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Original Article

Randomized Comparative Study of Drug Regimens: Fentanyl with Propofol and Fentanyl with Midazolam as Sedating Agents in Day Care Oral Surgery

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Abstract

Introduction: Widespread use of general anesthesia is limited by the risk associated, requirement of adequate equipment, extensive training required, and the cost. The use of intravenous agents in conjunction with local anesthetics has a definite synergistic effect and is referred to as conscious sedation.

Aim: The aim of this study is to compare usefulness and toxicity by qualitative comparison between two combinations, fentanyl + propofol, and fentanyl + midazolam, as agents for conscious sedation in patients undergoing maxillofacial surgical procedures.

Materials and Methods: The present study was conducted on 10 adult patients, 5 in each group (fentanyl + propofol and fentanyl + midazolam), between 14 and 50 years of age irrespective of sex. The comparison was made in terms of onset of action, recovery anterograde amnesia, patient cooperation, surgeons' convenience, side effects, and other parameters.

Result: Although the therapeutic efficacy of both the combinations was satisfactory, fentanyl + propofol combination showed better amnesic property and tolerance to the surgical procedure, whereas fentanyl + midazolam combination showed greater respiration depression. Fentanyl + propofol was found to be superior sedating agent having rapid onset and predictability of action, profoundness of amnesia, and faster recovery periods, offering advantage of early patient discharge and better patients compliance agent in day care maxillofacial surgical procedures.

Conclusion: Propofol + fentanyl combination as a superior sedating agent compared to fentanyl midazolam combination having rapid onset and predictability of action, profoundness of amnesia, and a faster recovery period, offering advantages early patient discharge and better patient compliance.

Key words: Conscious sedation, Day care procedures, Fentanyl, Maxillofacial surgery, Midazolam, Propofol

INTRODUCTION

Anxiety toward dental procedure varies from a suppressed fear of pain to phobia. This may make dental therapy difficult. Not only do many patients find these procedures unpleasant but also they may exhibit enhanced sympathetic activity such as xerostomia, tachycardia, sweating, and tremors, which in some cases may lead to anxiety-induced arrhythmia and vasovagal reaction.[1,2] Local anesthetics and new advances in technology have rendered dental treatment experience and often painless. However, in certain situations, pain and anxiety control become unattainable by local anesthetics, and the administration of local anesthesia is considered to be a traumatic procedure by many patients. General anesthesia is also not practical for many ambulatory patients undergoing minor surgical procedures, and hence, the alternative approach is the use of anxiolytic and sedative agents as adjunct to local

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anesthesia. Intravenous sedative hypnotics are commonly used during day care maxillofacial surgical procedures to enhance patient comfort, improve operating environment, and prevent recall of unpleasant events during surgery.[3,4] Conscious sedation is a technique in which the use of a drug or drugs produce a state of depression of central nervous system, which enables an operator to carry out a surgical procedure but during which verbal contact with the patient is maintained and patient retains protective reflexes. Among the methods used for conscious sedation intravenous sedation are perhaps the most popular, as it has rapid onset and enables the dose of the drug to be titrated according to the need of the patient, with maximum safety.[5]

Aim

The objective of the present study is to clinically evaluate the usefulness and toxicity by qualitative comparison between two combinations, fentanyl + propofol and fentanyl + midazolam, as agents for conscious sedation in patients undergoing maxillofacial surgical procedures including simple fracture reduction and fixation, impaction, and cyst enucleation on a day care basis.

MATERIALS AND METHODS

The present study was conducted in the Department of Oral and Maxillofacial Surgery, Tamil Nadu Government Dental College and Hospital on an outpatient basis. The study included 10 adult patients, 5 in each group, age between 14 and 50 years irrespective of sex. Apprehensive and uncooperative patients requiring surgery for removal of impacted mandibular third molars, cyst enucleation, and simple mandibular fracture reduction and fixation were included in the study. The procedure was explained to the patients, and a written informed consent was obtained. A detailed case history, including postexposure to anesthetics, sedative agents, and previous surgical procedures were collected and recorded. Routine blood investigation, chest-ray, and electrocardiogram (ECG) were done for all the patients. A pre-anesthetic evaluation and physicians clearance were obtained for all the patients.

