

Low-dose ketamine for supplement analgesia during minor day-case gynaecological surgery

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Background. Preemptive low-dose Ketamine IV has been found to reduce anaesthetic drugs requirement, exert an excellent analgesia and may therefore be a useful component of general anaesthesia. Meanwhile, these data in literature are interpreted with caution. **The aim** of this study was to evaluate the efficacy and safety of preventive low-dose Ketamine as an adjuvant in the multimodal total intravenous anaesthesia (TIVA).

Materials and methods. In this prospective study 40 women, ASA I-II, undergoing day-case minor gynaecological surgery, were enrolled. After premedication with Droperidol, Midazolam and Fentanyl in the study group (gr.), the patients (pts) received 0.2 mg/kg Ketamine (K gr., n = 20) and in the control gr. (C gr., n = 20) the patients received isotonic saline 30 sec before the induction of anaesthesia with Propofol. Anaesthesia was maintained with additional intermittent doses of Propofol, if required. The demand for a Propofol initial hypnotic dose and the requirement for additional intermittent doses, respiratory and cardiovascular reactions just after injection of drugs and during the perioperative period; times for response to verbal commands (early recovery) and for late recovery (physical capability), side-effects were registered perioperatively.

Results. The results demonstrate that K gr. required significantly less Propofol, necessary for sleep (48.25 ± 12.69 mg vs. 101.50 ± 16.94 mg in C gr. which was by 47% more; $t = 11.27$, $p = <0.001$) as well as the additional doses for maintainance. In K gr. respiratory depression and need for assisted ventilation was 3 times lower ($p = 0.02$). There was no significant difference in the haemodynamic values, emergence from anaesthesia and in discharge from hospital. Unharmful colorful vivid dreams were recorded in 3 pts after use of K. Early postoperative pain frequency was 50% less ($p = 0.01$).

Conclusions. Low-dose Ketamine is an effective and safe adjuvant in TIVA consisting of Midazolam, Fentanyl and Propofol for reducing the demand for hypnotics and analgesics, for preventing their side-effects and for performing adequate analgesia.

Key words: anaesthesia, low-dose ketamine, day-case surgery

INTRODUCTION

Drug combinations used for day-case surgery anaesthesia usually include short-acting preoperative anxiolytic, intravenous anaesthetics for induction and maintenance, moderate or short-acting opioids for analgesia. Fentanyl is the most popular one (1). Unfortunately, agents used in general anaesthesia can lead to respiratory depression and hypotension, especially if large doses are used for providing adequate analgesia. It was proved that preventive low-dose Ketamine can potentiate effects of hypnotics and opioids Fentanyl and Remifentanyl, reduce anaesthetic drugs requirement, promote patient's faster awakening and prevent side-effects of anaesthesia drugs. A single Ketamine dose during surgery reduced pain and opioid consumption (2–9). However, in literature the use of Ketamine for anaesthesia is controversial and conflicting (10–12). For this reason, the aim of this study was to evaluate the efficacy and safety of preventive low-dose Ketamine as an adjuvant in multimodal total intravenous anaesthesia (TIVA) in patients undergoing minor day-case gynaecological surgery.

MATERIALS AND METHODS

After the Ethics Committee approval and the written Informed Consent, in this prospective study 40 patients (pts), aged from 19 to 64, ASA I-II, scheduled for elective day-case gynaecological minor surgery involving cervix and uterus (e. g. cervical dilatation, curettage, polypectomy, biopsy), lasting for up to 20 minutes, were randomized to an intravenous subhypnotic dose of Ketamine or placebo (saline) 30 sec before injection of Propofol. Exclusion criteria were patients of ASA III or more, with a history of chronic pelvic pain, taking opioids, nonsteroidal antiinflammatory drugs, acetomenophen, psychotropic drugs, and had contraindications to Ketamine. Patients (pts) were divided into 2 groups (gr.) according to anaesthetic technique. After premedication with antiemetic butirophenon Droperidol 0.6 mg i/m, anxiolytic drug Midazolam 1 to 1.2 mg/70 kg i/v and opioid Fentanyl 100 mkg/70 kg i/v boluses, Ketamine gr. of pts (K gr., n = 20) received Ketamine 0.2 mg/kg 30 sec before Propofol injection. Placebo gr. or Control (C gr., n = 20) received the same volume of saline.

Basic anesthesia was provided with Propofol titrated to sleep – verbal contact and eye reflexes disappear. In all pts oxygen was supplied with a non-rebreathing mask reservoir system. The ventilation of pts was assisted with a bag and mask, if necessary. Respiratory rate (RR), oxygen saturation (SpO_2), heart rate (HR), noninvasive blood pressure (NIBP), ECG were registered preoperatively, after premedication and induction, during a traumatic episode and on awakening. The demand for a Propofol initial hypnotic dose and the requirement for additional intermittent doses, respiratory and cardiovascular reactions just after injection of drugs and during the perioperative period; times for response to verbal commands (early recovery) and for late recovery (physical capability), side-effects were registered. Bradipnea was defined as $RR < 6 \times 1$ min; hypoxia as $SpO_2 < 90\%$; hypotension as the systolic blood pressure (SBP) < 80 mm Hg, hypertention as $SBP > 170$ mm Hg; bradycardia as $HR < 50 \times 1$ min; tachycardia as $HR > 120 \times 1$ min. Patients satisfaction with anesthesia and hospitalization characteristics were controlled. For the discharge readiness the modified Aldrete scale was used (13). The type and duration of surgery were documented. Statistical analysis was performed with the Package for the Social Sciences (SPSS 14.0). For all statistical tests a value of $P < 0.05$ was taken as statistically significant.

