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Comparative Study Of Efficacy Of Propofol Auto Co-Induction Versus Midazolam-Propofol Co-Induction Using The Priming Principle In Patients Undergoing Surgeries Under General Anaesthesia

DR.CHRISH LENIL[1], DR.CHETANA CHAPARALA[2], DR. BHAGYAVARDHAN BOTTA3, DR. MANISH MANCHIREDDY[4]

Abstract

Background:*Anaesthesia is a balance between anaesthetic drug requirement and state of arousal of patient. Inadequate doses of the drug lead to increased incidence of awareness, while generous administration of drugs leads to hemodynamic instability, delayed recovery, and increase other complications.*

Aim: *The aim of this study was to assess the effect of the priming principle on dosage response in patients undergoing general anaesthetic surgery utilisingPropofol auto co-induction and Propofol – Midazolam co-induction using bispectral index (BIS).*

Objective : *The main goal is to calculate total Propofol dose requirement to achieve a BIS value of 45.*

Methods: *The study contains eighty patients who were admitted for elective surgeries under general anaesthesia. Patients were randomized into two groups PP and PM where one of the group PP received the priming dose of Propofol 0.4mg/kg body weight followed by induction dose of Propofol(2mg/kg)-10mg every 15 seconds until BIS value of 45 is attained whereas in the other group PM, priming dose of Midazolam 0.05mg/kg body weight followed by induction dose of propofol(2mg/kg)- 10mg every 15seconds was given until BIS value of 45 is achieved.*

Results: *All the groups had comparable demographic parameters. The total propofol dose to achieve BIS of 45. The total amount of propofol required to obtain a BIS of 45 was less in Midazolam-Propofol co-induction group with a statistical significance (P<0.05).*

Conclusion: *Priming Principle decreases the dose requirement of propofol required for induction without affecting haemodynamic stability.*

INTRODUCTION

Anaesthesia is a delicate balance between the need for anaesthetic drugs and the patient's level of arousal.[1]In the absence of central nervous system monitoring, hypnotic drugs have typically been provided using a set dose regimen that is adjusted according to the patient's response as measured by clinical parameters such as lack of vocal response.[1]

The "Priming Principle"[2] is a method of administering a pre-calculated amount of an induction agent before the complete required dose of the same induction agent. This technique is known as "Auto-Co-Induction"[3].

“Co-induction”[4] is the administration of two or more medications simultaneously administered to facilitate anaesthesia induction and document synergism[5]. The synergy of propofol and midazolam, given with or without fentanyl, lowers the total requirment of propofol needed and reducing the negative cardiovascular consequences of monotherapy[6]

Propofol is an intravenous anaesthetic that induces a quick and consistent loss of consciousness [7]. It induces a widespread metabolic and vascular depression in the human brain, which is followed by a fast and painless recovery. Propofol, Iipid-soluble anaesthetic and rapidly transported and metabolised in the liver[8].

Midazolam, a benzodiazepine - has sedative, anxiolytic, and amnestic properties and are used widely in the induction of general anaesthesia. [9] Midazolam is an anti-emetic that is utilised as a co-induction agent with propofol/opioids[10].

The bispectralindex(BIS) calculates a dimensionless value from a single frontal electroencephalographic signal to determine patient's level of awareness. With BIS monitoring, clinically adjusted medication administration to a specific requirement of patients leads in lower dosages of anaesthetic agents and quicker return of consciousness.[1]
The goal of this study was to calculate the total requirement of Propofol for induction and to examine the hemodynamic changes between PropofolAutoinduction and Propofol-Midazolam Co-induction utilising the Priming Principle and the Bispectral Index.

MATERIALS AND METHODS

After obtaining approval from the Institutional Human Ethics committee (IHEC) dated 5th,December,2019 , CTRI registration was done before the commencement of the study.
Study Population: Patients scheduled for surgery under General Anaesthesia in the Department of Anaesthesiology, who met the inclusion criteria.
Study design: A Prospective Randomised study
Sample size: Sample size calculation for continuous end point two independent sample study is as follows:
Based on previous study findings, mean induction dose of propofol for achieving BIS score of 45 in the PP group was 76 and the mean induction dose of propofol producing BIS score of 45 in the group PM was 61.
INCLUSION CRITERIA:

- American Society of Anaesthesiologists (ASA) grade I, II&III.
- Age 18-65 years.
- Both Elective and Emergency procedures
- Duration of surgery ≥ 60 minutes.

