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COMPARATIVE STUDY OF PROPOFOL WITH KETAMINE AND PROPOFOL WITH BUTORPHANOL FOR TOTAL INTRAVENOUS ANAESTHESIA IN SHORT SURGICAL PROCEDURES

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Study Protocol

Conflict of Interest: None

Abstract

Background: Total intravenous anaesthesia is technique which uses various drugs in combination, given exclusively by IV route to provide general anaesthesia to the patient. TIVA provides a good surgical plane, rapid induction, smooth the emergence from anaesthesia and rapid recovery. Thus making it a desirable alternative for day care surgeries. Propofol is IV anaesthetic agent, having a pharmacological profile favorable for TIVA. However it is known to cause respiratory depression and dose-dependent hypotension, and due its lack of analgesic properties there is a limitation on its employment. Ketamine known for its hypnotic, analgesic and amnesic properties. Butorphanol seems to provide good analgesia but is associated with adverse effects like cardio depressant action, dizziness and sedation.

Methods: A total of 60 patients who will be undergoing surgeries under TIVA in the age group of 20-60yrs will be taken up for this study. They would be further divided in two groups, Group PK will receive ketamine 1mg/kg 1 min prior to administration of propofol and propofol and group PB will receiving butorphanol 20µg/kg 1min prior to administration of propofol. Propofol will be given at a dose of 1.5ml/kg to both the groups during induction . In both the groups anaesthesia will be maintained with propofol 9mg/kg/hr . Patient will be monitored for various parameters such as non-invasive heamodynamic, respiratory parameters. Incidence of pain on injection Propofol, post-operative sedation, nausea, vomiting will also be looked for.

Results and Conclusion : Expected outcome of this study is that the combination of Propofol-ketamine, offers a better haemodynamic and respiratory stability over propofol-butorphanol combination. Pain on injection will be better attenuated by butorphaol than ketamine.

Keywords : Total intravenous anaesthesia, Propofol, Ketamine, Butorphanol, heamodynamic and respiratory parameters

INTRODUCTION

BACKGROUND: Total intravenous anaesthesia (TIVA) is a type of general anaesthesia technique in which a combination of anaesthetic drugs are used and each drug has its own distinguishing role. As the name TIVA itself is self-explanatory, states that all the agents that are used are given exclusively by IV route.[1] The knowledge perceived from various studies on TIVA state that the agents used must have certain pharmacological features such as rapid clearance rate and a little to no delay between change in infusion rates, plasma levels and actions. Major advantage of TIVA is that it lets in rapid induction, a good plane of surgical stage of anaesthesia and on the stop of surgery TIVA allows a clean emergence and early recovery.[2]

TIVA overcomes a number of negative aspects of conventional inhalation anaesthesia by the following ways.

1. Volatile anaesthetic agents such as sevoflurane, isoflurane and nitrous oxide use is negligible in TIVA, thus causing minimal Operation theatre pollution. Certain studies have shown that these inhalation agents have hazardous effects on operating room personnel, such as bone marrow depression, an increased incidence of miscarriage.
2. vaporisers use can be considerably reduced.
3. The components of TIVA can be regulated independently as the need of each component changes during surgery.
4. Gives a better surgical field to the surgeon by avoiding distension of air filled spaces.[2]

Propofol is a more recent IV anaesthetic agent, possessing a pharmacological profile beneficial for TIVA. It already has a massive reputation for induction and upkeep of anaesthesia for short duration surgeries[3] Propofol is considered a pleasant induction agent for most patients. Propofol is considered eminently suitable for infusion since it has a high profile of surgical clearance rate thus a rapid decline in blood concentration and a speedy recovery from anaesthetic state. Propofol due to its rapid clearance property and as it does not leave residual CNS effects[2] makes it a popular choice for maintaining anaesthesia in short surgical procedures or day care surgeries under TIVA.However it cannot be used as a sole anaesthetic agent due its hypotensive effect and its property to depress the respiratory drive. Propofol is not known to provide any analgesia thus an additional agent is needed for analgesia.[4]

Ketamine a phencyclidine group of drug ,a water soluble intravenous anaesthetic agent. It is the only intravenous anaesthetic which has hypnotic, analgesic and amnesic properties thus making it a complete anaesthetic agent .[5] Ketamine has certain limitations like its property to increase MAP. Thus neither propofol nor ketamine can be used as sole anaesthetic agents as Propofol reduces mean arterial pressure and ketamine increases them in contrast.

