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A Study On Clinical Outcome Of Propofol And Ketamine-Midazolam As Procedural Sedative Agent In Patients Undergoing Abdominal Surgeries

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Abstract

Benzodiazepine receptors are closely linked with GABA receptors and appear to facilitate the activity of the latter. Activated GABA receptors open chloride ion channels which then either hyperpolarize or short-circuit the synaptic membrane. Propofol is one of a group of alkylphenols. The alkylphenols are oils at room temperature and insoluble in aqueous solution, but they are highly lipid soluble. It has pH of 7 and pKa of 11, appears as a slightly viscous, white milky substance. It is stable at room temperature and is not light sensitive. Detailed pre-anaesthesia check-up was be done on the day prior to surgery and appropriate investigations was be carried out. The anaesthesia technique and questionnaire was explained to the patient and written informed consent was be taken. Time to induce spinal in A+B group is 25.85 Seconds. Number of attempts on an average in A+B group is 1.35.Patient Comfort score in A+B group 8.33. Patient satisfaction score in A+B 86.42.

Keyword: Nanoparticle, ferrite, structural, morphological and spectroscopy properties

Introduction

Ketamine is a water-soluble molecule that structurally resembles phencyclidine. The presence of an asymmetric carbon atom results in two optical isomers The left- Handed optical isomer of ketamine is designated S(+)-ketamine and the right-handed optical R(-) Most commonly available as racemic mixture [1].

Ketamine interacts with μ, δ and k opioid receptors. In contrast, other studies have suggested that ketamine may be an antagonist at mu receptors and an agonist at k receptors.

Ketamine anaesthesia is partially antagonized by anticholinesterase drugs. The fact that ketamine produces anticholinergic symptoms (emergence delirium, bronchodilation, sympathomimetic action) suggests that an antagonist effect of ketamine at muscarinic receptors. Benzodiazepines are thought to act via specific benzodiazepine receptors found at synapses throughout the CNS [2, 3].

Benzodiazepine receptors are closely linked with GABA receptors and appear to facilitate the activity of the latter. Activated GABA receptors open chloride ion channels which then either hyperpolarize or short-circuit the synaptic membrane.
Midazolam decreases the tidal volume. Apnoea occurs in 10-77% of patients when midazolam is used as an induction agent.
It impairs ventilatory response to hypercapnia. It produces hypnosis, sedation and anterograde amnesia.

The cerebral oxygen consumption and cerebral blood flow are decreased in a dose-related manner. When administered intrathecally or epidurally, the drug has anti-nociceptive effects mostly due to the kappa-opioid receptor agonistic action.

Midazolam is virtually completely metabolized in the liver to hydroxylated derivatives which are then conjugated to a glucuronide. Metabolites bind to CNS benzodiazepine receptors and are pharmacologically active.
The short duration of action of midazolam is due to its high lipophilicity, high metabolic clearance and rapid rate of elimination. However, this may not be the case after prolonged dosing on intensive care [4]. The use of midazolam in premedication decreases the MAC of volatile agents by approximately 15%.
The clinical effects of the drug can be reversed by physostigmine, glycopyrronium bromide and flumazenil.

Propofol is one of a group of alkylphenols. The alkylphenols are oils at room temperature and insoluble in aqueous solution, but they are highly lipid soluble. It has pH of 7 and pKa of 11, appears as a slightly viscous, white milky substance. It is stable at room temperature and is not light sensitive. If a dilute solution of propofol is required, it is compatible with 5% dextrose in water [5].

1% propofol contains 10% soya bean oil, 2.25% glycerol, 1.2% purified egg phosphide. Propofol is available as 1% solution in 10ml, 20ml, 50ml & 100ml vial. 2% solution is also availableinEurope.Inaddition,50mlprefilledsyringesof1%&2%solutionareavailable[6].

Methodology

Detailed pre-anaesthesia check-up was done on the day prior to surgery and appropriate investigations was carried out. The anaesthesia technique and questionnaire was explained to the patient and written informed consent was be taken.
Patient was remain fasting overnight prior to surgery and was premedicated with Tab Ranitidine 150mg on the night prior to surgery.

In operation theatre,
Standard pre-use checks of anaesthesia workstation and ancillary equipment was performed. Patients was be shifted to OT, standard monitor was be attached and basal vital parameters was be noted (Heart rate, bp spo2, Respiratory rate). Good flowing IV cannula was be secured.