EXCLUSION CRITERIA:

- Patients not willing to be in study group
- History of allergic reaction to study drug
- Pregnant patients.
- Weight less than 50KG

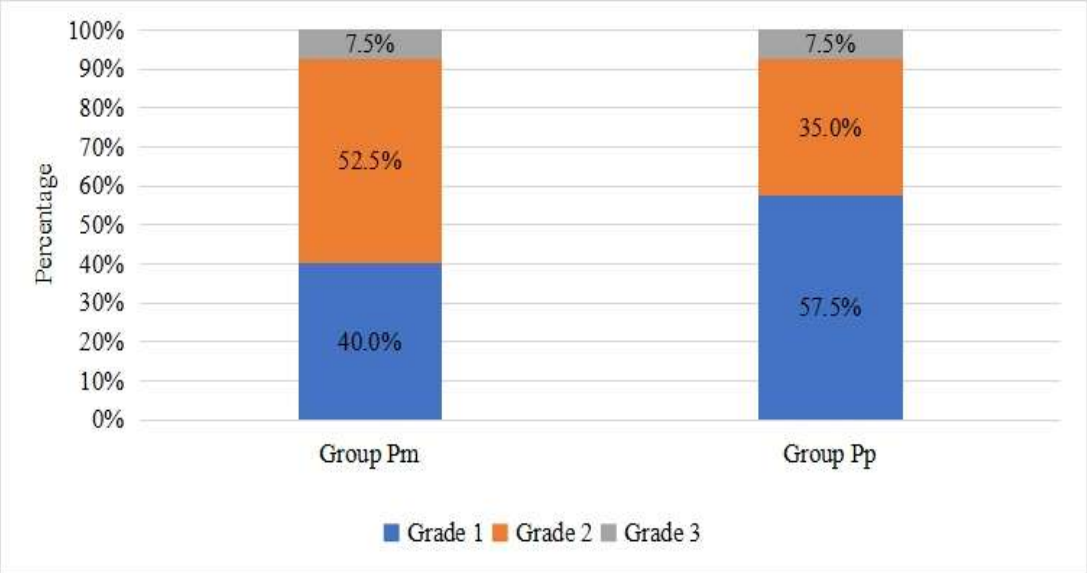
Results and Analysis

A total of 80 subjects were included in the final analysis, with 40 subjects in each study group. Among the study population, 40 (50%) participants were belonging to group PM and remaining 40 (50%) participants were belonging to group PP
The difference in mean age (years) between two study groups was statistically not significant (p value 0.447)
The proportion of males was slightly higher in PP group as compared to PM (30% Vs 22.5%). But the difference in proportion of male and female population was statistically not significant (p value 0.446)
The difference in mean weight (kg) between two study groups was statistically not significant (p value 0.839)

Table 1: Comparison of ASA grade between the study groups (N=80)

ASA Grade	Study Group		Chi square	P value
	Group PM (N=40)	Group PP (N=40)		
Grade I	16 (40%)	23 (57.5%)	2.656	0.265
Grade II	21 (52.5%)	14 (35%)		
Grade III	3 (7.5%)	3 (7.5%)		

Figure 1: Staked bar chart of comparison of ASA grade between the study groups (N=80)