RESULTS

The demographic and intraoperative characteristics did not differ between the groups. The age of K gr. pts was 40.60 ± 3.34 and the age of C gr. pts was 39.55 ± 11.31 , but the weight of K gr. pts was 68.80 ± 7.47 and the weight of C gr. pts was 71.70 ± 7.40 .

Requirement for Propofol. The average hypnotic dose of Propofol required for sleep and starting of surgery in the K gr. was 48.25 ± 12.69 mg, while in the C gr. it was 101.50 ± 16.94 mg, which was by 47% more ($t = 11.27$, $p = <0.001$). The requirement for the additional doses of Propofol in the most traumatic episodes was detected in the C gr. for 75% of pts, while in K gr. it was only for 45%, that was less by 1.66 times.

Vital functions. Respiratory reactions. In the K gr. bradipnea up to apnea and the need for assisted ventilation with O_2 was three times lower than

in the C gr. ($p = 0.02$). Hypoxic episodes were not seen in both groups.

Haemodynamic reactions. Bradycardia, more often seen after injection of Propofol in pts of C gr., did not need any treatment. There were no significant difference between the groups ($p > 0.05$). Severe tachycardia was not registered in both groups. Hypotensive reaction after the induction of Propofol was pronounced in C gr. (by $20 \pm 9\%$), but it was statistically insignificant. Changes in ECG during surgery were not recorded in both groups.

Emergence from anaesthesia. Early recovery time after injection of the last dose of Propofol did not differ significantly between the groups: in C gr. after 8.00 ± 2.36 min and in K gr. after 7.00 ± 2.36 min ($t = 1.41$, $p = 0.16$). The late recovery time (physical capability) was approximately similar: 11.65 ± 3.06 min for K gr. and 12.40 ± 2.28 min for C gr. ($t = 0.87$, $p = 0.38$). Early postoperative pain frequency in K gr. was 50% less in comparison with C gr. ($p = 0.01$). All 100% pts after waking up were satisfied, and they informed that felt no pain during surgery. In K gr. 3 patients after waking up reported about colorful, vivid dreams and were a bit euphoric. A harmful hallucinogenic effect of the Ketamine sub-hypnotic dose was not registered. All K gr. and C gr. pts fully met the criteria for assessing awakening and discharge from hospital 2–4 h later after surgery and anesthesia.

DISCUSSION

There are few data on combining subhypnotic Ketamine dose with Midazolam, Propofol and Fentanyl for perioperative anaesthetic management of minor and major operations that improve the quality of anaesthesia. Some authors concluded that addition of Ketamine for combined TIVA for day-case surgery remained unclear. Our study design was based on trials, that reported excellent analgesic effect of Ketamine and its properties to diminish antihyperalgesic effects of opioids and Propofol [14, 15, 16]. **The purpose of our study** was to investigate whether addition of Ketamine 0.2 mg/kg to TIVA consisting on Midazolam, Fentanyl and Propofol would decrease requirement for Propofol thus preventing its unfavorable respiratory and haemodynamic reactions. In our investigation, single low-dose Ketamine as an adjuvant in multimodal TIVA was shown to have advantages including superior

analgesia, reduced requirement for Propofol, absence of complicated respiratory, haemodynamic and psychomotor effects.

CONCLUSIONS

1. Ketamine when administered in the preventive subhypnotic single low-dose as an adjunct in multimodal TIVA in gynaecological day-case surgery appears to be an effective and safe agent for reducing the demand for propofol hypnotic doses and for performing adequate analgesia.

2. Ketamine predicts propofol induced haemodynamic fluctuations and does not affect other vital functions, reduces the frequency of the episodes of apnea, does not affect the recovery time and discharge time from hospital; prevents early post-operation pain and does not cause serious complications. It is associated with high patient satisfaction.

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MAŽŲ KETAMINO DOZIŲ SKYRIMAS PAPILDOMAI ANALGEZIJAI DIENOS CHIRURGIJOJE

Santrauka

Dienos chirurgijos anestezijoje dažniausiai skiriami trumpai veikiančios priešoperaciniai anksiolitikai, indukcijai skirti intraveniniai anestetikai ir analgeziją palaikantys vidutiniškai arba trumpai veikiančios opioidai. Pats populiariausias yra fentanilis. Deja, bendrai anestezijai naudojami preparatai gali sukelti hipotenziją, slopinti kvėpavimą, ypač jeigu adekvačiai analgezijai pasiekti naudojamos didelės dozės. Įrodyta, kad prevencinis mažų ketamino dozių vartojimas gali sustiprinti hipnotikų ir opioidų – fentanilio ir remifentanilio – poveikį, sumažinti anestezinių vaistų poreikį, skatinti greitesnę paciento atsibudimą ir apsaugoti nuo nepageidaujamo anestetikų poveikio. Viena ketamino dozė operacijos metu sumažina skausmą ir opioidų suvartojimą. Visgi ketamino naudojimas anestezijoje vertinamas kontroversiškai ir prieštaringai. Mūsų studijos tikslas buvo įvertinti mažų ketamino dozių, kaip adjuvanto multimodalinėje visiškoje intraveninėje anestezijoje (TIVA), veiksmingumą ir saugumą pacientams, kuriems atliekamos nedidelės dienos chirurgijos ginekologinės operacijos.

Raktažodžiai: anestezija, mažos ketamino dozės, dienos chirurgija