Side Effects and Surgeon-Patient Satisfaction with Total Intravenous Anaesthesia Using Propofol-Ketamine and Propofol-Fentanyl for Day-Case Surgery

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Abstract

Background: Various drugs combination has been tried for short surgical procedures to evaluate the side effects and surgeon-patient satisfaction.

Aims: This study compared the side effect and surgeon-patient's satisfaction with total intravenous anaesthesia with Propofol-ketamine vs Propofol-fentanyl Anaesthesia for short surgical procedures as a day-case.

Methods: one hundred and eight adults aged 18 to 50 years of either gender with ASA I or II scheduled for elective short surgical procedures as a day-case were randomly allocated into group K and F, comprising of 54 patients each. Group K received propofol-ketamine while group F received propofol-fentanyl for induction and maintenance of anaesthesia. Vital signs were recorded at the time of induction, maintenance and recovery. Postoperatively surgeon and patient’s satisfaction with the anaesthesia technique for the procedure was assessed on two scales as either satisfied or not satisfied. Side effects of the anesthetic technique were compared among the two groups.

Results: Fifty-one surgeons (94%) were satisfied with propofol-ketamine anaesthesia while fifty surgeons (93%) showed satisfaction with propofol-fentanyl Anaesthesia for short surgical procedures as a day-case.

Incidence of side effects recorded include PONV (P = 0.32), apnoea (P = 0.04), hypotension (P = 0.08), abnormal movement (P = 0.07) and excessive salivation (P = 0.04) compared among the two groups were observed with statistically significant apnoea in propofol-fentanyl group and excessive salivation in propofol-ketamine group.

Conclusion: Propofol-ketamine has a higher satisfaction rating among surgeons (p = 0.32) and patients (p = 0.16) compared to propofol-fentanyl, but the difference between the two groups is not statistically significant. Incidence of side effects is not generally significant. But when compared between the two groups it shows some statistical significance.

Keywords: Propofol; Fentanyl; Ketamine; Short Surgical Procedures

Introduction

General anaesthesia thus implies the loss of all forms of sensation throughout the body and is associated with unconsciousness. An ideal anaesthetic agent should provide quick and pleasant induction, predictable loss of consciousness, analgesia with stable operating conditions, minimal adverse effects, rapid and smooth recovery of protective reflexes and psychomotor functions [2]. These effects are commonly produced by administering different drugs, each for its own specific derived action rather than the use of a single agent.

Total intravenous anaesthesia (TIVA) is the induction and maintenance of general anaesthesia using drugs administered by the intravenous route only [1]. TIVA has undergone much improvement ever since its introduction into clinical practice. A number of advantages have been ascribed to TIVA over inhalational anaesthesia which includes absence of operating room pollution, minimal cardiac depression, less neuro-humoral response and decreased oxygen consumption [1-3]. TIVA can be used at remote locations with only oxygen and ventilation facilities.

Propofol was introduced in 1977, whose advantage in short surgical procedures relates to its rapid elimination from the blood leading to rapid recovery of cognitive and psychomotor functions with a very low incidence of postoperative nausea and vomiting (PONV). Lack of analgesic properties of propofol has necessitated the need for supplementary analgesia during TIVA.

Ketamine in subanaesthetic doses, combined with propofol, is gaining more attention as an analgesic for TIVA as demonstrated by Guit., et al. [3] Ketamine has very potent analgesic properties as well as being an induction agent. It also has a very long recovery period and it may cause psychomimetic events during recovery. Fentanyl is used extensively in TIVA in combination with propofol for its analgesic property [4]. It belongs to the opioid group of drugs. The combination of these drugs provide adequate hypnosis and analgesia and has advantages such as high potency, lower dosages, rapid recovery and fewer side effects [2,4,5].

Materials and Methods

The study was a prospective randomized double-blind trial conducted on 108 adult patients scheduled for elective day case surgery. An ethical approval was obtained from the Ethical Committee of the hospital, to conduct the study Patients’ informed consent to participate in the study was obtained using a structured consent form.