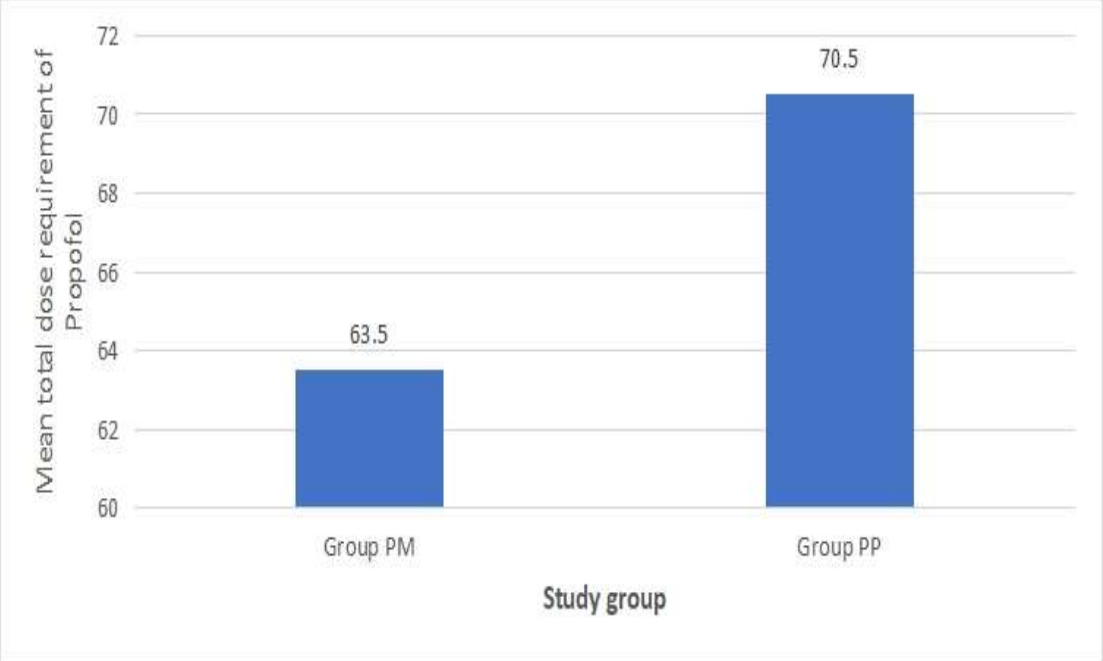


In group PM, highest proportion of participants were in ASA grade II, but in group PP higher proportion of subjects were in ASA grade I, but the difference in proportion of people in different ASA grades was statistically not significant (p value 0.265) (table 1 & figure 1)

Table 2: Comparison of mean total dose requirement of propofol between the study groups (N=80)

Study group	Total dose requirement of Propofol (mg) (Mean± SD)	Mean difference	95% CI		P value
			Lower	Upper	
Group PM	63.5 ± 14.42	7.00	0.64	13.36	0.031
Group PP	70.5 ± 14.13				

Figure 2: Comparative bar chart of mean total dose requirement of propofol between the study groups (N=80)



The mean dose of propofol was lower in group PM as compared to PP group (63.5 ± 14.42 Vs 70.5 ± 14.13). The mean difference was 7 mg , 95% CI 0.64,13.36, P value 0.031). The difference was statistically significant. (Table 2 & figure 2)

Table 3: Comparison of Bispectral index (≤45) at different time periods between the study groups (N=80)

Bispectral index (<=45) at	Study Group		Chi square	P value
	Group PM (N=40)	Group PP(N=40)		
Induction 0 sec	0 (0%)	0 (0%)	*	*
Induction 15 sec	0 (0%)	0 (0%)	*	*
Induction 30 sec	0 (0%)	0 (0%)	*	*
Induction 45 sec	6 (15%)	1 (2.5%)	3.914	0.18
Induction 60 sec	12 (30%)	5 (12.5%)	3.66	0.056
Induction 75 sec	19 (47.5%)	16 (40%)	0.457	0.499
Induction 90 sec	29 (72.5%)	27 (67.5%)	0.238	0.626
Induction 105 sec	39 (97.5%)	33 (82.5%)	5.000	0.057
Induction 120 sec	40 (100%)	37 (92.5%)	*	*
Induction 135 sec	0 (0%)	39 (97.5%)	*	*
Induction 150 sec	0 (0%)	40 (100%)	*	*

*No statistical test was applied- due to 0 subjects in the cells

The proportion of people getting bi-spectral index (≤45) was higher in PM group at all time points and all the 40(100%) of the subjects reached a bispectral index of ≤45 at 120 seconds in PM group as compared to 150 seconds in PP group. The difference in proportion of Bispectral index (≤45) (at different time periods i.e., from induction at 60 sec to 150 sec) between two study groups was statistically not significant (p value >0.05) (table 3)

Table 4: Comparison of mean Systolic blood pressure(SBP) in mmHg at different time periods between the study groups (N=80)

Systolic blood pressure (Mean± SD)	Study group		P value
	Group PM	Group PP	
Baseline	131.33 ± 17.67	127.5 ± 12	0.261
Post priming	126.08 ± 18.3	121.75 ± 11.54	0.210
Before intubation	111.43 ± 20.05	108.53 ± 8.8	0.405
After intubation	117.1 ± 14.88	117.58 ± 11.22	0.872
3 mins after intubation	113.43 ± 15.81	115.08 ± 11.83	0.599
5 mins after intubation	110.53 ± 13.91	112.18 ± 11.33	0.562
10 mins after intubation	109 ± 14.05	108.33 ± 10.19	0.806
15 mins after intubation	106.2 ± 13.94	105.65 ± 9.79	0.839

