50%) at 15 minutes. In group B, 5 (10%) patients had score of six at one minute, 5 (10%) at 3 minutes, 30 (60%) at 5 minutes, 8 (16%) at 10 minutes and 2 (4%) at 15 minutes post operatively. In group A, 25 patients had score of six at15 minutes post operatively while in group B, 30 patients had a score of six, at 5 minutes post operatively Therefore recovery was better in group B as compared to group A "TableVII".

Post operative complications : One patient (2%) from group A and 3 patients (6%) from group B had nausea post operatively. 2 patients (4%) from group A had emergence delirium while no patient in group B had emergence delirium. "TableVIII".

The **discharge time** in both the groups were comparable. In group A it was 112.80±4.17 minutes while in group B it was 110.64±4.59 minutes. No patient in either group complained of **awareness** through out the perioperative period and all the patients felt the anaesthetic technique to be pleasant.

V. Discussion

Ambulatory anaesthesia has become and more and more popular and now a days many minor procedures are done on an outpatient basis[9] .Thus an anaesthetic agent which provides rapid onset, short duration of action lack of cumulation on repeated administration , an absence of excitatory effects during induction and recovery and minimal post operative side effects is required[10].Propofol has been proven to be a suitable agent for T.I.V.A.as it has a fast onset of action and rapid metabolism without accumulation[11]. However it has no analgesic effect. The combination of ketamine and propofol has been used for T.I.V.A[12]as they maintain stable haemodynamics and minimal ventillatory depression .Opiods interact synergistically and markedly reduce the dose of propofol required for the loss of consciousness and during noxious stimulation such as skin incision[13]. Patients in both the groups did not differ significantly with respect to the demographic data, type and the duration of surgery consistent with the findings of **Guit J.B.M. et al (1991**) who found no statistically significant difference in gender, age, weight and duration of surgery in both the groups[14].

The heart rate increased in Group A and decreased in group B but post operatively in both the groups it returned towards the pre induction value and the difference between them was statistically non-significant ($p>0.05$).Heart rate does not change significantly after an induction dose of propofol[15] .Whereas ketamine stimulates the cardiovascular system and is usually associated with increases in heart rate[16]. Fentanyl reduces the heart rate by vagomimetic action and depressed the cardiac conduction by direct membrane actions[17]. **Moffat A.C. et al (1989)** in their study found a significant decrease in heart rate from induction to minutes[10]. **Kaushik Saha et al (2001)** in their study found a significant decrease ($p<0.001$) in heart rate at one minute after induction in the propofol- fentanyl group[18]. Our findings are consistent with the findings of A.C. Moffat et al, and Kaushik Saha et al.

Ketamine stimulates the cardiovascular system and is associated with increases in blood pressure, heart rate and cardiac output and these changes are not related to the dose of ketamine[16].Fentanyl decreases the B.P by decreasing the systemic vascular resistance .The combination of propofol with fentanyl was a particularly potent stimulus for hypotension[19].Intraoperatively there was a significant fall in systolic blood pressure in group B as compared to group A post induction and the maximum fall was at 1 minute post induction. Also there was a fall in diastolic blood pressure in group B compared to group A post induction with the maximum decrease at 1 minute post induction and postoperatively the blood pressure returned to the baseline in both the groups. The stable systolic and diastolic blood pressure in propofol- ketamine group could have been because ketamine causes sympathetic stimulation which tends to counter balance the cardiovascular depressant effects of propofol. The decrease in both the systolic and diastolic blood pressure in the propofol-fentanyl group could be because of the cumulative cardio-depressant effects of propofol and fentanyl.**Guit, J.B.M. et al (1991)** in their study found that stable arterial pressure was present in the propofol-ketamine group and decreases in systolic and diastolic pressures were present in the propofol-fentanyl group[14].**Singh Bajwa SJ, et al(2010)** found an increase in mean systolic and diastolic B.P in propfol fentanyl group during induction[20].The findings in our studies are consistent with the findings of Guit J.B.M. et al and Singh Bajwa et al .

There was a significant fall in respiratory rate in propfol-fentanyl group as compared to propofol – ketamine group and the maximum fall was at 1 minute post induction but postoperatively it returned to the baseline.Propofol is a profound respiratory depressant and apnoea usually occurs after an induction dose of propofol and its onset is usually preceeded by marked tidal volume reduction and tachypnoea[21].Whereas ketamine has minimal effects on central respiratory drive [22].The incidence of prolonged apnoea by propofol is increased further by addition of an opiate either as a premedication or just before induction of anaesthesia[21].Our findings are consistent with those of Gill SS, Wright E M et al[23].The higher incidence of apnoea in propofol fentanyl group may be because of the combined apnoeic effects of propofol and fentanyl.

