Research Article

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Effect of Propofol, Midazolam and Their Combination in Day Care Patients Undergoing Oral and Maxillofacial Surgical Procedures

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ABSTRACT

Background: The purpose of the study was to compare and assess the clinical efficiency of sedation by Propofol, Midazolam & Propofol-Midazolam combination on 60 subjects of either sex and age between 18-50 years.

Materials and Method: This is a prospective, randomized, double blind, controlled study, which is clinically oriented with 60 subjects of either sex which needed a minor oral surgical procedure. Group A: This received Propofol bolus & continuously maintained by infusion of Propofol. Group B: This received Midazolam bolus & continuously maintained by infusion of Midazolam. Group C: This received induction by Propofol & continuously maintained by infusion of Midazolam. Ten minutes after the infusion of sedative agent/s, the local anesthetic was injected. Minor elective surgical procedures were carried out. Patient's verbal response was determined both by the surgeon & anaesthelogist. After surgery the patient was sent to the recovery room & monitored for 2 hours, before being discharged. The patient were assessed starting with preoperative baseline vitals, then peri-operative baseline vitals every ten minutes and then, postoperative baseline vitals and other parameters were recorded on a relevant data sheet

Result: The anxiety score was less in group-A (21.5 ± 2.48, graph-1), proportion of Deep, Eye closed, rousable on mild stimulation was more in Group C as compared to Group A & Group B(graph-2). The proportion of incidence of side effects is less in Group A than other groups (graph – 3), patient satisfaction group C (4.15±0.49) and discharge score were better in Group-A (9.30± 0.57 graph - 4,5) and Group A was more hemodynamically stable (graph 6,7,8)

Conclusion: Propofol as a sole agent provides better anxiolysis, hemodynamic stability and reduced side effects but patient satisfaction is more in combination of propofol – midazolam combination.

Keywords: Propofol, Midazolam, Oral surgery.

INTRODUCTION

Enigma of fear, anxiety and pain has been associated with surgical procedures for the time immorable. To improve acceptability and comfort for patients and to reduce stress it is common to use an altered state of consciousness in which person is more relaxed and care free during the procedure. Dentistry, in its surgical and restorative aspect, is in majority based on office practice. Majority of the dental procedures can be performed under local anesthesia which is inherently safe. Most dentists are skilled in techniques of local anesthetics and nerve blocks. General anaesthesia should not be used as a method of anxiety control but for pain

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control, because more specific methods (local anaesthesia with or without conscious sedation and behaviour management techniques)[1] are available. Intravenous administration of sedative drugs allows dose titration to produce adequate sedation of a patient without loss of consciousness. However, the degree of sedation a patient feels that is necessary to tolerate an operation may differ from the degree of sedation the anesthesiologist provides. Also, sedation requirements often vary during the course of the procedure.[2]

Sedative/anxiolytic drugs are known to create more suitable operative conditions for both the operator and patient[3]. Regional anesthesia is popular and offers several benefit to the patient. The top three from the patient's point of view is staying awake, early family contact, and early food intake[4].

MATERIALS AND METHODS

This is a prospective, randomized, double blind, controlled study, which is clinically oriented with 60 subjects of either sex who had to undergo a minor oral surgical procedure which included surgical extraction of impacted teeth, cyst enucleation /marsupilization, apicoectomy, undisplaced mandibular fracture reduction & fixation, intra oral biopsy, alveoloplasty. All these procedures were of maximum 150 minutes duration. Group A received Propofol bolus & continuously maintained by infusion. Group B received Midazolam bolus & continuously maintained by infusion. Group C received induction by Propofol & continuously maintained by infusion of Midazolam. Patient included in the study were of age range of 18-50 years, had ASA Physical status Class I & II, informed consent regarding the study and procedure was taken from the patient and and all the patients were hemodynamically stable patient with all routine investigations within normal limit. Patient unwilling or hesitant for the procedure, with known history of egg allergy, history of adverse reaction or allergy to any drug used during anesthesia, systemic disease, Pregnancy, Known alcoholic, with compromised airway or had recent administration of CNS depressant drugs were excluded from the study.