Inclusion Criteria

Age group was between 14 and 50 years, and only the American Society of Anesthesiology risk category patients after a complete medical history and physical examination were included in the study. Patients with no history of sensitivity to any of the drugs on their constituents were used in the study.

Exclusion Criteria

Patients who were pregnant, used sedative regularly, drug of alcohol dependent, and had been given general anesthetic previously for dental procedures were excluded from the study.

Patients were asked to remain nil orally 6 h before surgery. On arrival, patients were connected to a multifunction monitor, and a no 18G cannula inserted in a vein on the fore arm of the non-dominant arm. Surgery was performed with the patient in a reclining position on completion of the procedure that the patients were observed for 10 min and later shifted and allowed to recover in the recovery room.

Randomization of the cases was done by sealed envelope technique into 2 groups, namely, Group I (fentanyl + propofol) and Group II (fentanyl + midazolam).

Patients in Group I received propofol at 100-150 μg/kg/min, which is 6-9 mg/kg/hour + fentanyl 2 mg/kg as induction dose, and later, slow intermittent dose titrated to the required end point of sedation, i.e., ptosis and slurred speech.[6] Patient in Group II received intravenous doses of midazolam 1-5 mg + fentanyl 2/mg/kg titrated to the required end point. This end point was chosen because it was easy to observe.[7-9]

Repeat doses were given after the sign of warning of sedation was seen such as phonation, nystagmus, and purposeful movements on surgical stimulation. Patients were given a local anesthetic injection of 2% lignocaine with 1:80000 adrenaline after 2-3 min after the administration of intravenous sedation.

In the operating room, multifunction monitor with pulse oximeter, ECG monitor, and NIBP was connected to the patient. Real-time monitoring of heart rate, systolic, diastolic, mean arterial pressure, and oxygen saturation was made. ECG was monitored, and during the whole-operative period, recording was made of any abnormal rhythm detected.

Onset of Action

The onset of action was calculated by the time elapsed between induction and the onset of signs of the end point of sedation.

Amnesia

Amnesia period and quality were evaluated with the help of post-operative questionnaire regarding surgical procedures and by presenting separate visual and cutaneous stimuli during surgery. Amnesia was assessed after the surgery and just before discharge by means of a checklist asking if the patient remembered.

Visual and cutaneous stimuli were applied to check anterograde amnesia. Recall of venipuncture on the hand

before the administration of any medication was used to assess retrograde amnesia. The correct, partial, or no recalls of these parameters were used to grade the degree of anterograde amnesia as good, moderate, or poor.

Recovery

The recovery period was measured from the last dose of the drug to the time when the patient could walk in a straight line without support. Recovery was assessed by the patient performance in a Trieger Dot test.[10] It was used to measure the psychomotor activity of the patient following sedative administration. Patients performed the test once preoperatively and then postoperatively at 15 min. Patients were asked to walk in a straight line without support under supervision. If the patient could do this, they were assessed as fit for discharge. If they could not, patients were allowed to recover and again asked to walk in a straight line after 15 min.

RESULTS

The study comprised of 10 patients divided into two group 5 each Group I - patients received fentanyl + propofol, Group II - patients received fentanyl + midazolam.

The age and sex incidence shows a mean age of 37.6 years in Group I and 31.2 years in Group II. The male:female ratio was 3:2 in Group I and 2:3 in Group II. The mean duration of surgery shows no significant difference between Groups I and II. The onset of action was assessed with the onset of signs of sedation end point that is slurred speech and presence of ptosis (Verrill's sign). An increase in heart rate was seen in both the groups but the increase in heart rate at all stages was significantly higher in Group I. A sudden increase in heart rate was noticed immediately after local anesthesia administration in both the groups. The intraoperative increased heart rate gradually returned to base line values in the recovery room in both the groups (Figure 1).

