

RESEARCH ARTICLE

COMPARATIVE STUDY OF PROPOFOL AUTO-COINDUCTION VERSUS KETAMINE PROPOFOL COINDUCTION USING PRIMING PRINCIPLE BY BISPECTRAL INDEX ANALYSIS FOR DAY CARE SURGERY

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Abstract

Aim:The aim of our study was to do the comparison of Propofol Autocoinduction versus Ketamine Propofol coinduction using priming principle by bispectral index analysis for day care surgery.

Methods:150 patients participated in our study at Govt. Medical College and Rajindra Hospital, Patiala. Patients aged above 18 years and ASA Grade I and II scheduled to undergo elective surgery were included in this prospective, randomized controlled trial. All patients were randomly assigned into 3 groups of 50 each. Group A- patients were given Propofol 0.5mg/kg body wt., Group B- patients were given Netamine 0.5mg/kg body wt., Group C- patients were given normal saline 2.5ml 2 minutes before induction. Patients were induced with injection Propofol 1% at rate of 30mg/10 sec until BIS value reaches to 40. Induction dose requirements of Propofol, Haemodynamic parameters including HR, MAP, SBP, DBP,SPO2, ECG, RR were recorded. Incidence of post op complications / side effects were also recorded. Data was tabulated and subjected to statistical analysis.

Results: Groups were comparable to each other with respect to age, weight, gender, ASA status. Significant difference was found in HR, SBP, DBP between Group A and Group B at 1 minute and 2 minute after coinduction. MAP shows statistically highly significant (p < 0.001) results after 1 minute and 2 minute of coinduction. Total dose of propofol required and mean BIS value shows highly significant results when compared between groups.

Conclusion: In conclusion, our study identified that overall dosage of propofol was significantly lower when modest doses of propofol and ketamine were given beforehand than when a placebo was used. When used as an induction agent, ketamine offers better haemodynamic stability.

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Introduction:-

Propofol has emerged as an induction agent of choice over the last two decades due to its smooth induction and rapid recovery.¹ Compared with the conventional induction agents such as thiopentone and ketamine, propofol offers better intubating conditions and superior airway integrity with the added advantage of airway reflex suppression ¹ However the main concern for an anesthesiologist is the hemodynamic instability caused by the

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An ideal intravenous anaesthetic agent to be considered for day-care surgery should provide rapid recovery with lesser side effects and available at a reasonable cost. Both Propofol and Ketamine has all these characteristics but cause significantly opposing haemodynamic effects.⁵

Propofol is a short acting anaesthetic agent which is used widely for the induction of anaesthesia and for the sedation in minor surgical procedures. It produces unconsciousness within 30 seconds after intravenous injection. It is a non-barbiturate, non-opioid sedo-hypnotic agent with rapid onset and shorter duration of action. It produces good sedation and also has antiemetic effect. Its adverse effects are dose related cardiovascular and respiratory depression, bradycardia and pain during injection. Propofol is known to produce amnesia with sedative and hypnotic effects but it doesn't have analgesic property so combination of analgesic molecule is required with propofol for the sedation in surgical procedures.⁶

Ketamine is an intravenous anaesthetic developed in 1960s from its precursor phencyclidine and its mode of action is through causing dissociative anaesthesia. ketamine has several advantages starting from its analgesic and amnesic effects, protecting airway reflexes, maintenance of spontaneous respiration. However, Ketamine has many side effects that limited its frequent use as an anaesthetic. These side effects include nausea, vomiting, elevation of blood pressure, emergence hallucinations and elevation of heart rate due to its sympathomimetic effects and also increase in intracranial pressure.⁷ Bispectral Index monitoring system was introduced for clinical use in October 1996 as a technique of measuring the extent of Anaesthesia induced by Hypnotics and sedatives. The BIS index derives data from a complex EEG parameter, combining several variables from the frequency domain and time domain analysed in real time.⁸

The aim of our study was to do the comparison of Propofol Auto-coinduction versus Ketamine Propofol coinduction using priming principle by bispectral index analysis.

Materials and Methods:-

In the present clinical study 150 patients participated at Govt. Medical College and Rajindra Hospital, Patiala. Patients aged above 18 years and ASA Grade I and II scheduled to undergo elective surgery were included in this prospective, randomized controlled trial. All patients were randomly assigned into 3 groups of 50 each.