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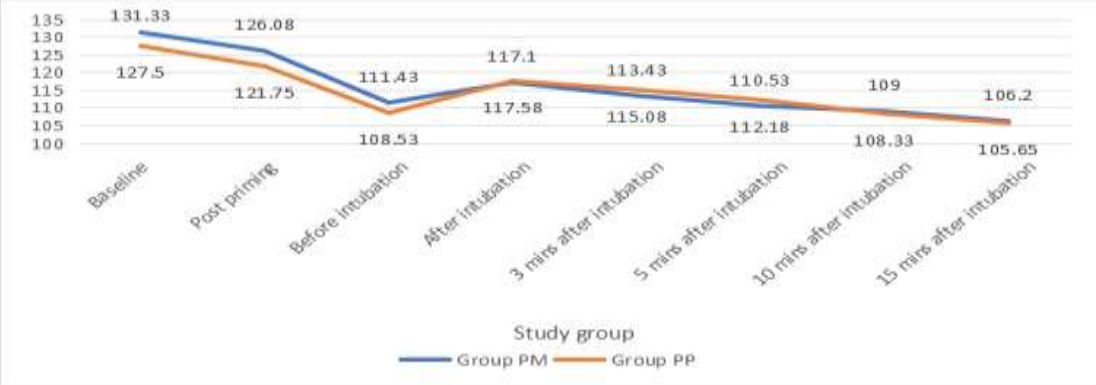
Figure 4: Line chart of mean Systolic blood pressure(SBP) in mmHg at different time periods between the study groups (N=80)

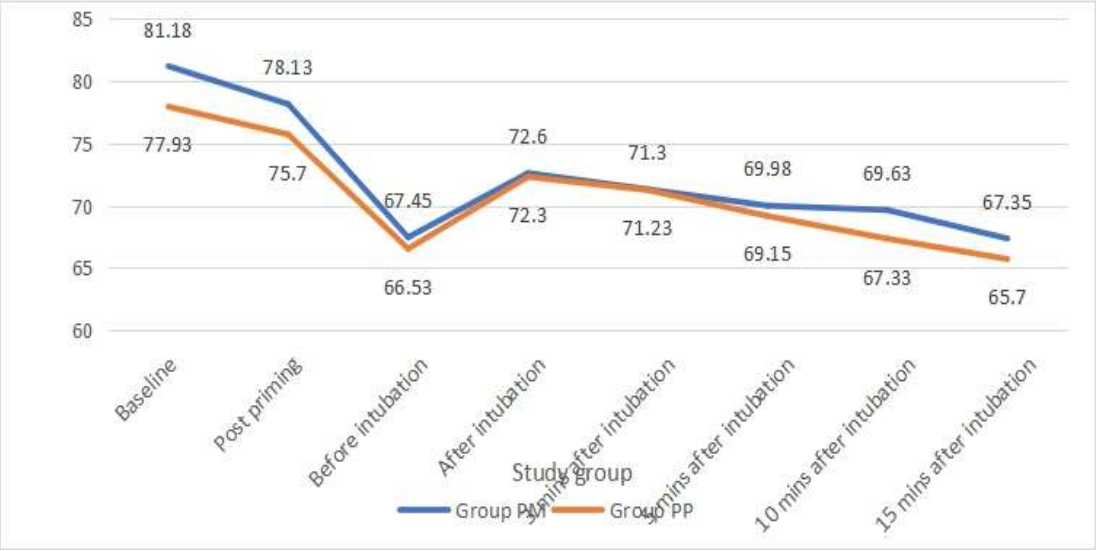


There was no statistically significant difference between the study groups in their systolic blood pressure at different stages of the procedure from baseline to 15 minutes after induction. (P value >0.05). (table 4 & figure 4)

Table 5: Comparison of mean Diastolic blood pressure(DBP) in mmHg at different time periods between the study groups (N=80)

Diastolic blood pressure (Mean± SD)	Study group		P value
	Group PM	Group PP	
Baseline	81.18 ± 9.21	77.93 ± 8.51	0.105
Post priming	78.13 ± 8.26	75.7 ± 7.76	0.180
Before intubation	67.45 ± 11.63	66.53 ± 8.16	0.682
After intubation	72.6 ± 8.07	72.3 ± 9.86	0.882
3 mins after intubation	71.3 ± 8.49	71.23 ± 9.27	0.970
5 mins after intubation	69.98 ± 8.39	69.15 ± 8.93	0.671
10 mins after intubation	69.63 ± 8.66	67.33 ± 9.07	0.249
15 mins after intubation	67.35 ± 8.93	65.7 ± 9.82	0.434

Figure 5: Line chart of mean Diastolic blood pressure(DBP)in mmHg at different time periods between the study groups (N=80)

