ORIGINAL ARTICLE

Recovery Time and Time of First Request for Postoperative Analgesia in Day-case Surgery: Propofol-Ketamine Vs Propofol-Fentanyl

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ABSTRACT

Background: The significance of recovery time and adequate postoperative analgesia for day case surgery has led to various trials of drug combinations in other to get the benefit of both early recovery with prolonged postoperative analgesia. Various intravenous analgesic agents in combination with propofol has been tried in an attempt at finding the ideal drug combination for short surgical procedures. **Objectives**: This study compared the recovery time and time of first request for postoperative analgesia of two drug combinations: propofol-ketamine and propofol-fentanyl used as the sole anaesthetic agents for short surgical procedures in adult's day case surgery. Methods: One hundred and eight adults aged 18 to 50 years of either gender with ASA physical status I or II scheduled for elective short surgical procedures 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. Recovery time was assessed using Steward Recovery Score. Postoperative analgesic requirement was assessed based on pain score using the Verbal Rating Scale. **Results**: Demographic and clinical characteristics such as age, sex, weight, duration of surgery and types of surgical procedures used were comparable between the two groups. Recovery time was prolonged in group K compared to group F (p=0.01). Time for first request of postoperative analgesia was found to be significantly shorter in group F (p=0.01). **Conclusion**: Both propofol-ketamine and propofol-fentanyl combinations produced effective postoperative analgesia and appreciable recovery time for daycase surgery. While Propofol-fentanyl has a shorter recovery time, Propofol-ketamine has a longer period of postoperative analgesia.

Keywords: Propofol, fentanyl, ketamine, postoperative, analgesia.

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Introduction

Total intravenous anaesthesia (TIVA) is the induction and maintenance of general anaesthesia using drugs administered by the intravenous route only.[1]

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 advantages in short surgical

procedures relates to its rapid elimination from the blood leading to rapid recovery from anaesthesia 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]

The short surgical procedure in this context refers to any surface surgery that is of 60 minutes' duration or less. These procedures cut across various specialties and ranges from circumcision, lumpectomy, closed reduction of fractures, herniorraphy, Examination under anaesthesia, ganglion removal, rectal biopsy, wound debridement, hydrocelectomies, colporrhaphy, incision and drainage of abscesses, radiological intervention etc.

This study, therefore seeks to compare recovery time and analgesic efficacy of propofol-ketamine vs propofol-fentanyl in patients undergoing short surgical procedures in Aminu Kano Teaching Hospital, Kano.

Materials and Methods

This was a prospective, randomized double-blind study conducted over a period of six months at Aminu Kano Teaching Hospital, Kano. Following ethical approval, 108 ASA 1 or 2 patients between the age of 18 – 50 years scheduled for elective surface surgical procedures not expected to exceed 60min and who consented to participate were enrolled into the study. Excluded from the study were patients with known allergy to any of the study drugs or constituents, patients on monoamine oxidase inhibitors, and those with history of jaundice or features of liver disease. Also excluded were pregnant women and psychiatric patients.

Sample size

The sample size was calculated using the formula for determining sample size in comparative studies

n = 48.6 patients per group

~ 49 patients per group

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

Study Protocol

Preoperative assessment including history, physical examination and review of results of relevant laboratory investigations was carried out a day before or on the day of the procedure, at this time necessary information was provided to every patient on the study and proposed technique of anaesthesia and informed consent was obtained. Patients were instructed to fast for at least 6 hours for solid food and 2 hours for clear liquid before the procedure. Demographic and clinical data that included patient's age as at the last birthday, sex, weight, diagnosis and type of surgery were recorded.

Randomization

One hundred and eight patients who consented to participate in the study were allocated randomly into two equal groups K (propofol/ketamine) and F

(propofol/fentanyl) by a senior registrar who was not involved in the evaluation and administration of anaesthesia to the patients. Both the investigating anaesthetist and the patient were blinded to the group allocated.

Study Procedure

Patients were weighed at the theatre reception by a research assistant. After positioning on the operating table, an intravenous line was set with size 16G or 18G cannulae on the dorsum of the hand 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 patient monitor.

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

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

Induction of anaesthesia in each of the two study group was achieved with a sleep dose of the drug combination after three minutes of pre-oxygenation with 100% oxygen. In both groups, the primary end point for induction was loss of verbal contact. Immediately after induction of anaesthesia, the vital signs of blood pressure was measured continually every 5 minutes while the pulse rate, respiratory rate and SpO2 were measured continuously but recorded 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 after induction of anaesthesia unless where oxygen saturation was observed to drop to 94% then oxygen supplement via facemask or nasal prong was administered. Where there was evidence of airway compromise, jaw thrust was applied to maintain the airway patency. Apnoea observed in some of these patients immediately on induction of anaesthesia was managed with Bag mask ventilation with 100% oxygen until patient regained spontaneous breathing. However, no patient was allowed to desaturate (SpO2 <94%) and no patient was intubated.