Butorphanol synthetic agonist-antagonist opioid is used along with Propofol to provide analgesia, other key positive characters of butorphanol are its minimal potential for toxicity and abuse.[6] Thus making it feasible for tiva. Butorphanol also provides good analgesia but is associated with adverse effects like cardiodepressant action, dizziness and sedation.[7]

Rationale: Ketamine even though it has all features of an ideal anaesthetic agent it has more potential for abuse and on the other hand butorphanol is a potent analgesic agent

and has a very low potential for abuse ,it does have drawbacks like cardiodressent action, dizziness. Thus we would like to compare and see which is more stable hemodynamically and for respiratory stability.

AIM AND OBJECTIVES

The aim of this prospective comparative randomised study is comparing the effects of administering propofol with ketamine and propofol with butorphanol for total intravenous anaesthesia in short surgical procedures.

Primary objective of the study is:-

1. To compare haemodynamic and respiratory stability.

Secondary objectives of the study are:-

To compare the two drugs i.e. ketamine, butorphanol with propofol for

1. The effect of abolishment of pain (caused by propofol).
2. Incidence of post-operative sedation.
3. Incidence of postoperative nausea and vomiting.

MATERIALS AND METHODS

Study design:

1. Study period :2 years
2. Study area : department of anaesthesiology JNMC &AVBRH.
3. Study design : prospective comparative randomised study.
4. Study population: Patients, 20-60yrs of age of either gender.

Study Settings

After the approval of the ethics and screening committee of Jawaharlal Nehru Medical College, DMIMS (DU), Acharya Vinoba Bhave Rural Hospital (AVBRH), Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha. This study will be conducted on 60 individuals.

Written and informed consent will be obtained from all the patients prior to procedure.

PARTICIPANTS:

Inclusion criteria:

1. Patients aged between 20- 60years of either gender
2. ASA Class I & II patients.
3. All the patients willing to give informed written consent
4. Duration of surgical procedure- 15mins to 30 mins

Exclusion criteria:

1. ASA Class III and above
2. Parents /Guardian's refusal
3. Age : <20 & > 60 years (male or female)
4. Patients having allergy to drugs
5. Duration of Surgical procedure: > 30 mins
6. Those patients who require muscle relaxation

7. patients with anticipated difficult mask
8. Patients with comorbidities such as cardiac diseases, and on thyroid medications

DATA SOURCE/ MEASUREMENTS

Data source: AVBRH, Sawangi Meghe, Wardha.

Data measurement:

1. Heamodynamic parameters : HR,SPo2,Systolic bp, Diastolic bp, MAP
2. Respiratory parameters: Respiratory rate, tachypnea, respiratory effort.
3. Pain on injection with propofol
4. Incidence of post op sedation by using ramsayscore
5. Incidence of post op nausea and vomiting.

MATERIALS REQUIRED:

2. Drugs - glycopyrolate, Midazolam, fentanyl,butorphenol,Propofol .

Sample Size & Design:

Sample size is calculated using WWW.OpenEpi.com .The mean MAP after 10 mins of induction is taken to be 88.30 (+or -) 6.77 keeping power at 80% an alpha of 0.05 , and a 10% difference in mean MAP between the two groups, a sample size of 60 patients will required. The patients selected will be divided into two groups of 30 each randomly.

60 patients of belonging to age group of 20- 60 years fulfilling all the inclusion and exclusion criteria and posted for surgery under TIVA are divided into two groups (i.e.30mins in each groups) as follows:

Group PK(n-30) : will be receiving propofol-ketamine

Group PB (n-30) : will be receiving propofol-butorphanol

PREOPERATIVELY:

Pre operatively a through history taking and general examination will be done for all the patients. The procedure will be explained and written consent will be taken. Patients will be kept NBM overnight prior to the day of procedure. Vitals like PR (pulse rate), RR (respiratory rate), oxygen saturation (SpO_2), BP and ECG will be evaluated in pre-operative room. The selected patients will allocated into one of the two groups of 30 each .Before the commencement of TIVA, patients will be instructed on the methods of study. Monitors will be connected and baseline values of heart rate, blood pressure , respiratory rate and oxygen saturation will be noted .

METHODOLOGY

A total of 60 patients in the age group of 20–60 years patients, who will be undergoing surgeries under total intravenous anaesthesia, will be enrolled in the study. After obtaining written in- formed consent,

After entering the procedure room an Infusion line with 18 gauge cannula will be started, monitors will be attached to patients for continuous monitoring of HR, electrocardiogram, non-invasive blood pressure and oxygen saturation (Spo2)

Patients will be randomly administered one of the two different sedative infusions propofol-ketamine (group k; n = 30) or Propofol-butorphanol (group b; n = 30).Patients will receive standardized premedication in the form of inj. Glycopyrrolate 0.2mg and inj.