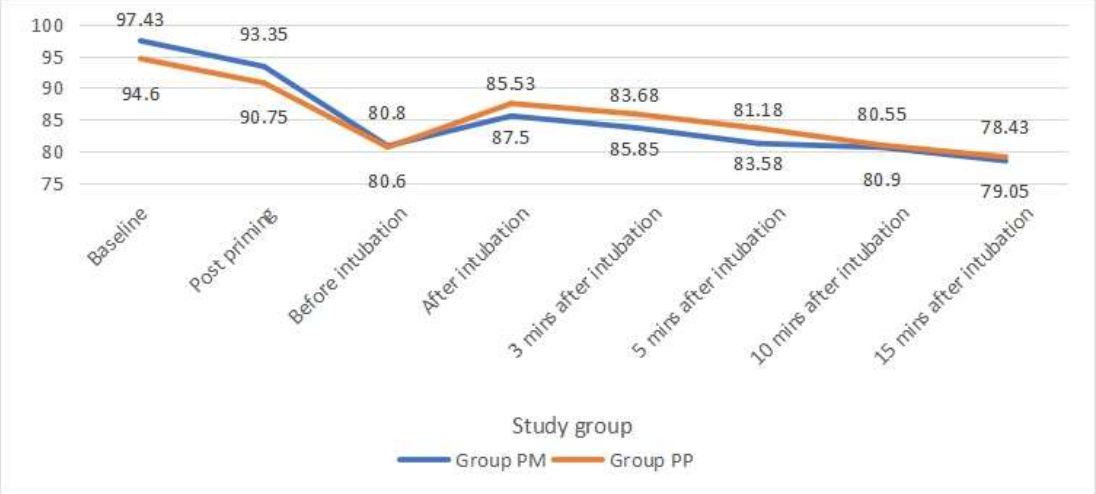


There was no statistically significant difference between the study groups in their diastolic blood pressure at different stages of the procedure from baseline to 15 minutes after induction. (P value >0.05). (table 5 & figure 5)

Table 6: Comparison of mean of Mean arterial pressure(MAP) in mmHg at different time periods between the study groups (N=80)

Mean arterial pressure (Mean± SD)	Study group		P value
	Group PM	Group PP	
Baseline	97.43 ± 12.08	94.6 ± 7.69	0.216
Post priming	93.35 ± 12.54	90.75 ± 7.19	0.259
Before intubation	80.8 ± 15.51	80.6 ± 7.68	0.942
After intubation	85.53 ± 10.62	87.5 ± 10.33	0.402
3 mins after intubation	83.68 ± 11.98	85.85 ± 9.87	0.378
5 mins after intubation	81.18 ± 11.61	83.58 ± 9.23	0.309
10 mins after intubation	80.55 ± 11.38	80.9 ± 9.05	0.879
15 mins after intubation	78.43 ± 11.45	79.05 ± 9.15	0.788

Figure 6: Line chart of mean of Mean arterial pressure(MAP) in mmHg at different time periods between the study groups (N=80)



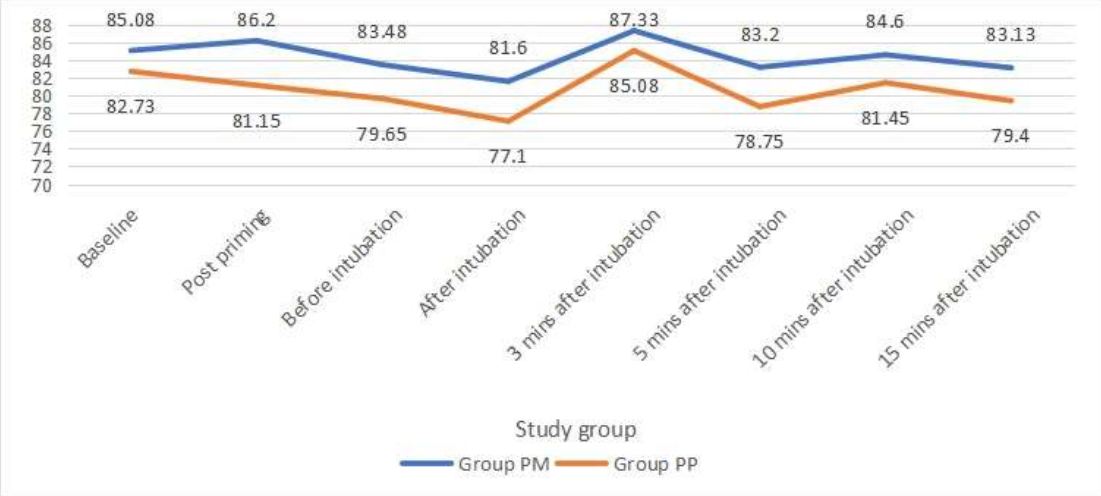
There was no statistically significant difference between the study groups in their mean arterial pressure at different stages of the procedure from baseline to 15 minutes after induction. (P value >0.05). (Table 6 & figure 6)

Table 7: Comparison of mean of Pulserate(PR) in rate/minute at different time periods between the study groups (N=80)