Patients with American Society of Anesthesiologists (ASA) physical status I and II, aged 18 to 50 years, scheduled for day case surgery were included in the study.

Patients with known allergy to any of the study drugs or constituents, Psychiatric disorders, Pregnancy, patients on monoamine oxidase inhibitors and patient with history of jaundice or liver disease were excluded from the study.

The sample size was calculated using the formula for determining sample size in comparative studies [6]:

\[
n = \frac{2(Z_\alpha + Z_\beta)^2 \pi (1- \pi)}{\Delta^2}
\]

\(n\) = Minimum sample size for each of the component groups
\(Z_\alpha\) = Standard normal deviation set at 95% confidence level = 1.96
\(Z_\beta\) = Standard normal deviation for power of test to detect difference between propofol-ketamine and propofol-fentanyl set at 80% power corresponding to 0.84
\(\pi\) = Arithmetic average of the two proportion \((P_2 + P_1)/2\)
\(\Delta\) = Arithmetic difference between \(P_2 - P_1\)
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P = Proportion of patients satisfied with the administration of propofol-ketamine 95.5% = 0.955 [2]

P = Proportion of patients satisfied with the administration of propofol-fentanyl 75.5% = 0.755 (based on previously published study by Bajwa, et al. [2]) therefore

\[ \pi = \frac{(0.955 + 0.755)}{2} = 0.855 \]

\[ \Delta = (0.955 - 0.755) = 0.200 \]

\[ n = \frac{2(1.96 + 0.84)^2 \times 0.855(1 - 0.855)}{(0.200)^2} = 48.6 \text{ patients per group} \]

\[ \sim 49 \text{ patients per group} \]

10% attrition was added along the course of the research making the overall sample size 108 patients for the two groups.

Preoperative assessment including history and physical examination was carried out a day before or on the day of the procedure by the researcher to provide information to the patient on the study and technique of anaesthesia. Basic investigations which include full blood count and differential, serum urea, electrolyte and creatinine and ECG were checked. Patients were instructed to fast for at least 6 hours for solid food and 2 hours for clear liquid before the procedure. Informed consent was obtained after a thorough explanation of the study procedure. Demographic data were gathered from the case note and the patients, these includes patient’s age as at the last birthday, sex, weight, diagnosis and types of surgery. These were recorded in the preformed data collection form.

Patients enrolled into the study were randomly allocated to one of the two study groups by a senior registrar who was not involved in the evaluation and administration of anaesthesia to the patient. One hundred and eight pieces of uniformly sized sheets of paper were labelled K and F, fifty four each, representing the two study groups: propofol/ketamine and propofol/fentanyl respectively. These papers were folded and shuffled in a large box. For each patient, an assistant instructed the patient to take one folded sheet of paper from the box and the patient assigned to the treatment group indicated on the paper. The patient’s hospital file number was recorded on the sheet of paper. The paper was sealed in a separate envelope that will only be opened after the completion of evaluation. The investigating anaesthetist and the patient were blinded to the group allocated.

Patients were weighed at the theatre reception by a research assistant. On the operating table an intravenous line was set with size 16G or 18G cannulae and 0.9% saline set running. Baseline vital signs including respiratory rate, pulse rate, non-invasive blood pressure, oxygen saturation and ECG were monitored using GE Dash 4000 Automated multi parameter monitor. The anaesthetic machine and resuscitative equipment was checked. Glycopyrrolate 0.2 mg was given to all patients as antisialagogue.

The preparation of study drugs was done by a registered nurse anaesthetist who was not allowed to take part in the study. The drugs were prepared as follows:

- **Group K:** Using a 20 ml syringe, 2 ml of ketamine (50 mg/ml) was withdrawn and diluted by 8 ml of 0.9% saline to make a solution of 10 mg/ml of ketamine. 10 ml of 1% Propofol (10 mg/ml) was withdrawn using the same syringe containing ketamine to make a Propofol/Ketamine solution (Propofol: 5 mg/ml and ketamine: 5 mg/ml).