Maintenance of anaesthesia was achieved in both groups with an average of 0.4ml/kg/hr infusion of the study regimen using B Braun syringe pump. However, a bolus dose of 1-2 ml of the study regimen was administered when a patient showed sign of discomfort. 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 and the values obtained were recorded every 5 minutes.

Recovery from anaesthesia using Steward Recovery Score was assessed every 5 minutes until patient achieved a score of 6 and time at which this score was achieved is recorded. Postoperative pain assessment using the Verbal Rating Scale (no pain =0, mild =1,

moderate =2 and severe =3) was used after the patient had fully recovered and assessment continued every 15 minutes thereafter. Rescue analgesia with parenteral paracetamol 1g infusion was given for patients with VRS ≥ 2, or on the patient's request for pain medication.

Data Analysis

Data were collected using a structured data collection form. All results obtained were analyzed using statistical package for social science (SPSS) version 22.0 for windows. Values were expressed in numbers, means, standard deviations 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 value less than 0.05 was regarded as statistically significant.

RESULTS

A total of 108 patients took part in the study. No patient was dropped from the study, resulting in zero attrition rates. Therefore 108 subjects were included in the final analysis (propofol-ketamine group 54; propofol-fentanyl group 54)

Table I shows the demographic characteristics of the two study groups. There is no statistically significant difference with respect to ages, weight and sex 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 58.8kg (±9.7) in the propofol-ketamine (K) and 58.76kg (±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=0.68).

Table II showed the distribution and duration of surgical procedures. The types of surgical procedures were comparable between the two groups (P>0.05). 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 III showed the mean time for first request of postoperative analgesia. Time of first request for postoperative analgesia is the time from the end of Anaesthesia to the time the patient achieved a VRS pain score of ≥ 2 or on patient request for pain medication. The mean time for first request of post-operative analgesia was shorter in propofol-fentanyl group (F) 48.3(±5.9) minutes compared to propofol-ketamine group (K) 55.8(±5.9) minutes. The difference between the two groups was statistically significant (p=0.01).

Table IV showed the mean recovery time among the two groups. Recovery time is time from the end of Anaesthesia until patient attains a Steward Recovery Score of 6. The mean recovery time in propofol-ketamine group was (42.7±8.7) min, which was longer than the recovery time in propofol-fentanyl group (36.4±7.8) min and

Table I Demographic and clinical characteristic of group K and F

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

K; Propofol-ketamine F; Propofol-fentanyl

Table II. Distribution and duration of surgical procedures among group K and F

Types of surgery	K	F	Pvalue
Herniorraphy	7	5	0.16
Cystoscopy/EUA	12	13	0.32
Stent removal	11	13	0.16
excision of lipoma/ganglion	7	8	0.32
Closed reduction of fractures	3	2	0.32
Wound debridement	4	5	0.32
Circumcision	1	0	0.32
Others	8	9	0.32
Total	54	54	

K; Propofol-ketamine F; Propofol-fentanyl

Table III. Mean recovery time from anaesthesia

	K	F	P value
Recovery time (min)	42.7±8.7	36.4±7.8	0.01

K; Propofol-ketamine F; Propofol-fentanyl

Table IV. Mean time of first request for postoperative analgesia

	K	F	P value
Time of first request of postoperative analgesia (min)	55.8±5.9	48.3±5.9	0.01

K; Propofol-ketamine F; Propofol-fentanyl

Discussion

An ideal anaesthetic technique which is used for patients undergoing short surgical procedures, should provide adequate depth of anaesthesia, analgesia and ensure rapid recovery with good residual postoperative analgesia and minimal or no side effect.[1,24] This study showed that propofol-fentanyl and propofol-ketamine combinations provide safe and effective anaesthesia in adults undergoing short surgical procedures.

The addition of fentanyl and ketamine to propofol in this study was clinically relevant. Patients who received propofol-fentanyl as TIVA showed a significantly better recovery score profile than the propofol-ketamine group as measured by Steward Recovery Score (36.4minutes vs 42.7minutes; p=0.01). The analgesic efficacy of ketamine addition to propofol was observed in the propofol-ketamine group in which the time of request of postoperative analgesia was significantly prolonged (55.8minutes vs 48.3minutes; p=0.01).