Inclusion Criteria -

- ASA I and II patients
- Age group: 18 years and above
- Either sex posted for day care procedures -Approximate duration of 30 minutes and less

Exclusion Criteria –

- Patients who refused to give consent to the study.
- Age < 18 years
- Patients having allergy to drugs used during the study

• Patients with Comorbid conditions like cardiovascular diseases, Acute respiratory tract infections, acute and chronic hepatic diseases, renal diseases, CNS diseases, psychiatric diseases and the patients with alcohol and drug addiction.

- Pregnant women
- Patients with ASA grade 3&4

• Surgical procedures lasting more than 30 minutes

Informed consent:

Prior to inclusion in this study, a written informed consent was taken in their own vernacular language after explaining the technique from each patient.

Pre- anaesthetic check up

Preanesthetic check-up was done in every patient which includes:

- Detailed clinical history from the patient
- Detailed general physical examination and baseline pulse rate, blood pressure.

• Systemic examination which includes: Cardiovascular system, Respiratory System, Central Nervous System, Hepato Renal System, Genito Urinary System, Airway examination.

• Investigations- Haemoglobin, bleeding time, clotting time, PTI / INR, urine complete examination, fasting blood sugar, renal function tests, liver function tests and ECG. Each patient was kept fasting at least six hours pre-operatively.

Intraoperative

After review of pre anaesthesia checkup, patients were shifted to operating room as scheduled. After I/V cannulation, premedication with Inj. Glycopyrrolate 0.2mg I/V was given. All routine monitors – ECG, NIBP, pulse oximetry were attached to the patient. BIS electrodes were placed on the skin of the forehead after cleansing with alcohol. Thereafter baseline vital parameters were recorded and BIS reading taken to obtain baseline value while the patients were fully awake. Patients were pre oxygenated with 100% O2 for 5 minutes. Patients were given Inj. Midazolam 0.03mg/kg, Inj. Butrum 1mg i/v and Inj. Lignocaine 2cc. Then according to group stratification:

Group A – Received Propofol 0.5 mg/kg i/v

Group B – Received Ketamine 0.5 mg/kg i/v

Group C – Received normal saline 2.5ml.

After 2 minutes, all patients were induced with Propofol 2mg/kg until BIS value reaches to 40. Speed of injection is 30mg/ 10 sec which was kept constant in all the groups. Complications like apnoea, laryngospasm, vomiting, coughing were noted. Anaesthesia was maintained by using O2 : N2O and volatile agents – isoflurane.

Parameters like HR, SBP, DBP, MAP, SpO2, RR were recorded just after premedication, coinduction, 1,2,5,10 minutes after coinduction. Overall dosage of Propofol used was noted.

BIS values were recorded at following intervals-

- Baseline
- After priming
- After induction

Sedation was assessed postoperatively by Ramsay Sedation Scale(RSS) at 0,1,2,4,6 hours.

Results:-

All groups were comparable to each other with respect to age, weight, gender, ASA physical status. **Table 1:-** Mean Heart Rate (BPM).

				p value		
HR	Grp A	Grp B	Grp C	A vs B	A vs C	B vs C
Baseline HR	87.56±14.97	89.01±14.92	87.00±13.21	0.622 (NS)	0.843 (NS)	0.471 (NS)
HR After Premedication	89.78±15.04	90.56±14.65	89.76±13.38	0.793 (NS)	0.994 (NS)	0.776 (NS)
HR After Coinduction	89.00±15.00	90.94±14.55	90.22±13.63	0.513 (NS)	0.671 (NS)	0.799 (NS)
HR After 1 Min of Coinduction	87.14±15.11	93.12±14.51	91.02±13.60	0.046 (S)	0.180 (NS)	0.457 (NS)
HR After 2 Min of	86.18±14.79	93.16±14.77	91.58±13.67	0.020 (S)	0.061 (NS)	0.580 (NS)

Coinduction						
HR After 5 Min of Coinduction	84.14±13.95	89.76±14.69	88.84±14.06	0.053 (NS)	0.097 (NS)	0.750 (NS)
HR After 10 Min of Coinduction	83.32±13.75	88.92±14.84	88.81±14.35	0.053 (NS)	0.087 (NS)	0.800 (NS)

The mean Heart rate variation between three groups in recordings taken just after premedication, after coinduction, after 5 min of coinduction, after 10 mins of coinduction was non-significant (P>0.05). These Heart Rate variations showed statistical significance (p<0.05) in recordings taken after 1 min of coinduction and 2 min of coinduction in group A versus group B.