- **Group F:** Using a 20 ml syringe, 2 ml of Fentanyl (50 mcg/ml) was withdrawn and diluted by 8 ml of 0.9% saline to make a solution of 10 mg/ml of fentanyl. 10 ml of 1% Propofol (10 mg/ml) was withdrawn using the same 20 mls syringe containing fentanyl to make a Propofol/Fentanyl solution (Propofol: 5 mg/ml and Fentanyl: 5 mcg/ml).

Induction of anaesthesia in each of the two study group was achieved with a sleep dose of the drug combination. In both groups, the primary end point for induction was loss of verbal contact. Immediately after induction, the vital signs of blood pressure, pulse rate, respiratory rate and SpO\textsubscript{2} were recorded and subsequently measured at five minutes intervals using the multi parameter monitor until the...
end of the procedure. Continuous ECG monitoring was ensured. Patients were allowed to breathe room air spontaneously. Where there was evidence of airway compromise, jaw thrust was applied to maintain the airway patency. Transient apnoea observed immediately on induction of anaesthesia was managed with Bag mask ventilation until patient regained spontaneous breathing. However, no patient was intubated.

Maintenance of anaesthesia was achieved in both groups with an average of 0.4 ml/kg/hr infusion of the study regimen using B Braun syringe pump.

Administration of all anaesthetic drugs was stopped at the end of the procedure. The postoperative recovery nurse, who was also blinded to the regimen used, monitored the patient postoperatively; assessing pulse rate, blood pressure, SpO₂ and respiratory rate every 5 minute.

Postoperatively, surgeon and patient satisfaction with the anaesthesia technique for the procedure was assessed on two scales as either satisfied or not satisfied. Complications such as postoperative nausea and vomiting, excessive secretions, abnormal movement, hypotension, apnoea at induction and during maintenance were recorded and treated accordingly.

Data were collected using a structured data collection form. Results obtained were analyzed using statistical package for social science (SPSS) version 22.0 for windows. Values were expressed in numbers, percentages and results presented as tables. Chi-square test was used for analysis of categorical variables and student’s t-test was used for analysis of continuous variables. P values less than 0.05 was regarded as statistically significant.

**Results**

Table 1 shows the demographic characteristics of the two study groups. There is no statistically significant difference with respect to ages, weight, sex and the duration of surgery between the two groups (p > 0.05). The mean age of the patients in the propofol-ketamine (K) group was 33.1 years (± 9.3) and 31.6 years (± 9.1) in propofol-fentanyl (F) group (p = 0.44). The mean weights was 58.80 kg (± 9.7) in the propofol-ketamine (K) and 58.76 kg (± 9.7) in propofol-fentanyl (F) groups (p = 0.98). The Male/Female distribution was 35/19 in group K and 38/16 in group F (p = 0.83). The mean duration of surgery was 37.5 minutes (± 10.3) for propofol-ketamine (K) and 37.4 minutes (± 10.0) for propofol-fentanyl (F) (p = 0.77).

<table>
<thead>
<tr>
<th>Variables</th>
<th>K (mean ± SD)</th>
<th>F (mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>33.1 ± 9.3</td>
<td>31.6 ± 9.1</td>
<td>0.44</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male/female</td>
<td>35/19</td>
<td>38/16</td>
<td>0.83</td>
</tr>
<tr>
<td>Weight</td>
<td>58.8 ± 9.7</td>
<td>58.7 ± 9.7</td>
<td>0.98</td>
</tr>
<tr>
<td>Duration of surgery</td>
<td>37.5 ± 10.3</td>
<td>37.4 ± 10.0</td>
<td>0.77</td>
</tr>
</tbody>
</table>

*Table 1: Demographic and clinical characteristic of group K and F.*  
*K: Propofol-ketamine; F: Propofol-fentanyl.*

Table 2 shows the types of surgical procedures which were comparable between the two groups (P > 0.05).