Procedure:

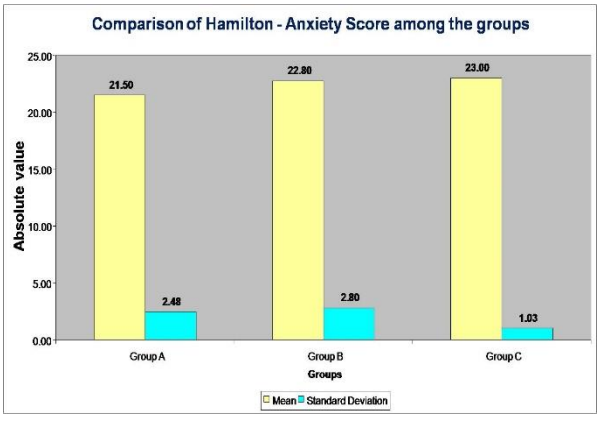
Ten minutes after the infusion of sedative agents, the local anesthetic was injected. Minor elective surgical procedures were carried out. Patient's verbal response was determined both by the surgeon & anaesthelogist by talking to the patient continuously during the procedure. The drug administration was stopped when the surgeon completes the surgical procedure. After surgery the patient is sent to the recovery room & monitored for 2 hours, before being discharged. The patients were assessed starting with preoperative baseline vitals, then peri-operative baseline vitals every ten minutes and then, postoperative baseline vitals, and all were recorded on a relevant data sheet. Apart from base line vitals, other parameters were also recorded like Degree of sedation (table-1), Operating conditions (table -2), Incidence of side effect (table-3), Degree of amnesia (table -4), Discharge score (table – 5), Patients satisfaction (table – 6).

Stastical analysis

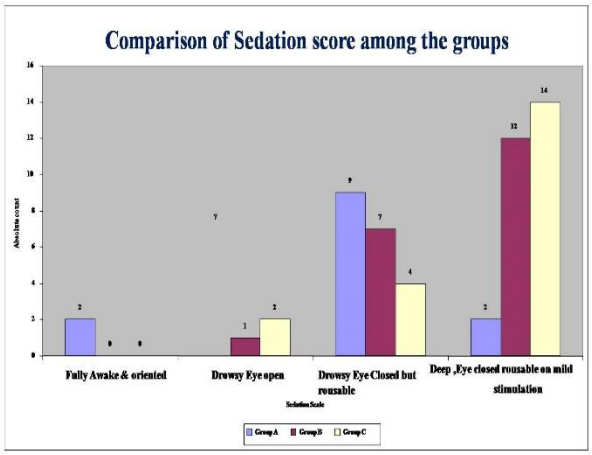
Analysis of variance (ANOVA) was applied to test the hypothesis of the significant difference among the groups. Application of Chi-square Test of association to determine the association between the categorical variables. Student's t – test to test the hypothesis of significant difference for inter-comparisons of groups.

RESULT

The anxiety score was less in group-A (21.5 ± 2.48, graph-1), proportion of Deep, Eye closed, rousable on mild stimulation was more in Group C as compared to Group A & Group B(graph-2).

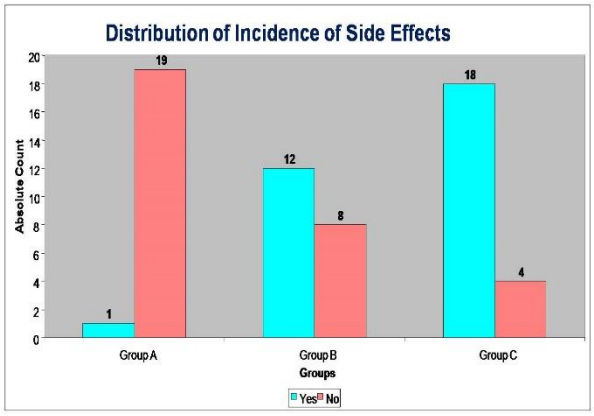


Graph 1: anxiety score among the group



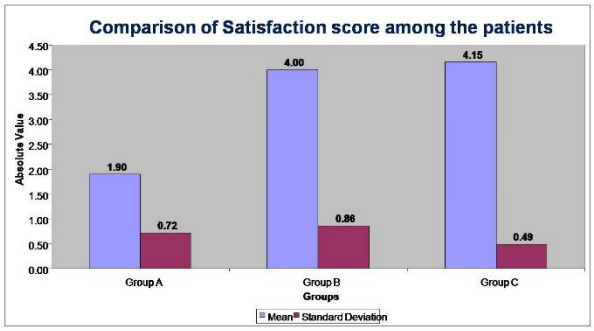
Graph 2: Comparison of sedetion score

The proportion of incidence of side effects is less in Group A than other groups (graph – 3),

