International Scientific Journal of Engineering and Management (ISJEM) ISSN: 2583-6129
Volume: 04 Issue: 04 | April – 2025 DOI: 10.55041/ISJEM02599
An International Scholarly || Multidisciplinary || Open Access || Indexing in all major Database & Metadata

TOPIC: PROPOFOL AND PROPERTIES, MECHANISMS OF ACTION, ADMINISTRATION TECHNIQUES, MONITORING AND TOXICITY

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SUMMARY

As the part of the development of a model for the study of propofol, we have investigated the propofol properties, administration techniques, monitoring & adverse effects. A systematic search for any type of report published and unpublished, was made to review the evidence that propofol increases the risk of hypotension, bradycardia, hypertriglyceridemia, apnea, myocardial depression etc. So, its safe use is necessary to drive optimal patient outcomes. We reviewed some published journals in 2009, there are 97 cases of propofol associated deaths also 108 publications documenting that showed 168 cases of propofol infusion syndrome. The study found that nearly 60% deaths from accidental overdose of propofol than remaining cases were interlinked to drug interaction or any other factors that leads death. This activity outlines the appropriate use of propofol based on categorized patients, so anesthesiologist or any other anesthesia practioners can direct patient anesthesia, where it is indicated as part of the interprofessional team and improving patient outcomes.

CONTINUING STUDY

propofol is an intravenous anesthetic agent used as induction agent for general anesthesia or procedural sedation during monitored anesthesia care. It administered as a bolus or an infusion or may be combination of both. The chemical name of propofol is 2,6 di-isopropyl phenol. It is available as 1% & 2% milky white solution that prepared in soyabean oil. The soyabean oil making propofol injection painful, so lignocaine should be added with propofol to reduce or prevent pain during propofol injection administration. Propofol also contains glycerol and egg lecithin. Propofol has been available since the early 1980s. First clinical trials of propofol began in 1977 and later it is entered the market in 1986. Propofol has gained widespread popularity because it is thought to have specific advantages as compared with other induction anesthetics, such as favorable kinetics, smooth and rapid induction characteristics, a recovery profile with a low incidence of adverse effects and non-hypnotic therapeutic properties. It was suggested that the excellent hemodynamic state was of particular use in pediatric patients. Main objective of this activity to identify the pharmacokinetics and pharmacodynamic of propofol to improves patient outcomes from anesthesia.

MECHANISMS OF ACTION

The mechanisms of action for propofol to be related with effect on gamma-aminobutyric acid (GABA) receptors in brain. Propofol mediates their action through GABA receptors and GABA-A, increasing the membrane conductance to chloride ions causing hyperpolarization of membranes. Propofol also acts by inhibiting the the glycine receptors. The electrophysiological studies shown that propofol acts at β subunit of GABA-A receptors and enhancing receptors response to GABA that leads increased chloride influx, neuronal hyperpolarization and subsequent inhibition of neurotransmission. Functional MRI shown that propofol decreased connectivity between thalamocortical and corticocortical networks that resulting the patient undergoes sedation and hypnosis.

Early studies indicate propofol can affect the neurotransmitter system by inhibiting excitatory neurotransmission that reduces the activity of N-methyl-D-aspartate (NMDA) receptors. Moreover, propofol decreases synaptic release of excitatory neurotransmitter like glutamate, acetylcholine that take places in anesthetic properties. Propofol blocks NMDA receptors-mediated excitatory transmission and contribute to unconsciousness and amnesia beyond its GABAergic effects.

ADMINISTRATION

Routes of administration: Intravenous
Onset of action: Less than one minute
Dose: 2-3 mg
Duration of action: An induction dose for propofol approximately 10 minutes. Prolonged or repeated administration will accumulate in peripheral tissues and will causes on increased duration of action.
Distribution: Large volume of distribution
Protein binding: 97% to 99%
Metabolisms: Propofol is metabolized by hepatic and conjugation to sulfate and glucuronoid conjugates.
Clearance: Hepatic clearance occurred approximately 60% and remaining 40% extrahepatic clearance take place via kidney and lungs.
Excretion: Primarily Renal
Pharmacokinetics: Propofol achieved the induction in one arm brain circulation time i.e. 15 second. Patient regained the consciousness after 2-8 minutes due to its rapid redistribution. Propofol having elimination half-life is about 2-4 hours. Context-sensitive half-life may be up to 1-3 days after 10 days infusion.

INDICATIONS

Clinical use of propofol: Propofol use in induction for general anesthesia and sedation during monitored anesthesia care for patients undergoing procedures. Propofol having early and smooth recovery, inactive metabolites and antiemetic effects, so it is intravenous agent of choice for day care surgery. Propofol is choice for total intravenous anesthesia along with opioids and maintenance of anesthesia in patients. Sedation is produced in intensive care unit (ICU) by propofol infusion and agent of choice for induction in susceptible individuals for malignant hyperthermia.
Off label use: Propofol having the properties that can treat the epileptic activity in brain. It is also used for treatment of refractory post operative nausea and vomiting by decreasing the central serotonin releases.

CONTRAINDICATION

Contary to the previous recommendation of not using propofol in pregnancy, lactation and children < 3 years but in current studies proved that propofol can be safely used. However, because of increased possibility of propofol infusion syndrome in children, it not recommended for long-term infusion in children < 16 years. Propofol can also use in egg allergy patient because egg allergy is almost from egg white not from lecithin, which is prepared from egg yoke. Same as the patient with soy allergy can safely use propofol because an allergic reaction occurs secondary to exposure to specific protein from soy sources not the fat or oil that make up emulsion. The oil used to manufacture propofol are unlikely to contain quantities of protein significant enough to produce on allergic cross-reaction. However, it is advisable to not use propofol in patient with history of anaphylaxis to egg and oil.