Systolic, diastolic, and mean arterial pressure were increased in both the groups following drug administration. No statistically significant difference was found in the level of increase in systolic pressure at various time interval except post local anesthesia administration period, where the raise is 15% in Group I and only 5% in Group II. The rise in systolic blood pressure ranged from 8% to 15% in Group I and 5-10% in Group II (Figure 2).

Oxygen saturation was measured from a pulse oximeter and shows no statistically significant difference between the two groups (Figure 3).

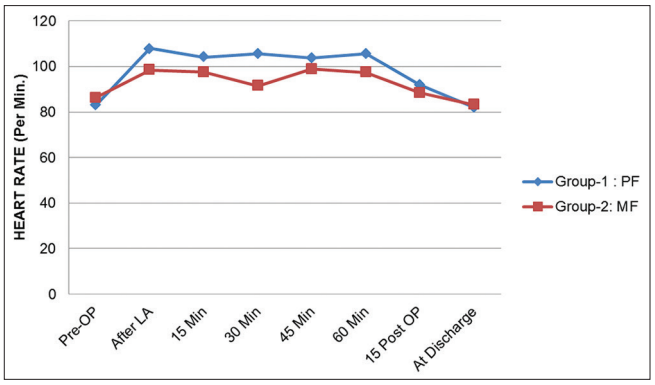

Figure 1: Heart rate

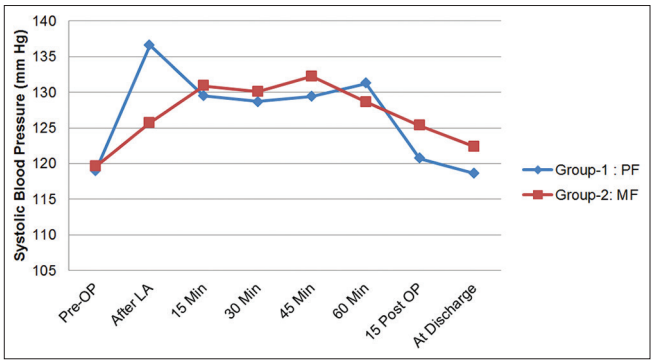

Figure 2: Systolic blood pressure

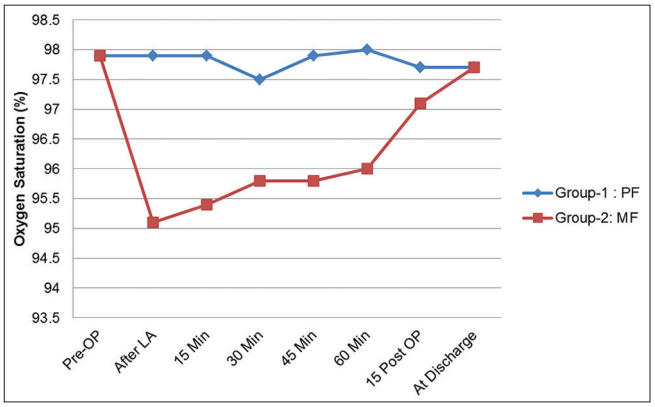

Figure 3: Oxygen saturation

Arrhythmias of any kind were not noticed on the ECG monitor lead II both the groups throughout the procedure.

When the patient was questioned at the post-operative period, the patients could remember vein puncture, and therefore, no retrograde amnesia was established in any of the two groups. From the data, it may be inferred that the patients in Group I experienced early and profound amnesia than the patients in Group II. 80% of patients in Group I experienced profound amnesia for tactile and visual stimuli as compared to 10% in Group II. From the checklist, anterograde amnesia was evaluated as good, moderate, and poor for each group. 90% of the

patients experienced good amnesia as compared to 10% of patients in Group II. The difference between the two groups is statistically significant suggesting a greater degree of intraoperative amnesia with Group I as compared to Group II.

Postoperatively, all patients in both the group were oriented to person, place, and time. Recovery was measured from the last dose of the drug to the time when the patient could walk in a straight line without support. Vital signs were recorded postoperatively which gradually reduced dose to predrug base line values during recovery. The mean recovery period shows that the average recovery time of Group I patient is 10-11 min more than the Group II which was statistically insignificant.