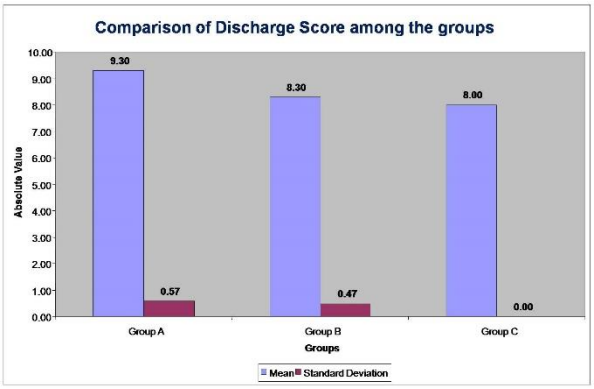


Graph 3: Distribution of incidence of side effect.

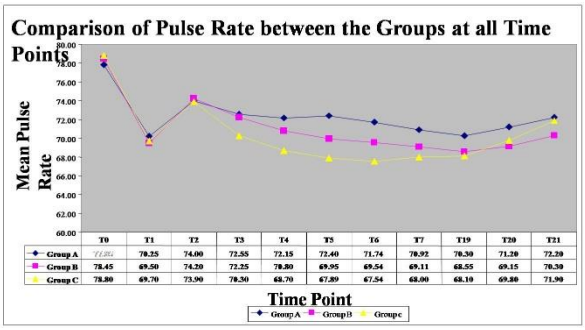
patient satisfaction group C (4.15±0.49) and discharge score were better in Group-A (9.30± 0.57 graph- 4,5) and Group A was more hemodynamically stable (graph 6,7,8).



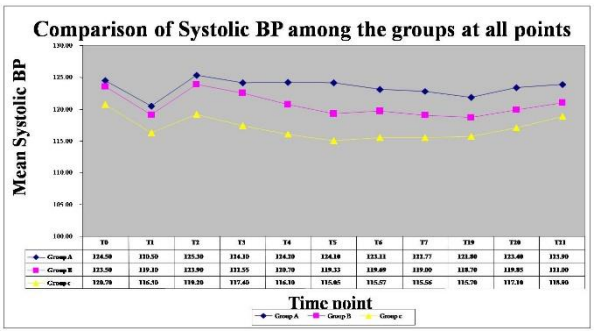
Graph 4: Comparison of satisfaction score



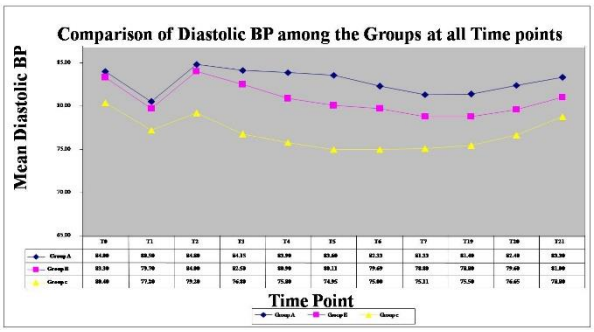
Graph 5: Comparison of discharge score



Graph 6: Comparison pulse rate.



Graph 7: Comparison of systolic blood pressure



Graph 8: Comparison of diastolic blood pressure.

DISCUSSION

Sedation can be described as a continuum ranging from minimal sedation, such as anxiolysis, through to general anaesthesia. In contrast to general anaesthesia, verbal contact is usually maintained or is possible when needed. The term 'conscious sedation' is used for sedation for therapeutic or diagnostic procedures, and 'monitored anaesthesia care' for sedation to supplement local or regional anaesthesia.

Unfortunately, these terms are not consistently applied. Sedation is part of the general management of a patient receiving a regional block and being awake during the whole surgical procedure. The aims include general patient comfort, freedom from specific discomfort, and some amnesia for both the block procedure and the surgical operation, in order to meet the patient's preference and safety[4].