Intraoperatively there was a fall in SpO_2 in both the groups and the difference between them was statistically significant. The decrease in group B was more than that in group A. In group A no patient while in group B 10 patients required O_2 supplementation by face mask when the SpO_2 fell below 90%. **Sicignano et al (1990)** did a comparative study of propofol-ketamine vs propofol-fentanyl in short gynaecological surgery and did not find any changes in arterial oxygen saturation throughout the surgery and recovery period[24]. **Escarment et al (1996)** observed no change in oxygen saturation during the operation and no hypoxemia during the post operative period[25] .The finding of the present study are not consistent with the above findings because in the above studies patients were receiving 100% O_2 by mask.

In group A, maximum number of patients i.e. 25 patients had score of six, 15 minutes postoperatively,whereas in group B, 30 patients had score of six, 5 minutes postoperatively. **Guit J.B.M. et al (1991)** in their study on 18 patients who underwent non-cardiac surgery using ketamine propofol in one group and comparing it with fentanyl propofol in the second group as TIVA found that the awakening after stopping TIVA was 17 minutes in propofol-ketamine group and 13 minutes in propofol-fentanyl group which was statistically nonsignificant[14] .**Hernandez C et al (1999)** compared the characteristics of induction, maintenance and awakening of three techniques of combined total intravenous anaesthesia (TIVA) using propofol-ketamine, midazolam- ketamine and propofol-fentanyl, found that the time of awakening was 11.8±5 minutes in group I and 20.2±12.5 min in group II and 16.6±5.6 minutes in group III[26]. **Kaushik Saha et al (2001)** in their study found that recovery time in propofol-ketamine group was 11.71±7.17 minutes and in propofol-fentanyl group it was 8.7±3.28 minutes and the difference was statistically significant[18]. The findings in our study are comparable to Kaushik Saha et al .The prolonged recovery in group A could be because of the prolonged duration of action of ketamine.

In our study the mean time to discharge in group A 112.80±4.17 minutes while in group B it was 110.64±4.59 minutes which was comparable and non-significant ($p>0.05$). **Jakobsson J et al (1993)** in their study on 200 female patients (ASA grade I) scheduled for termination of pregnancy found that the mean time to discharge was 93 minutes for propofol-ketamine group and 96 minutes for propofol-fentanylgroup [9].The findings in our study is comparable to the above study.

At the time of discharge none of the patients had awareness of the perioperative period , no patient had dreams and all the patients were satisfied with the anaesthestic techniques.

VI. Tables

Table I :Comparison Of Patient Characteristics And Duration Of Surgery In Both Groups.

	GroupA	GroupB	P value	Stastistical significance
Mean age (years)	37.62±9.06	37.60±9.64	>0.05	N.S
Mean weight (kg)	57.34±6.14	55.14±5.67	>0.05	N.S
GenderM/F(%)	20/80	16/84	>0.05	N.S
Mean duration of surgery (minutes)	22.42±3.37	23.72±3.31	>0.05	N.S

Table II: Comparison Of Pulse Rate At Different Stages Of Anaesthesia In Both Groups.

Anaes.Stage	Time intervals	Group	Mean ± SD	t	p	S
Pre-Induction		A	84.20±5.22		>0.05	NS
		B	84.16±4.99			
Induction	1M	A	84.52±5.32	19.97	<0.05	S
		B	74.44±4.37			
	5M	A	84.56±5.08	20.82	<0.05	S
		B	76.96±4.34			
Intra-Operative	10M	A	84.92±5.19	15.56	<0.05	S
		B	78.60±4.38			
	15M	A	84.80±4.56	15.17	<0.05	S
		B	78.38±4.50			
	20M	A	84.82±4.74	7.47	<0.05	S
		B	81.85±4.13			
Post-Operative	1M	A	84.92±5.25	1.26	>0.05	NS
		B	83.92±4.74			
	5M	A	84.68±5.30	0.46	>0.05	NS
		B	84.88±3.89			
	10M	A	84.48±5.41	0.98	>0.05	NS
		B	84.92±4.66			
	15M	A	84.68±5.49	0.57	>0.05	NS
		B	84.94±4.85			

TableIII : **Comparison Of Systolic Blood Pressure Of Both Groups At Different Stages Of Anaesthesia**

Anaes.Stage	Time intervals	Group	Mean ± SD	t	p	S
Pre-Induction		A	125.96±9.40	0.47	>0.05	NS
		B	126.84±9.55			
Induction	1M	A	127.48±9.32	5.01	<0.05	S
		B	116.36±9.51			
	5M	A	128.24±9.73	3.69	<0.05	S
		B	121.28±9.42			
Intra-Operative	10M	A	128.24±9.74	1.61	<0.05	S
		B	125.20±9.27			
	15M	A	127.48±8.76	0.81	>0.05	NS
		B	125.95±9.13			
	20M	A	127.44±9.21	0.51	>0.05	NS
		B	126.47±8.85			
Post-Operative	1M	A	127.06±9.73	0.46	>0.05	NS
		B	126.20±9.21			
	5M	A	126.28±9.71	0.06	>0.05	NS
		B	126.37±9.15			
	10M	A	126.22±9.63	0.49	>0.05	NS
		B	125.28±9.26			
	15M	A	126.04±9.62	0.45	>0.05	NS
		B	125.20±6.78			