Recovery time is the time from stoppage of all anaesthetic drugs to the time of achieving Steward Recovery score of 6. The difference in recovery time between the two groups observed in this study was statistically significant as patients in group F demonstrated a shorter recovery time compared to group K (42.7 vs 36.4 min: p=0.01). This is consistent with the findings of Brajesh et al[23] who compared propofol-ketamine and propofol-fentanyl for day case surgeries and found that recovery time in propofol-fentanyl group was significantly less than that of propofol-ketamine group (22.8 vs 20.2 min; p<0.05). Other researchers have, however reported contrasting findings.[4,22] Zeynep et al found no significant difference in recovery time between propofol-ketamine group and propofol- fentanyl group (4.5 vs 2.9min; p>0.05). The findings of early recovery which though was not significant between the two groups compared to this study could be attributed to the shorter duration of the procedures (10.9min vs 10.7min) in their series. And moreover the drugs were administered as boluses. Nalini et al[22] reported similar findings with that of Zeynep et al, they compared propofol-fentanyl and propofol-ketamine for patients undergoing puerperal sterilization and they reported that there was no statistically significant difference in recovery time between propofol-fentanyl group (8.3 min) vs propofol-ketamine group (9.7 min) (p>0.05). The prolonged recovery time observed in this study with propofol-ketamine group may be linked to the high volume of drug used during maintenance of anaesthesia (27.9ml vs 25.4ml; p=0.01).

The combination of propofol and fentanyl used in short surgical procedures is quite popular and is accepted widely.[25] Fentanyl provides adequate analgesia, which extends into the post-operative period, while minimally affecting the psychomotor functions.[1,2,25] Fentanyl has short duration of action (30 min) however following prolonged administration or with higher doses, its duration of action is significantly prolonged.[19]

In this study, the mean time for first request of postoperative analgesia was shorter in propofol-fentanyl group compared to propofol-ketamine group, which is statistically significant (48.3 vs 55.8 min; p=0.01). This could be due to the prolonged sedative effect of ketamine and not necessary the analgesic effect because the mode of pain assessment depend on the cognitive state of the patient. Similarly, Nalini et al[22] in a randomized controlled study of sixty patients undergoing puerperal sterilization anaesthetized with propofol-ketamine and

propofol-fentanyl, found that the mean time for first request of postoperative analgesia was shorter with propofol-fentanyl group compared to propofol-ketamine group. But Nalini et al reported that the time of first request for postoperative analgesia to be 4.4hr in propofol-fentanyl group and 5.2hr in propofol-ketamine group. This finding of prolonged ''time of first request for postoperative analgesia'' by Nalini et al could be explained by the addition of local infiltration with 1.5mg/Kg of plain bupivacaine at the site of surgery. Taheri et al[26] found that patients who received propofol-ketamine at induction of anaesthesia had shorter time to first request of postoperative analgesia compared to those induced with propofol-fentanyl (15 vs 30 min; $p<0.05$). They randomized 60 patients, ASA I and II undergoing adenotonsillectomy, in a double blind study, aged 3 – 12years and grouped them into group I and II. Group I received 0.5mg/kg of ketamine and propofol titrated till loss of verbal contact. Group II received fentanyl 1 mcg/kg and propofol for induction till loss of verbal contact. Both groups were intubated with atracurium and anaesthesia maintained on 1.2% isoflurane and 50% nitrous oxide in oxygen. The shorter time for first request of postoperative analgesia observed in propofol-ketamine group by Taheri et al,[26] may be as a result of low dose of ketamine (0.5mg/kg) used compared to this study where not only 2mg/kg was used at induction of anaesthesia, but ketamine infusion was continued till the end of anaesthesia. Also Taheri et al[26] conducted their study on children where differences in physiology may affect drug metabolism and elimination. A previous study[3] also reported similar findings with this study. Guit et al[3] found that fewer patients who received propofol and ketamine had required rescue doses of analgesics as compared to those who had received propofol and fentanyl. Kennedy et al[27] found that children on ketamine/midazolam had lower pain scores than those on fentanyl/midazolam in paediatric emergency room. The results in this study suggested that small doses of ketamine, an N-Methyl-D-Aspartate antagonist, may exert a prolonged antinociceptive effect in the postoperative period.

Conclusion

This study confirms that both propofol-fentanyl and propofol-ketamine combinations are ideal techniques for TIVA in patients undergoing short surgical procedures. Propofol-fentanyl has a shorter recovery time than propofol-ketamine which is significant. However, propofol-ketamine combination provided longer duration of postoperative pain relief.

Recommendations

It may be recommended that either propofol–ketamine or propofol–fentanyl can be used as an excellent combination in TIVA for elective short surgical procedures. Where postoperative pain is expected to be high, propofol-ketamine will be advantageous and where early recovery is of concern e.g. day case surgery; propofol-fentanyl is an option.

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