Graphical representation of SBP: Graph-1



Graphical representation of DBP: Graph-2

Systolic and Diastolic blood pressure was statistically significant in group A versus group B after 1 minute and 2 minute of coinduction.

				A vs B	A vs C	B vs C
	Grp A	Grp B	Grp C	(p value)	(p value)	(p value)
Baseline MAP	95.13±6.38	93.67±6.65	93.19±6.73	0.264 (NS)	0.141 (NS)	0.721 (NS)
MAP After	95 25+5 90	94 09+6 13	93 23+6 46	0.338 (NS)	0.105 (NS)	0.493 (NS)
Premedication	<i>93.23</i> <u>-</u> <i>3.9</i> 0	>1.02±0.15	<i>y</i> 3.25±0.10	0.550 (115)	0.105 (105)	0.195 (115)
MAP After	94.89+5.81	94.36+6.08	93.63+7.08	0.655 (NS)	0.331 (NS)	0.580 (NS)
Coinduction	>	>	20100=7100	01000 (1.03)	0.001 (1.0)	01000 (110)
MAP After 1 Min	92.65±5.64	96.71±6.06	94.28±6.73	0.001 (HS)	0.193 (NS)	0.061 (NS)
of Coinduction						()
MAP After 2 Min	92.38+6.02	97.02+6.27	94.88+6.21	0.001 (HS)	0.064 (NS)	0.090 (NS)
of Coinduction	/210020102	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	>	01001 (115)	01001 (113)	01090 (113)
MAP After 5 Min	89 91+5 38	92 12+6 07	89 59+6 91	0.057 (NS)	0.797 (NS)	0.054 (NS)
of Coinduction	07.71±5.50	<i>92.12</i> ±0.07	07.57±0.71	0.057 (115)	0.777 (115)	0.051 (115)
MAP After 10						
Min of	89.65±5.42	91.77±5.74	90.36±5.98	0.061 (NS)	0.537 (NS)	0.231 (NS)
Coinduction						

 Table 2:- Mean Arterial Blood Pressure (MMHG).

MAP was statistically highly significant (p<0.001) after 1 minute and 2 minute of coinduction in group A versus group B and group B versus group C.

Mean SPO2 and mean RR remained stable and comparable at all measured time intervals and difference between them was statistically non-significant as p value was >0.05.

 Table 3:- Mean Bis Value.

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Mean BIS	Grp A	Grp B	Grp C	p value			

				A vs B	A vs C	B vs C
Baseline Mean BIS	98.28±1.29	98.32±1.32	98.54±1.22	0.879 (NS)	0.303 (NS)	0.387 (NS)
Mean BIS Post Priming	75.86±1.54	78.86±2.04	98.74±1.03	0.001 (HS)	0.001 (HS)	0.001 (HS)
Mean BIS After Induction	40.00±0.00	40.00±0.00	40.00±0.00			

At post priming interval, fall in BIS values was observed in group A (75.86 \pm 1.54), group B (78.86 \pm 2.04) and in group C (98.74 \pm 1.03) which was statistically highly significant (p<0.001) in group A versus group B, in group A versus group C and in group B versus group C.

Total				p value (F			
Dose of	Group A	Group B	Group C	value)	A vs B	A vs C	B vs C
Propof	90.40±9.8	53.20±11.5	106.40 ± 9.4	0.001	0.001	0.001	0.001
ol	9	1	2	(0.350.297)	(17.337)	(8.282)	(25.292)

To maintain BIS at 40 during induction, overall dosage of propofol was decreased in group A and group B in comparison to control group which was statistically highly significant (p<0.001) in group A versus group B, in group A versus group C and in group B versus group C.

Mean RAMSAY sedation score was comparable between group A, group B, group C and was statistically nonsignificant (p>0.05). The incidence of post operative complications like nausea, vomiting, shivering, fever, urinary retention, bleeding, shock was statistically non-significant (p>0.05).