Table 3 showed the incidence of adverse events among group K and group F. Three patients (5%) from propofol-ketamine group (K) and two patients (4%) from propofol-fentanyl group (F) had nausea without vomiting during recovery phase (p = 0.32).

Apnoea after induction of anaesthesia was observed in ten patients (22%) among propofol-fentanyl group and six patients (12%) among propofol-ketamine group (p = 0.04).

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<table>
<thead>
<tr>
<th>Types of surgery</th>
<th>K</th>
<th>F</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herniorraphy</td>
<td>7</td>
<td>5</td>
<td>0.16</td>
</tr>
<tr>
<td>Cystoscopy/EUA</td>
<td>12</td>
<td>13</td>
<td>0.32</td>
</tr>
<tr>
<td>Stent removal</td>
<td>11</td>
<td>13</td>
<td>0.16</td>
</tr>
<tr>
<td>excision of lipoma/ganglion</td>
<td>7</td>
<td>8</td>
<td>0.32</td>
</tr>
<tr>
<td>Closed reduction of fractures</td>
<td>3</td>
<td>2</td>
<td>0.32</td>
</tr>
<tr>
<td>Wound debridement</td>
<td>4</td>
<td>5</td>
<td>0.32</td>
</tr>
<tr>
<td>Circumcision</td>
<td>1</td>
<td>0</td>
<td>0.32</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
<td>9</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>54</td>
<td>54</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** Distribution of surgical procedures among group K and F.

*K: Propofol-ketamine; F: Propofol-fentanyl.

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Group K</th>
<th>Group F</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 54</td>
<td>n = 54</td>
<td></td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Apnoea</td>
<td>6 (11%)</td>
<td>10 (22%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Aspiration</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>0 (0%)</td>
<td>3 (5%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Abnormal movement</td>
<td>11 (20%)</td>
<td>4 (10%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Excessive secretions</td>
<td>4 (7%)</td>
<td>0 (0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hallucination</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3:** Complications reported in both groups.

*K: Propofol-ketamine; F: Propofol-fentanyl.

Three patients (4%) in propofol-fentanyl group (F) had hypotension while none of the patient in propofol-ketamine group (K) experienced hypotension (p = 0.08).

Eleven patients (20%) in propofol-ketamine group (K) had abnormal movement while only four patients (7%) in propofol-fentanyl group (F) had abnormal movement (p = 0.07).

Four patients (7%) in propofol-ketamine group (K) had oral secretions, while none in propofol-fentanyl group (F) (P = 0.04).

Table 4 shows that 51 surgeons (94%) were satisfied with the use of propofol-ketamine while 3 surgeons (6%) were not satisfied with the use of propofol-ketamine. 50 surgeons (93%) were satisfied with the use of propofol-fentanyl while 4 surgeons (7%) were not satisfied with the use of propofol-fentanyl. There is no difference statistically between the number of surgeon satisfied with propofol-ketamine with that of propofol-fentanyl (p = 0.32). Fifty-four patients (100%) were satisfied with the use of propofol-ketamine while 52 patients

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(96%) recorded their satisfaction with propofol-fentanyl. There is no significant difference statistically between the number of patients satisfied with the use of propofol-ketamine with that of propofol-fentanyl anaesthesia ($p = 0.16$).

<table>
<thead>
<tr>
<th></th>
<th>Group K</th>
<th>Group F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfied</td>
<td>51 (94%)</td>
<td>50 (93%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Not satisfied</td>
<td>3 (6%)</td>
<td>4 (7%)</td>
<td></td>
</tr>
<tr>
<td>Surgeon</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td>54 (100%)</td>
<td>52 (96%)</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>(4%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Surgeon and patient satisfaction rating.

K: Propofol-ketamine; F: Propofol-fentanyl.