Pulse rate	Study group		P value
	Group PM	Group PP	
Baseline	85.08 ± 12.41	82.73 ± 12.28	0.397
Post priming	86.2 ± 14.24	81.15 ± 12.13	0.092
Before intubation	83.48 ± 14.97	79.65 ± 10.25	0.186
After intubation	81.6 ± 12.35	77.1 ± 9.65	0.073
3 mins after intubation	87.33 ± 11.58	85.08 ± 10.12	0.358

5 mins after intubation	83.2 ± 12.8	78.75 ± 10.65	0.095
10 mins after intubation	84.6 ± 12.18	81.45 ± 10.36	0.216
15 mins after intubation	83.13 ± 12.19	79.4 ± 10.01	0.139

Figure 7: line chart of mean of Pulserate(PR) in rate/minute at different time periods between the study groups (N=80)



There was no statistically significant difference between the study groups in their pulse rate at different stages of the procedure from baseline to 15 minutes after induction. (P value >0.05). (Table 7 & figure 7)

DISCUSSION

PHARMACOLOGY OF PROPOFOL

Propofol(2,6-diisopropylphenol), used for anaesthetic induction, maintenance, and sedation in the intensive care unit, as well as day care treatments. It has rapid onset, short duration of action, and low risk of side effects and it provides a rapid return of consciousness with fewer lasting effects on the central nervous system (CNS). [11]

Molecular Formula: C12H18O **Molecular Weight:**178.27072 g/mol

Formulations:

Propofol consists of (10%)Soyabean oiland 1.2 % egg lecithin and 2.25% glycerol and long-chain triglycerides. This combination encourages bacterial growth and triglyceride production.[11]

Mechanism of Action:

At therapeuticdosages, propofol preferentially regulates gamma aminobutyric acid (GABA) receptors and does not modulate other ligand-gated ion channels. Propofol's sedative-hypnotic actions are mediated via a GABA A receptor subtype interaction.When GABA A receptors are activated, they cause hyperpolarization of the postsynaptic cell membrane and functional inhibition of the postsynaptic neuron.[12]

DOSAGE :

- 1.5-2.5mg/kg iv for induction of anaesthesia[11]
- For intravenous infusion and sedation, 25-75 mcg/kg/min and for hypnosis, 100-200 mcg/kg/min.[11]
- Half-life of elimination of Propofol: 0.5–1.5 hours
- Contextsensitive half time: less than 40 minutes for an 8-hour infusion.[11]
- 3.5–4.5 l/kg volume of distribution
- 30–60 ml/kg/min clearance rate. [11]

Pharmacokinetics:

Absorption:

Propofol has a low bioavailability due its high first pass effect and a high hepatic extraction ratio(>90%). [13] The first half-life of distribution is 2–8 minutes, while the elimination half-life is 4–7 hours. Propofol infusions lasting up to 8 hours have a context-sensitive half-life of 40 minutes. [14]

Metabolism:

Propofol clearance from plasma surpasses hepatic blood flow, implying that tissue absorption, as well as hepatic oxidative metabolism by cytochrome P-450 which plays a role in the drug's removal from the plasma.[14]Propofol, ring hydroxylated by cytochrome P-450, resulting in 4-hydroxypropofol, which can subsequently be glucuronidated or sulfated. The glucuronide and sulphate conjugates of propofol appear to be inactive pharmacologically, 4-hydroxypropofol has about a third of propofol's hypnotic effect. Less thanunaltered 0.3 percent of a dosage is eliminated in urine. [15]

Excretion:

After metabolism, 88% of propofol is eliminated in the urine, but onlyunaltered 0.3% of propofol given is excreted. The phenolic metabolite of propofol (1%) is responsible for the greenish colouring visible after delivery.[12]

Pharmacodynamics:

Cardiovascular

Propofol lowers preload, cardiac contractility, and systemic vascular resistance. The activation of baroreceptor-mediated compensatory mechanisms in response to low cardiac output and systemic vascular resistance raises heart rate.[14]

Respiratory:

Propofol decreases upper airway reflexes and cause respiratory depression. In the absence of paralysis by neuromuscular blocking medications, lowering upper airway reflexes has been useful during intubation or supra-glottic airway placement.[14]

Cerebral

Propofollowers the amount of oxygen requirement in the brain. It has largely anticonvulsant property and enhances EEG burst suppression at high infusion levels. Also used in the treatment of status epilepticus. [16]

Other characteristics:

Propofol has no effect on evoked myogram or twitch tension, and it does not improve neuromuscular blockade. Propofol is useful in patients who are sensitive to volatile drugs or have a family history of malignant hyperthermia.