Propofol, (2, 6 di-isopropylphenol) is a general anesthetic agent that is delivered intravenously. It is prepared as a 1% (10 mg/mL) emulsion in an aqueous solution of 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide.4-7 It acts by enhancing the GABA-activated chloride ion channel function. The blood-brain equilibration half-life is approximately 2 to 3 minutes with a distribution half-life of 2 to 4 minutes. Propofol has several advantages when used in the outpatient setting and can be used with the bolus technique familiar to most oral surgeons, or an infusion pump. It has a rapid onset of action and a short duration of action. This leads to rapid recovery with earlier cognitive and psychomotor function.

Propofol goes through hepatic metabolism and renal excretion. The metabolites, glucuronide and sulfate conjugates are not metabolically active. Up to 90% of propofol is excreted in the urine and less than 1% is excreted unchanged in the feces. It is safe to use in patients with moderate hepatic or moderate renal disease.[5]

Midazolam is water soluble and therefore is not painful on intravenous administration. Midazolam is the only benzodiazepine approved by the food and drug administration for use in neonates. It should be noted that because of its water solubility, midazolam takes three times as long to reach a peak electroencephalograph effect.[6]

In our study p value = 0.07 > 0.05 implies that, there is no significant difference in Hamilton anxiety score among the groups (graph -1) which concurs with the study of Karandikar et al[3], however, the proportion of sedation in our study was more in Group C as compared to Group A & Group B (graph -2) but in their study their score was the same[3]. In our study Midazolam was a more potent amnesic, however incidence of side effects was less for Propofol even the patient satisfaction and discharge score favored propofol.

Propofol is an intravenous sedative hypnotic agent that has gained wide acceptance for outpatient oral and maxillofacial surgery because it quickly produces loss of consciousness and is associated with a rapid and smooth recovery. It is both a cardiovascular and respiratory depressant that can produce dose-dependent hypotension but has been shown to provide hemodynamic stability, particularly when combined with midazolam[7,8]. In our study several vital signs were routinely monitored during intravenous sedation but no hemodynamic exacerbations were observed (graph-6,7,8). Having established that propofol produced equivalently effective sedation to midazolam in the study by havel et al , it is clear that the major advantage to the use of propofol for procedural sedation is rapid recovery[9]. Propofol compared favorably with midazolam in each of these measures of effectiveness evaluated in the study.[9]

However leitch et al found that Propofol has several pharmacokinetic parameters that potentially make it a superior sedative agent to midazolam; more rapid onset and offset being two. However its routine use has been restricted to anaesthetists, as in high doses, general anaesthesia is produced with possible loss of the patient's patent airway. Carrasco believe that propofol is an agent with the same safety, a higher clinical effectiveness, and a better cost-benefit ratio than midazolam in the continuous sedation of critically ill patients undergoing mechanical ventilation[11].

Conscious sedation for minor oral surgery procedures is becoming increasingly popular as general anaesthesia becomes less so. In combination with local anaesthesia it potentially

forms a pain-free and anxiety-free technique for both the patient and the surgical team. Any new drug delivery system must be carefully assessed for safety and efficacy in this specific environment.[10]

Ustun et al suggest dexmedetomidine, a highly selective alpha (2)-adrenoreceptor agonist may be a remarkable alternative to midazolam for intravenous sedation because it seems to be a reliable and safe method, with additional analgesic effect providing a satisfactory sedation level without any serious side effects during impacted third molar surgery. Taniyama K et al in 2009 in their study concluded that dexmedetomidine's sedative actions resemble physiologic sleep, and respiratory depression is less marked; this differs from the features of benzodiazepines and propofol, which have been used in the dental field for psychosedation. It has been reported that this agent causes cardiovascular and psychiatric/neurologic side effects such as hypertension and bradycardia[13]. Further studies should be done to investigate the efficacy of dexmedetomidine in geriatric patients or medically compromised patient populations where this drug may be of value[12].