MONITORING

Therapeutic effects of propofol: Propofol has a rapid and smooth onset of action, having antiemetic and antiprurytic properties that is extremely predictable in its duration. It has low organ toxicity and is very compatible with a wide range of other commonly used drugs in the settings of anesthesia like thiopentone sodium, etomidate etc.
Central Nervous System: Propofol will causes a decrease in cerebral blood flow, intracranial pressure, cerebral metabolic rate and cerebral oxygen consumption in brain. Propofol variable dose effects the level of consciousness. Its higher dose decreases the level of consciousness, used for moderate sedation to general anesthesia. This decreased sensorium leading to loss of protective airways reflexes. Propofol causes increased latency and decreased amplitude during somatosensory evoked potential monitoring. Propofol at higher dosage can lead to burst suppression and even an isoelectric EEG. Propofol can suppress the convulsion and seizure activity in brain.
Respiratory System: Propofol having dose-dependent respiratory depression effects by inhibiting the hypercapnic ventilatory drive. Propofol can induce apnea at induction dose, so it is carefully used in respiratory disorders

patients. Propofol has been induce bronchodilation in chronic obstructive pulmonary disorders (COPD) patient and causes a low incidence of bronchospasms in asthmatic patients.

Cardiovascular system: Propofol inhibiting the sympathetic vasoconstriction activity and mild depression of myocardium causes decreased systemic arterial pressure and systemic vascular resistance that leads to hypotension. It can decrease myocardial blood flow and myocardial oxygen consumption. Propofol also achieved the hypotension by impairs the baroreceptors response to hypotension.

Propofol significantly produced bradycardia by affecting the myocarduim which is most common complication induced during propofol anaesthesia. There are 65 published and 187 spontaneous reports to drug monitoring centers described with different strengths of evidence a biological basis for propofol-induced bradycardia, 1444 bradycardias, 86 asystole aand 24 deaths. Controlled clinical trials indicates that propofol significantly increased the risk of bradycardia compared to another anesthetic. 1 of 660 patients undergoing propofol anesthesia had an asystole. The risk of bradycardia-related death during propofol anesthesia was estimated to be 1.4 in 1000,000. Data from phase lV study of propofol did not agree with data from controlled studies. The propofol carries a finite risk for bradycardia and hypotension with potential for major harm. So propofol should be cautiously used in catecholamine-depleted patients and in hypovolemic patients.

GIT: Propofol decreases the central serotonin releases and act as a potent antiemetic agent by preventing post operative nausea and vomiting.

ADDITIONAL MONITORING

Propofol can causes respiratory as well as cardiovascular depression, so that anesthesiologist or anesthesia practioners must be qualified to be care of patient at any level of sedation. The American Society of Anesthesiologist (ASA) guidelines recommend, oxygenation, circulation, ventilation and temperature for all anesthetics should be continuously monitored. The anesthesia practioners must be present during all anesthetic procedure from sedation to general anesthesia to prevent and reduces the risk of complications, when patients undergo anesthesia. Additionally, some rescue instruments and equipments should be available there to manage anesthesia like bag valve mask, sources of oxygen, laryngeal mask airways, endotracheal tube of different sizes, laryngoscopes, defibrillator and some emergency drugs like atropine, glycopyrolate, tranexa, etc. The ASA guidelines recommend to follow NPO status due to loss of protective airways reflexes carries the risk of gastric content aspiration. These all techniques are vital for reducing the complications associated with anesthesia.

TOXICITY

Propofol infusion syndrome: It is a serious side effect occurring through the prolonged infusion of propofol more than 48 hours. This effect causes metabolic acidosis, hyperkalemia, hyperlipidemia, rhabdomyolysis and can lead renal and cardiac failure or death. The main cause of propofol infusion syndrome is alteration in mitochondrial metabolism and electron transport chain functions but the exact mechanisms of propofol infusion syndrome is still unknown. This is mainly seen in mechanically ventilated patient or in ICU. Mortality associated with propofol infusion syndrome has been around 33% and increases at delayed diagnosis.

Propofol has dose dependent effects, at higher dose can increases risks of complications and decreases the patient outcomes from anesthesia by affecting the nerve system, cardiovascular system as well as respiratory system.

CONCLUSION

Propofol having rapid and smooth recovery, short half-life, antiemetic, antipruritic, bronchodilation properties making it choice of induction agent. But either propofol having most of the disadvantages likes profound and larger apnea, hypotension, bradycardia, less stable solution, myoclonic activity, sexual fantasies, hallucination etc. So all the anesthesiologist nurse anesthetist, or any other anesthesia practioners, who uses the propofol should be familiar with its adverse effects and should be incharge of monitoring the patient during induction via propofol. Anesthesia practioners should also monitor the patients in post operative wards or sedation in ICU to preventing the propofol

associated complications. A coordinated efforts between all procedural team members including clinicians, specialists, nurses and surgical assistant or other anesthesia practioners will help drive optimal patient outcomes from propofol anesthesia. This activity outlines review interprofessional team strategies for improving care coordination and communication to adverse propofol, where it is indicated and improved patient outcomes from propofol anesthesia.