Discussion

This study showed that propofol-fentanyl and propofol-ketamine combinations provide safe and effective anaesthesia in adults undergoing day case surgeries. The study further demonstrated that propofol-ketamine group showed a significant side effect of abnormal movement and excessive secretions. Both techniques were acceptable by the surgeons and patients as they showed high satisfaction with the conduct of anaesthesia. Although significant side effects of apnoea ($p = 0.04$) was reported with propofol-fentanyl and abnormal movement ($p = 0.01$) and excessive secretions ($p = 0.04$) with propofol-ketamine, there were high satisfaction rating by the surgeons and patients.

In this study Propofol-fentanyl combination showed a significant increase in respiratory depression, as ten (20%) patients developed apnoea compared to six (11%) patients in propofol-ketamine group after induction of anaesthesia.

This study reported an increased incidence of oral secretions, four patients (7%) in group K as compared to none in group F. This may be due to the salivary effect of ketamine.

Nausea was reported in three patients in group F compare to one patient in group K. This significant difference may be due to the central emetic effects of fentanyl [5,7]. In a related study Zeynep, et al. [4] reported 10% incidence of nausea among propofol-ketamine group and 11% incidence of nausea among propofol-fentanyl group. They also reported 15% incidence of vomiting among propofol-ketamine group and no incidence of vomiting among propofol-fentanyl group. But, as a whole, lower incidence of nausea and no incidence of vomiting when compared to 20 - 30% incidence of PONV where volatile anaesthesia was used.* The decreased incidence may be attributed to the antiemetic effect of propofol.* Propofol has been used successfully to treat postoperative nausea in a bolus dose of 10 mg and has been successfully used to treat refractory PONV [9].

Eleven patients (20%) in group K and ten patients (10%) in group F had abnormal movement during maintenance phase of anaesthesia ($p = 0.07$). This finding is similar to what was observed by Brajesh., et al. [10] who found the incidence of abnormal movement among propofol-ketamine and propofol-fentanyl groups to be 20% and 12% respectively. No patients had excitation postoperatively in both groups, and this can be explained on the basis of lower dosage of ketamine used (1 mg/kg) in this study [11].

The study was unable to establish a significant difference in satisfaction score in the two groups. All the fifty-four patients (100%) in group K and fifty-two patients (96%) in group F were satisfied with the anaesthetic technique used and described it as pleasant. These findings are consistent with the findings of Brajesh., et al. [10] where all the patients (100%) in the two groups were satisfied with the technique. These may be attributed to the good postoperative analgesia, decreased incidence of nausea and vomiting and absence of agitation. Fifty-one surgeons (94%) were satisfied with propofol-ketamine anaesthesia and fifty surgeons (93%) were satisfied with propofol-fentanyl anaesthesia and described it as good. In a previous study [11], in contrast with this study, Nalini., et al. [11] reported satisfactory surgical conditions with adequate muscle relaxation in 60% of patients in Propofol/Fentanyl group and in 90% of patients in Propofol/Ketamine group. In either group (30 patients each), the number of times bolus dose of propofol was administered was found to
be more in Propofol/Fentanyl group than in Propofol/Ketamine group (3 versus 1). This could be attributed to the complementary effects of propofol and ketamine, wherein propofol provides better muscle relaxation, while ketamine contributes towards superior analgesia, resulting in a balanced anaesthesia.

**Conclusion**

Although significant side effects were recorded in both groups’ i.e. apnoea and excessive salivation, the high satisfaction with the technique of anaesthesia by the patients and surgeons supports adoption of these techniques for day case surgery. The absence of hypotension and lower incidence of respiratory depression in propofol-ketamine group further suggest that propofol-ketamine combination could be a better choice in the hands of an anaesthetist for patients undergoing day case surgery.

**Recommendations**

It may be recommended that either propofol-ketamine or propofol-fentanyl can be used as an excellent combination in TIVA for day case surgery.

**Bibliography**