Table IV : Comparison Of Diastolic Blood Pressure Of Both Groups At Different Stages Of Anaesthesia

Anaes.Stage	Timeintervals	Group	Mean± SD	t	p	S
Pre-Induction		A	79.64±3.44	0.86	>0.05	NS
		B	80.04±3.56			
Induction	1M	A	80.48±3.47	9.83	<0.05	S
		B	73.60±3.61			
	5M	A	81.28±3.95	8.69	<0.05	S
		B	75.20±3.48			
Intra-Operative	10M	A	81.28±3.99	4.74	<0.05	S
		B	77.96±3.44			
	15M	A	80.91±4.74	3.83	<0.05	S
		B	78.43±2.93			
	20M	A	80.37±4.27	2.52	>0.05	NS
		B	79.61±3.61			
Post-Operative	1M	A	80.04±4.03	0.74	>0.05	NS
		B	79.52±3.49			
	5M	A	79.12±4.93	1.45	>0.05	NS
		B	80.52±3.56			
	10M	A	79.40±4.40	1.38	>0.05	NS
		B	80.76±3.0			
	15M	A	79.56±4.22	1.03	>0.05	NS
		B	80.72±3.52			

Table V: Comparison Of Mean Respiratory Rate Of Both Groups At Different Stages Of Anaesthesia

Anaes.Stage	Timeintervals	Group	Mean±SD	t	p	S
Pre-Induction		A	17.20±0.81	0.26	>0.05	NS
		B	17.12±1.47			
Induction	1M	A	17.24±1.23	14.31	<0.05	S
		B	12.64±1.79			
	5M	A	17.72±1.46	11.41	<0.05	S
		B	14.10±1.71			
Intra-Operative	10M	A	17.60±1.28	7.87	<0.05	S
		B	15.44±1.46			
	15M	A	17.49±1.31	5.34	<0.05	S
		B	15.55±1.76			
	20M	A	17.48±0.97	5.04	<0.05	S
		B	15.62±1.75			
Post-Operative	1M	A	17.44±1.28	2.07	<0.05	S
		B	16.48±1.18			
	5M	A	17.24±1.23	0.65	>0.05	NS
		B	16.88±1.15			
	10M	A	17.24±1.25	0.51	>0.05	NS
		B	17.08±1.29			
	15M	A	17.22±1.31	0.06	>0.05	NS
		B	17.20±1.45			

Table VI: Comparison Of Spo_2 At Different Stages Of Anaesthesia In Both The Groups

Anaes.Stage	Timeintervals	Group	Mean± SD	t	p	S
Pre-Induction		A	97.48±1.70	0.55	>0.05	NS
		B	97.28±1.92			
Induction	1M	A	97.40±1.63	4.51	<0.01	S
		B	95.88±1.73			
	5M	A	97.16±1.52	11.59	<0.01	S
		B	91.68±2.97			
Intra-Operative	10M	A	97.04±1.41	13.36	<0.01	S
		B	92.72±1.79			
	15M	A	96.00±1.41	4.67	<0.01	S
		B	94.10±2.04			
	20M	A	95.47±1.31	1.38	<0.05	S
		B	94.67±2.22			
Post-Operative	1M	A	96.48±1.48	2.13	<0.05	S
		B	95.24±1.80			
	5M	A	97.72±1.34	1.76	>0.05	NS
		B	96.68±1.37			
	10M	A	97.92±1.45	1.30	>0.05	NS
		B	97.16±1.57			
	15M	A	97.92±1.45	1.12	>0.05	NS
		B	97.32±1.54			

TableVII : Distribution Of Patients Having Steward Coma Score Of Six

Variations in Recovery profile of patients acquiring modified Steward Coma Score of six.

Time interval (minutes)	Group A	Group B
PO1	0 (-)	5 (10)
3	2 (4)	5 (10)
5	8 (16)	30 (60)
10	15 (30)	8 (16)
15	25 (50)	2 (4)
Mean±SD	11.42±4.10	5.50±3.14

Figures in parentheses are percentages

t value = 8.11p <0.01 (significant)

Table VIII: Post-Operative Side Effect In Both The Groups

Side Effects	Group A		Group B	
	No.	%age	No.	%age
Nausea	1	2	3	6
Vomiting	-	-	-	-
Secretions	-	-	-	-
Laryngospasm	-	-	-	-
Bronchospasm	-	-	-	-
Venous sequelae	-	-	-	-
Emergence delirium	2	4	-	-
Any other	-	-	-	-

VI. Conclusion

Both propofol-ketamine and propofol-fentanyl are comparable to each other in terms of haemodynamic variables and recovery characteristics Thus it can be concluded that both propofol-ketamine and propofol-fentanyl are suitable combinations as TIVA techniques,as they produce rapid, pleasant and safe anaesthesia with only a few untoward side effects and only minor haemodynamic effects.

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