Remifentanil is one such drug that has the potential to significantly change currently accepted protocols in outpatient anesthesia for dentistry and oral and maxillofacial surgery[14]. Lacombe et al in their study found that the anesthetic regimen composed of midazolam with an admixture of propofol/remifentanil (ratio, 1:500) provided faster emergence and recovery without increased adverse reactions compared with a standard regimen where fentanyl is administered by bolus.[14]

In Australia the current conscious sedation techniques commonly use the benzodiazepine midazolam and fentanyl. The midazolam is delivered in a titrated manner to give the desired "end-point" where the patient is suitably sedated for treatment to proceed. Combining the midazolam and fentanyl give a synergistic effect that can provide profound sedation and also allow for a smaller overall dose of each drug to be administered. Some practitioners may also introduce propofol that gives enhanced and deeper sedation for a brief period when it may be required during certain procedures, such as dental extraction.[15]

CONCLUSION

Midazolam is a commonly used intravenous benzodiazepine that has had an effective and excellent safety record for outpatient intravenous sedation, particularly for elderly and CAD patients. Propofol is gaining wide acceptance in minor oral surgical procedures because of rapid onset and recovery and good hemodynamic stability. However we should always be open to newer drugs which have a potential to further improve the safety index in minor oral surgical procedure and add on to ease and comfort of the patient.

PERFORMA OF STUDY

STUDY PERFORMA

Table -1 SEDATION SCALE

- 1. (No).....Fully Awake & Oriented
- 2. (Mild).....Drowsy. Eye Open
- 3.(Moderate)...Drowsy, Eye Closed but rousable
- 4.(Deep).....Drowsy, Eye Closed, rousable on mild stimulation
- 5.(Over).....Unrousable on mild physical stimulation

SCORE =

Table – 2 COOPERATION BY PATIENT AS ASSESSED BY SURGEON

OPERATIONCONDITION..DEFINITION ..SCORE

- GOOD.....Patient fully cooperative, optimum degree of sedation for the patient.....1
- FAIR.....Minimum interference from the patient by virtue of slight over sedation or under sedation 2
- POOR.....Operating difficult by virtue of over sedation or under sedation 3
- IMPOSSIBLE....Operation not possible by virtue of over sedation or undersedation.....4

SCORE =

Table - 3

SIDE EFFECT..... REMARKS

Nausea
Vomiting
Drowsy /Sleepy
Headache
Pain On Injection Site
Others (If Any)

Table – 4 DEGREE OF AMNESIA

1. Do you remember the prick of needle for local anesthesia?.....Yes/No
2. Do you remember the operator incising/cutting your gums?....Yes/No
3. Do you remember sound of motor/ drilling of bone? .....Yes/No
4. Do you feel pressure/pain during removal of tooth/curettage/bone Plating/homeostasis maneuvering.....Yes/No
5. Do you remember when the stitches were placed?..... Yes/No
6. Do you remember being shifted out of the operating room?.....Yes/No
7. Do you remember the questions asked to you during the procedure .....Yes/No

STUDY PERFORMA

TEST

If the patient remembers

- 7-5 Nos. of questions then he is non-amnesic.
- 2-4 Nos. of questions then he is partially amnesic.
- 0-1 Nos. of questions then he is totally amnesic.

Table – 5 DISCHARGE PROFORMA (ALDRETE SCORE)

ACTIVITY.

- 0=unable to lift head or move extremities voluntarily or on command
- 1=moves two extremities voluntarily or on command. And can lift head.
- 2=able to move 4 extremities voluntarily or on command. And can lift head and has controlled movements.

RESPIRATION

- 0=Apenic; condition necessitates ventilation or assisted respiration
- 1=labored or limited respiration. Breathes by self but has shallow, slow respirations. May have oral airway.
- 2=can take a deep breath and cough well; has normal respiration rate & depth.

CIRCULATION

- 0=has abnormally high or low blood pressure. B.P of 50 mm of Hg of pre anesthetic level.
- 1= B.P of 20-50 mm of Hg of pre anesthetic level.
- 2=stable B.P & pulse. B.P of 20 mm of Hg of pre anesthetic level. (Min 90 mm of Hg- systolic).

NEUROLOGIC STATUS

- 0=Not responding or responding only to painful stimuli
- 1=Responds to verbal stimuli but drifts off to sleep easily.
- 2=Awake and alert, oriented to time, place & person.

COLOR

- 0=Cyanotic, dusky
- 1=pale
- 2=pink

TOTAL SCORE

MAXIMUM SCORE: 10

SCORE REQUIRED FOR DISCHARGE =8-9,

Table - 6 PATIENT SATISFACTION

- Modified Visual Analogue Scale (VAS), Scoring 0-10

0.....totally calm & relaxed

10.....worst fear imaginable

SCORE=

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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