Discussion:-

The tendency for day care surgery has increased with the administration of short-acting intravenous medications. Outpatient anaesthesia requires a safe anaesthetic method and an anaesthetic agent that provides rapid anaesthesia depth, haemodynamic stability, rapid metabolism and minimum adverse effects in recovery period.⁹ Auto-coinduction also known as priming technique involves administering a small initial dose of an induction agent followed by full dose of same agent. This method aims at taking advantage of amnesic, sedative and anxiolytic properties at sub-hypnotic doses of i/v induction agents.¹⁰

In this study, the distribution of patients according to Age, Weight, Gender and ASA status were comparable in group A, group B and group C and statistically no significant difference was found between the groups. (p>0.05). In our study. HR was comparable between all the three groups at baseline. After 1 min of coinduction, HR decreased in group A, increased in group B and group C in comparison to baseline, premedication interval and after coinduction. The difference between all the groups was analysed and was significantly significant(p<0.05) between group A and group B. After 2 min of coniduction, HR decreased in group A, increased in group B and group C as compared to baseline, premedication interval, after coinduction and after 1 minute of coinduction. Statistically significant(p<0.05) difference was found when group A compared with group B. Hailu S et al¹¹ conducted a randomized controlled trial (RCT) to study effectiveness of Ketofol versus Propofol induction on haemodynamic profiles in adult elective surgical patients. In this study, decrease in HR was significant in propofol group in comparison to Ketofol group.HR was higher in Ketofol group compared with Propofol group at all measurement times. These results are in accordance with our study. In our study, after 1 min of coinduction and after 2 min of coinduction, SBP decreased in group A and increased in group B and group C. Propofol lowers peripheral vascular resistance and myocardial contractility which lowers SBP and DBP. While Ketamine stimulates the myocardium,it raises peripheral vascular resistance and inevitably raises both the SBP and DBP. Group B patients had shown significant increase in systolic BP. After 1 min of coinduction and 2 min of coinduction, SBP was statistically significant (p<0.05) when group A compared with group B and when group B compared with group C. Hailu S et al¹¹ conducted a RCT on effectivity of Ketofol versus Propofol induction in adult elective surgical patients. After induction, SBP was Significantly higher in ketofol group as compared to propofol group. There was significantly decrease in SBP for the Propofol group. These findings support the results of our study. Ketamine stimulates the

cardiovascular system and increases the HR, BP and systemic vascular resistance. In our study, after 1 min of coinduction and 2 min of coinduction, DBP decreased in group A and increased in group B and group C. The difference between the groups was analyzed and was statistically significant (p<0.05) in group A versus group B. Işık Y et al¹² conducted a comparison study of Ketofol and Propofol in minor gynaecologic interventions. After induction, diastolic blood pressure in groups receiving ketofol and propofol decreased and increased respectively. These findings are in accordance with our study.

In our study, SPO2 and RR were compared between all the groups at baseline, after coinduction, after 1 min, 2 min, 5 min, 10 min of coinduction. These were comparable at all the time intervals between all the groups and were statistically not significant. Patil VP et al¹³ conducted a study: ketamine and propofol- safe for short surgical procedures. SPO2 preoperatively was 98 \pm 0.3, intraoperatively was 97 \pm 0.4. These were statistically not significant. These findings are in accordance with our study. Baseline mean BIS value was 98.28 ± 1.29 in group A, 98.32 ± 1.32 in group B and 98.54 ± 1.22 in group C which was comparable in all three groups. At post priming interval, maximum fall in BIS value was found in propofol auto-coinduction group (75.86 ± 1.54) in comparison to group B (78.86 \pm 2.04) and group C (98.74 \pm 1.03). Reduction in BIS value shows statistical highly significant difference (p < 0.001) in group A versus group B and in group A versus group C and in group B versus group C. Aboeldahab H et al¹⁴ conducted a comparison study between Ketamine, Propofol and Ketofol (ketamine+propofol) as an induction agent. Maximum fall in BIS value was in propofol group in comparison to other groups after induction and was significant. These findings are in accordance with our study. In group A, only 2 patients experienced nausea, 3 patients experienced vomiting and 4 patients shivering. In group B, 6 patients experienced nausea, 5 experienced vomiting and 3 patients shivering. In group C, 2 patients experienced nausea and 2 patients vomiting and 1 experienced shivering. Other complications like fever, bleeding, urinary retention, shock was absent in group A, group B and group C. These were comparable between all the groups and were statistically not significant (p>0.05). Karki SB et al¹⁵ conducted a comparison of anaesthetic properties of Ketofol and Propofol in day care procedures. Postoperative nausea vomiting was seen in total 8 patients where 5 patients developed nausea in Ketofol group and 2 in Propofol group, however vomiting seen only in 1 patient of Ketofol group which were statistically not significant. These findings are in accordance with our study.

Conclusion:-

In conclusion, our study identified that overall dosage of propofol was significantly lower when modest doses of propofol and ketamine were given beforehand than when a placebo was used. When used as an induction agent, ketamine offers better haemodynamic stability.

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