Midazolam 2mg iv Once in the operating theatre 2 mins prior to administration of propofol., Anaesthesia will be induced with propofol- ketamine in group K and with propofol butorphanol in group B with appropriate dosage according to body weight. standard monitoring will be done with the help of pulse oximetry, ECG, and NIBP at regular intervals.

Group PK will receive ketamine1mg/kg 1 min prior to administration of propofol and propofol 1.5mg/kg as inducing agent and group PB will receive butorphanol 20µg/kg 1min prior to administration of propofol and then propofol 1.5mg /kg. In both the groups anaesthesia will be maintained with propofol 9mg/kg/hr . Haemodynamic parameters such as heart rate, SBP, DBP and respiratory parameters such as respiratory rate and spo2 will be monitored at baseline, immediately after induction and in the post induction period after at 5,10,20,30 minutes. Respiratory efforts ie presence of laboured breathing ,with respect to presence or absence of nasal flaring, use accessory muscles for respiration and chest rise. Incidence of tachypnea ie more than 20 breaths per minute will also be compared between the two groups.

While injecting propofol, Pain on injection will be noted by vocal response, facial grimace, arm withdrawal or tears suggesting.

Incidence of Sedation will be assessed in post-operative period using standard sedation score, Ramsay hunt sedation scoring.

Table 1 - **Ramsay scale for the assessment of the level of sedation**

LEVEL OF ACTIVITY	POINTS
Patient anxious, agitated or restless	1
Patient cooperative, orientated and tranquil	2
Patient responding only to verbal commands	3
Patient with brisk response to light glabella tap or loud auditory stimulus	4
Patient with sluggish response to light glabella tap or loud auditory stimulus	5
Patient with no response to light glabella tap or loud auditory stimulus	6

Incidence of Post-operative nausea and vomiting will be noted in both the groups.

Statistical methods:

Statistical analysis could be done by using by using descriptive statistics ie mean, standard deviation, standard error of mean and by using inferential statistics like chi squre test, students unpaired t test. All the results would be tested at 5% level of significance

EXPECTED RESULTS:

Expected outcome of this study is that the combination of Propofol-ketamine, offers a better haemodynamic and respiratory stability over propofol- butorphanol combination. Pain on injection will be better attenuated by butorphaol than ketamine.

DISCUSSION

Dr. Nabin Regmi et al[8] have done a randomised double blinded study on combination of propofol with ketamine and propofol with butorphanol for day care surgeries. In this study they compared the two combinations in terms of hemodynamic and respiratory stability. The other objectives of this study were to compare the pain abolishment on injecting propofol, imvidence of postoperative sedation, nausea and vomiting .This study was conducted on 60 individuals between 16-60 yrs of age and belonging to ASA class I and ASA class II. Patients were divided into two groups of 30 each : Group-B and Group-K receiving Propofol-Butorphanol combination and Propofol-Ketamine combination respectively.Heart rate, MAP SPO2 were monitored at baseline and at every 5 mins interval after induction. The conclusion of this study was that Propofol in combination with Ketamine provided better hemodynamic and respiratory stability than Propofol in combination with Butorphanol ,however pain on injection with propofol was better controlled with Propofol-ketamine combination.[8]
P. Venkateswarlu et al[9] have done a comparative study on 60 patients undergoing short surgeries under TIVA with propofol with ketamine and propofol with butorphanol drug combination. Study population were divided into group K and group B randomly. Group K, received Propofol- Ketamine and Group B, Propofol Butorphanol. Either of the groups were induced and maintained with Propofol 1.5 mg/kg IV and Propofol 9 mg/kg/hr IV respectively. They recorded a fall in both SBP and DBP after induction in both the groups . Group B showed more variation in SBP & DBP during various intervals and no such significant difference was not found in group K. Pain on injection with Propofol was not attenuated by Butorphanol pre-treatment . Post-operative sedation was more in Group B (Propofol-Butorphanol) than in Group K (Propofol –Ketamine). They concluded that the group K ie combination of Propofol-Ketamine was found to be more effective than the other Group in terms of stability of the hemodynamic parameters as well as sedation was less after the surgery in group K. Few other studies related to general anesthetics have been reported [10-14]. Belekar reported on efficacy of Butorphanol as an adjuvant to epidural analgesia[15]. Palan and Agrawal also reported a comparative study of Butorphanol with Tramadol[16].

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