In GROUP A, the patients was receive inj. Propofol 0.7mg/kg IV with increments of 20mg till they achieve Ramsay sedation score of 4 along with oxygen via venti mask at 6-8ltr/min.
In Group B, the patients was receive inj. ketamine 0.5mg/kg and Inj midazolam 0.02mg/kg

IV along with increments of inj. Ketamine 10mg till they achieve Ramsay sedation score of 4 along with oxygen via venti mask at 6-8ltr/min. In Group C, the patients receive Normal Saline 5ml IV along with oxygen via venti mask at 6-8ltr/min.
Time to achieve Ramsay score 4 was be noted and was be considered as onset of sedation.
All patients were maintained on spontaneous Respiration.
Any unexpected fall in saturation with sedation was recorded and treated according to standard protocol.

Patient was placed with their back parallel to edge of the operating table, thighs flexed into the abdomen with neck flexed to allow the forehead to be as close as possible to knees with the help of an assistant in OT.

Results

Table 1: Socio-demographic and Sedation

Parameters	Group		p value
	A+B (n = 60)	C (n = 30)	
Age (Years)	37.78 ± 13.06	40.03 ± 12.21	0.431[1]
Age			0.732[2]
≤20 Years	4 (6.7%)	1 (3.3%)	
21-30 Years	18 (30.0%)	6 (20.0%)	
31-40 Years	13 (21.7%)	8 (26.7%)	
41-50 Years	11 (18.3%)	8 (26.7%)	
51-60 Years	14 (23.3%)	7 (23.3%)	
Gender			0.134[2]
Male	24 (40.0%)	17 (56.7%)	
Female	36 (60.0%)	13 (43.3%)	
BMI (Kg/m²)	26.29 ± 2.75	25.70 ± 2.72	0.231[1]
BMI			0.619[2]
18.5-22.9 Kg/m²	9 (15.0%)	6 (20.0%)	
23.0-24.9 Kg/m²	7 (11.7%)	5 (16.7%)	
25.0-29.9 Kg/m²	44 (73.3%)	19 (63.3%)	
Ease To Identify Space			1.000[2]
Easy	48 (80.0%)	24 (80.0%)	
Difficult	12 (20.0%)	6 (20.0%)	
Time to Induce Spinal (Seconds)	25.85 ± 13.84	18.17 ± 13.62	0.239[1]
Number of Spinal Attempts	1.35 ± 0.78	1.27 ± 0.58	0.728[1]
More Than 1 Attempt (Yes)	14 (23.3%)	6 (20.0%)	0.720[2]
Patient Comfort Score***	8.33 ± 1.47	7.13 ± 1.20	<0.001[1]
Patient Satisfaction Score***	86.42 ± 14.02	71.67 ± 12.27	<0.001[1]
Onset of Sedation (Seconds)	69.80 ± 12.62	-	-

Time to induce spinal in A+B group is 25.85 Seconds.
Number of attempts on an average in A+B group is 1.35.
Patient Comfort score in A+B group 8.33.
Patient satisfaction score in A+B 86.42.

Discussion

Propofol is presumed to exert its sedative hypnotic effects through interaction with GABA, the principal inhibitory neurotransmitter in the CNS. When the GABA receptor is activated, transmembrane chloride conductance increases, resulting in hyperpolarization of post synaptic cell membrane and functional inhibition of post synaptic neuron. Propofol interacts with specific components of GABA receptor complex, appears to decrease the rate of dissociation of GABA from its receptor. This increases the duration of GABA activated opening of the chloride channel with resulting hyperpolarization of cell membrane.

Propofol inhibits acetyl choline release in hippocampus and prefrontal cortex through acting on GABA a receptors producing sedation. Propofol produces central nervous system effects by inhibiting NMDA sub-type of glutamate receptor through modulation of sodium channel gating.

After a single bolus injection, propofol levels in blood decrease rapidly as a result of both redistribution and elimination. The initial distribution half-life of propofol is 2-8min. In two compartment model elimination half-life is around 1-3 hours. In three compartment model, the initial distribution half-life is around 1-8minutes and 30-70 min, elimination half-life is 4-23.5 hours. This longer elimination half-life indicates deep compartment with limited perfusion, which results in slow return of propofol back to central compartment. The volume of distribution of central compartment is around 20-40l and volume of distribution at steady state is 150-170l. The clearance of propofol is extremely high 1.5-2.2l/min. This clearance exceeds hepatic blood flow and extra hepatic metabolism has been demonstrated. Lungs seem to play a role in extra hepatic metabolism [7].