Although psychomotor performance was clearly affected by the drug, all patients were able to complete the post-operative testing regimen on schedule. Many patients slept during the post-operative rest period, but all were easily arousable as from natural sleep. The test scores show that psychomotor coordination is clearly affected in both the groups; however, in Group II, it is slightly more (Figures 4 and 5).

Burning sensation during injection of propofol was reported by a total of 4 patients but no incidence of postinjection thrombophlebitis. None of the patients reported headache or hallucination, and no patient complained of pain at the operated site for about 3 h in both the groups. One incidence of delirium, post-operative vomiting, and hiccup immediately after propofol administration was noticed. None had an incidence of ptosis or change in body temperature. No evidence of any delayed complication occurred.

No serious complication occurred intra- and post-operatively that required attention.

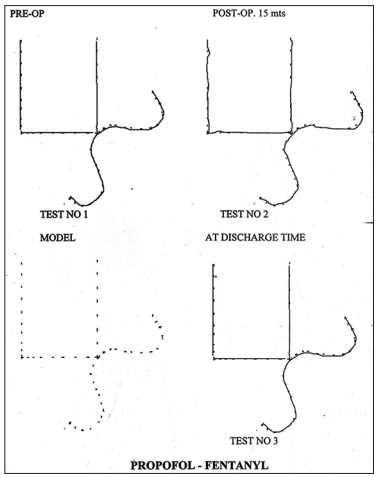

Figure 4: Trieger dot test - propofol and fentanyl

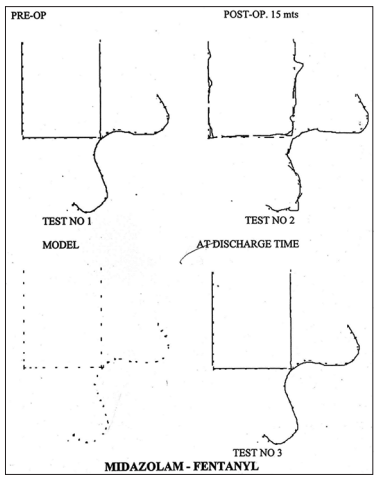

Figure 5: Trieger dot test - midazolam and fentanyl

DISCUSSION

Fear and anxiety about pain are common reasons for patients to delay dental care. Fear, apprehension, anesthesia, and surgery are also accompanied by various harmful cardiovascular, metabolic, and hormonal response.[11] Conscious sedation in combination with local anesthesia has been used as a safe alternative to general anesthesia for control of perioperative pain and anxiety in oral surgery.[12] The introduction of intravenous sedation by Pierre-Cyprian Ore of Bordeaux, France, in 1872 leads to various agents being used for analgesia, amnesia, anxiolysis, and patient cooperation.[13,14] The evaluation of a therapeutic modality of intravenous conscious sedation should start with a statement of the clinical goals of the treatment which can be divided into measures of efficacy and measures of clinical toxicity.

The identified measures of the efficacy of intravenous sedation agents are anxiolytic activity, analgesic activity, amnesic effect, and patient cooperation, whereas toxicity response variables of primary importance are cardiovascular and respiratory effects, prolonged recovery from psychomotor impairment, and side effect liability.[15] Currently, there are several medication regimens used for efficient, safe, conscious sedation during outpatient oral surgical procedures. In this context, we compared the clinical efficacy and toxicity response of two drug groups which may provide a satisfactory combination for conscious sedation.

CONCLUSION

The design of the present study permitted a qualitative comparison between the intravenous sedative drug combinations, i.e., propofol + fentanyl and

midazolam + fentanyl apprehensive and uncooperative patients undergoing oral and maxillofacial surgical procedure on a day care basis. Based on the parameters evaluated in the present study, we can conclude propofol + fentanyl combination as a superior sedating agent compared to fentanyl midazolam combination having rapid onset and predictability of action, profoundness of amnesia, and a faster recovery period, offering advantages early patient discharge and better patient compliance. However, further extensive double-blind studies over a larger population are required to accord fentanyl + propofol group as ideal sedating agent combination in the day care oral surgical procedure.

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