Clinical uses and dosage:

Induction of Anesthesia

Propofol inducing doses range from 2.0 to 2.5 mg/kg i.v. Awakeningoccurs atpropofol plasma concentrations of 1.0 to 1.5mcg/ml. [14]

Intravenous Sedation

Propofol, a titratable medicine for i.v sedation. With a normal conscious sedation dose of 25 to 100mcg/kg/minute i.v., analgesic and amnestic effects are limited.[14].

Maintenance of Anesthesia

Propofol is commonly used in combination with a short-acting opioid to maintain anaesthesia at a dose of 100 to 300mcg/kg/minute.

Antiemetic Effects

In the postanesthesia care unit, subhypnotic doses of propofol (10 to 15 mg i.v.) may be used to relieve nausea and vomiting.

Effects on the skin:
Pruritus caused by neuraxial opioids or cholestasis can be treated with 10 mg of propofol given intravenously.
Anticonvulsant properties:
Propofol at doses greater than 1 mg/kg intravenously decreasesthe seizure threshold by 35 to 45% in individuals undergoing electroconvulsive therapy. [14]
Attenuation of Bronchoconstriction:
Metabisulfite is used as a preservative in a propofol formulation. In asthmatic patients, metabisulfite may cause bronchoconstriction. [14]
Potential toxicity:
Propofol infusion syndrome is characterised by severe metabolic acidosis, lipaemia, renal failure, rhabdomyolysis, and heart failure in combination with critical illness when given at high doses for lengthy periods of time. Propofol infusion rates of no more than 4 mg/kg/hr are now recommended for long-term sedation in intensive care patients.[19]
PHARMACOLOGY OF MIDAZOLAM
In the peri-operative interval, midazolam is the most often utilized benzodiazepine.It has a water-soluble structure with imidazole ring, which accounts for its aqueous solution stability and fast metabolism. [18] Midazolam's amnestic effects are stronger than its sedative effects, so patients may be conscious yet forget about postoperative events and conversations.
Molecular Formula :C18H13ClFN3**Molecular weight**: 325.78 g/mol
Mechanism of action:
Benzodiazepines do not activate GABA receptors, although they do increase their affinity for GABA.[19] As a result, channel openings open more frequently, increasing chloride conductance and hyperpolarizing the post synaptic cell membrane.
Pharmacokinetics:
Absorption:
Midazolam,rapidly absorbed and passes across the blood-brain barrier. Only half of a Midazolam dose taken orally enters systemic circulation, indicating significant first-pass metabolism. [18]
Metabolism:
Cytochrome P450 (CYP3A4) enzymes in the liver and small intestine rapidly convert it to active and inactive metabolites. Midazolam's main metabolite, 1-hydroxymidazolam, has half the action of the parent molecule.[20]The kidneys are responsible for the elimination of 1-hydroxymidazolam glucoronide.
Pharmacodynamics:
Central Nervous system (CNS) :
Midazolam reduces the cerebral metabolic rate of oxygenand cerebral blood flow.It is a powerful anticonvulsant that can be used to treat statusepilepticus. [21]
Cardiovascular System:
Midazolam causes a reduction in systemic blood pressure as well as an increase in heart rate. [22] The decrease in systemic vascular resistance causes blood pressure fluctuations, although cardiac output is unaffected.[23]
Respiratory system:
With dosages of 0.15mg/kg, there are dose-dependent declines in ventilation. Resting ventilation has been proven to be suppressed by midazolam at doses of 0.05-0.075 mg/kg. It's possible to have apnea for a short time. Lowers upper airway activity and suppresses the swallowing reflex. [23]

Stress Response:
Midazolam lowers the adrenergic response to surgical stress, but not the cortisol or renin response. Midazolam premedication has been shown to reduce antidiuretic hormone levels in the blood.[24]

Other Effects Of Midazolam:

- Anxiolytic Effect
- Hypnotic Effect
- Anticonvulsant Effect
- Anterograde Amnestic Effect
- Anti Nociceptive Effect

Dosage:

1-2.5 mg for sedation[11]
0.1-0.5 mg/kgfor iv induction[25]
Premedication – 0.05-00.15mg/kg iv

Clinical benefits:

Preoperative medication:

The most oftenly used oral pre-operative drug for children, which produces drowsiness and anxiolysis with minimal effects on breathing and oxygen saturation at a dose of 0.25 mg/kg.[33] 0.5 mg/kg Midazolam, given orally 30 minutes before anaesthesia induction offers sedation and anxiolysis without causing a delay in awakening. [26]

Intravenous sedation:

During regional anaesthesia, midazolam at doses of 1 to 2.5 mg i.v is helpful for sedation. In the presence of opioids, the effects of midazolam on breathing are amplified.[27]

Induction of anaesthesia:

Midazolam 0.1 to 0.2 mg/kg i.v over 30 to 60 seconds can be used to induce anaesthesia.[25]