Pharmacokinetics of propofol may be altered by gender, weight, preexisting disease, age and concomitant medication. Propofol may impair its own clearance by decreasing hepatic blood flow. Increasing cardiac output leads to decrease in propofol concentration and vice versa. Women have a high volume of distribution and higher clearance rates, but elimination half-life is similar to males. Children have a longer central compartment volume (50%) and more rapid clearance (25%). Therefore in children >3years, volume and clearance should be adjusted by weight. Hepatic disease appears to result in larger steady state and central compartment volumes. Clearance is unchanged, but elimination half-life is slightly prolonged [8].

Propofol decrease cerebral metabolic rate for oxygen, cerebral blood flow and intracranial pressure. Large doses of propofol may decrease systemic blood pressure sufficiently to decrease cerebral perfusion pressure. Propofol acutely decreases intraocular pressure by 30-40%. Normal cerebral reactivity to carbon dioxide and auto regulation is maintained during propofol infusion. Propofol provides cerebral protective effects after an acute ischemic insult as same degree that of either halothane or thiopentone [9].

At sub hypnotic doses, propofol provides sedation and amnesia. Propofol alters mood after short surgical procedures. It also produces general state of well-being [10].
Propofol produces cortical EEG changes ranging from initial increase in alpha to gamma and theta frequency. It also produces burst suppression at higher doses. It also produces a decrease in early component of somato sensory and motor evoked potentials but not an early auditory evoked potential. Effect of propofol on epileptogenic EEG activity is controversial. Propofol has a direct anticonvulsant effect, which is dose dependent. Propofol produces shorter duration of motor and EEG seizure activity after electroconvulsive therapy. Propofol is associated with grand mal seizures and has been used for cortical mapping of epileptogenic foci.

Conclusion

Sedation has been shown to increase patient satisfaction during regional anaesthesia and may be considered as a means to increase the patient's acceptance of regional anaesthetic techniques.

References

1. Blouin RT, Seifert HA, Babenco HD, Conard PF, Gross JB. Propofol depresses the hypoxic ventilatory response during conscious sedation and isohypercapnia. Anesthesiology 1993;79:1177-82.
2. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96:1004-17.
3. Ge SJ, Zhuang XL, Wang YT et al. Changes in the rapidly extracted auditory evoked potentials index and the bispectral index during sedation induced by propofol or midazolam under epidural block. Br J Anaesth 2002; 89:260-4.
4. Minto CF, Schnider TW, Gregg KM, Henthorn TK, Shafer SL. Using the time of maximum effect site concentration to combine pharmacokinetics and pharmacodynamics. Anesthesiology 2003;99:324-33.
5. Malik, R., Nandal, Naveen and Gupta, Prakhar. (2021), The Impact of online shoppers to price and quality: a survey study in Delhi-NCR, Efflatounia, 5 (2), pp. 376 – 389.
6. Kurup V, Ramani R, Atanassoff PG. Sedation after spinal anesthesia in elderly patients: a preliminary observational study with the PSA-4000. Can J Anaesth 2004;51:562-5.
7. Wu CL, Naqibuddin M, Fleisher LA. Measurement of patient satisfaction as an outcome of regional anesthesia and analgesia: a systematic review. Reg Anesth Pain Med 2001;26:196-208.
8. Yotsui T, Kitamura A, Ogawa R. Addition of epinephrine to intrathecal tetracaine augments depression of the bispectral index during intraoperative propofol sedation. J Anesth 2004;18:147-50.
9. Smith I, Monk TG, White PF, Ding Y. Propofol infusion during regional anaesthesia: sedative, amnestic and anxiolytic properties. Anesth Analg 1994;79:313-9.
10. Taylor E, Ghouri AF, White PF. Midazolam in combination with propofol for sedation during local anaesthesia. J Clin Anesth 1992;4:213-6.
11. Sandler NA, Sparks BS. The use of bispectral analysis in patients undergoing intravenous sedation for third molar extractions. J Oral Maxillofac Surg 2000;58:364-8.