Post operative sedation:

Active metabolites may accumulate over a lengthy period of i.v treatment. Patients who are kept on greater doses of midazolam take longer to wake up. [28]

Overdose and Treatment:

Sedation, confusion, impaired coordination, diminished reflexes, coma, and unfavourable hemodynamic changes are symptoms of a midazolam overdose. The drug "Flumazenil" is a BZD antagonist that is used to reverse the effects of midazolam.[29]

BISPECTRAL INDEX MONITORING

The explicit memory of sensory impressions after general anaesthesia is known as anaesthesia awareness, also called inadvertent intraoperative awareness. Anaesthesia-related awareness is a significant condition with long-term psychological implications[30]

The goal of general anaesthesia is to achieve hypnosis, analgesia, areflexia, and a sufficient depth of anaesthesia without needing more anaesthetic drugs.

The level of hypnosis is statistically predicted in the bispectralindex monitor, which is obtained from EEG data.[31]

Levels of Intraoperative awareness:

Griffith and jones Classified awareness into:

1. Pain perception complaint with conscious awareness
2. Painless conscious awareness with explicit recollection
3. Awakeness or conscious awareness
4. There is no explicit recall or pain, but there is a possibility of implicit remembering.
5. Subconscious knowledge of intraoperative events without explicit recall but evidence of implicit memory
6. There is no awareness[32]

Clinical need for monitoring awareness:

Patients have recalled specific aspects of talks that had place while they were unconscious in operating room. Patients may have anxiety as a result of this awareness, which can lead to post-traumatic stress disorder. A very deep plane of anaesthesia, on the other hand, may cause hemodynamic irregularities, necessitating the use of vasoconstrictor medicines to keep blood

pressure and cardiac output normal and can lead to respiratory depression, necessitating the use of postoperative breathing assistance. Monitoring the level of anaesthesia should aid in avoiding intraoperative consciousness and ensuring that the correct amount of anaesthetic medicines is administered to avoid adverse cardiovascular effects caused by excessive doses.

Bispectral Index Monitoring:

It's an EEG parameter , a combination of measures from EEG signal from like bispectral index, power spectral analysis, and temporal domain analysis.[33] They combine these measurements into an algorithm to improve the association between the EEG and theeffects of anaesthesia clinically, as measured by the BIS index range.[34]

In anaesthesia and critical care, the bispectral index remains the most validated type of consciousness or brain function monitoring.

Bispectral index is the consequence of two innovations**:**

❖Bispectral analysis

❖ Bis algorithm.[35]

Clinical implications of BIS monitoring:

Using BIS monitor, reduce anaesthetic agent usage and enhance patient satisfaction by reducing postoperative nausea and minimising episodes of awareness.[36][37]

The present clinical study titled "Comparative efficacy of Propofol auto-induction versus Midazolam-Propofol co-induction using Priming principle in patients undergoing surgeries under general anaesthesia" was conducted to compare the required dosage of the induction agent to obtain the BIS value of 45 and hemodynamic parameters between the two study groups under ASA grade I,II,III of both sexes between 18-65 years of age, undergoing elective and emergency surgeries under GA were included in the study. Patients were randomly allocated into two groups- Group PM and Group PP.

Group PM (n=40) - 0.05mg/kg bodyweight of Midazolam as priming dose followed by induction dose of Propofol (2mg/kg) until BIS value 45 is attained.

Group PP (n=40) - 20% (0.4mg/kg bodyweight) pre-calculated dose of propofol(2mg/kg) as priming dose followed by remaining dose of Propofol until BIS value 45 is attained.

Appropriate statistical analysis revealed the following findings:

- Propofol dose requirement to obtain BIS score of 45 was compared between both the study groups and the requirement was less in Midazolam-Propofoco-induction group compared to Propofol auto-induction group with P=0.031 which is statistically significant.
- Systolic BP, diastolic BP and mean arterial pressure were compared between the two groups. After priming in both the groups, there was no any statistical difference (p>0.05).
- No statistical difference in comparing age (in years), weight(in kg) and ASA grading between both thegroups.
- No any statistical difference in male and female sexes, among Midazolam-Propofol co-induction group and Propofol auto-induction group.

11. CONCLUSION

- The final result of the study was that use of priming principle for induction reduced the requirement dosage of propofol to obtain BIS score of 45.
- Midazolam- Propofol co-induction, reducing dose requirement of propofol for induction without much change in haemodynamic parameters such as systolic and diastolic blood pressure and mean arterial pressure and heart rate.
- Henceforth Midazolam predosing along with titratable propofol dose with BIS monitoring lowersa the dose requirement to obtain adequate depth of anaesthesia without altering hemodynamic parameters.

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