PETHEDINE IN COMBINATION WITH KETAMINE TO ABOLISH ITS POSTOPERATIVE HALLUCINATION EFFECT

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ABSTRACT

Background: Ketamine is a potent analgesic and sedative and its analgesic effect persists after its sedation effect[(2)], but still there is controversy about using ketamine as analgesic due to its psychomimetic adverse effects like hallucinations or nightmares

Objectives: the target is to evaluate the effect of pethedine in combination with ketamine to decrease post sedation side effects of ketamine like hallucinations

Patients and methods: 150 patients divided into 3 groups,group A 50 patients received ketamine by dose of 1mg/kg.group B patients received ketamine by same dose in combination with midazolam by dose of 0.05mg/kg and group C received ketamine by same dose with pethedine by dose of 0.5mg/kg.

Results: the postoperative hallucinations were significantly higher in group A (16 patients, 32%) compared with groups B and C. Also, hallucination was significantly higher in group B (7 patients, 14%) compared to group C (3 patients, 6%)

Conclusion: pethedine is better than midazolam to control postoperative hallucinations of ketamine when used in combination for sedation in minor operations

Keywords: ketamine,pethedine,midazolam,hallucinations.

INTRODUCTION

The ideal sedation is one that safely relieves pain, anxiety and unpleasant memories for a variety of procedures. Administration of subhypnotic doses of IV anesthetics during local or regional anesthesia is a common technique.

One of them is the combination of ketamine with midazolam which is termed dissociative sedation[(1)].

Ketamine is a potent analgesic, and its analgesic effect continues after its sedative effect being disappeared[(2)].

The identification of N-Methyl-D-Aspartate (NMDA) receptor and its role in pain perception has brought a new interest to ketamine to be used as analgesic for postoperative pain management.[(3)].

Ketamine when used as a sole analgesic by high doses > 0.5 mg/kg is stimulating and is shown to resemble the dysphoric symptoms of psychosis as in schizophrenia[(4)].

Thus, there is controversy about using ketamine in this setting for analgesia and sedation due to the fear of psychomimetic adverse effects such as hallucinations or nightmares[(3)].

The combination of ketamine and a benzodiazepines, often midazolam is frequently used for sedation.

Midazolam is thought to reduce the adverse effects especially hallucinations of ketamine, but there are few objectives; data to confirm this benefit[(5)].

Many other sedatives can be used for sedation as chloral hydrate, intramuscular narcotics, and phenothiazines, but they are largely ineffective with prolonged recovery time[(6)].

Intravenous agents such as propofol generally require anesthesiology support due to respiratory depression that may be in need for endotracheal intubation[(7)].

So, the need for combination of two sedatives like ketamine and midazolam for children needing painful procedure in emergency situations[(8)].

Midazolam is a benzodiazepine. It has the advantages of rapid onset of action from one to five minutes with duration of action from one to two hours when given by intravenous route. Midazolam produces retrograde and antegrade amnesia. Midazolam in large dose causes respiratory depression which can be reversed by flumazenil[(9)].

Pethidine is a synthetic narcotic. It is commonly used as a pre-medication for painful procedures or as a treatment for postoperative pain. Pethedine produces prompt but short-lasting analgesia which lasts for three to four hours. Pethedine in overdose causes respiratory depression reversed by naloxone[10].

The target of our work is to evaluate the effect of combination of pethedine with ketamine for sedation in minor surgical procedures and to compare the postoperative hallucinations of ketamine when combined with midazolam and with pethedine.

PATIENTS AND METHODS

Patients:

150 patients undergo minor surgical operations under sedation only like abscesses, wound debridement, wound suturing, patient with appendectomy under spinal anesthesia nd in need for sedation. All patients between 12 and 60 years old. Patients are divided into three groups:

Group A: 50 patients undergo minor surgical procedures and will receive only ketamine by IV route by a dose of 1 mg/kg.

Group B: 50 patietns undergo same types of surgical procedures and will receive ketamine by same dose (1 mg/kg) followed by midazolam by a dose of 0.05 mg with maximum dose of 2.5 mg IV.

Group C: 50 patients undergo same types of surgical procedures and will receive ketamine by same dose (1 mg/kg) IV followed by pethedine by a dose of 0.5 mg/kg with maximum dose of 25 mg IV.

Method:

All patients are scheduled for minor surgical procedures as skin abscesses, wound debridement and dressing under sedation, a wound suturing under sedation is added to patients under spinal anesthesia like appendectomy and feeling peritoneal traction pain and in need for sedation.

All patients for three groups were monitored for O_2 saturation, blood pressure and heart rate, also intraoperative airway obstruction and patients in need for opening the airway by jaw thrust or using oral airway, also number of patients who suffered intraoperative vomiting and received metoclopramide ampoule by IV route.

Postoperative and in the recovery room, patients were monitored for heart rate, blood pressure and O_2 saturation added to estimation of:

- Post-sedation recovery time.
- Postoperative hallucinations.
- Postoperative vomiting.

Statistical analysis:

Statistical data are done by student t-test, the results are compared as percentage and mean ± standard deviation.

RESULTS

Table (1) showed the patient characteristic and demographic data with no statistically significant results according to age, sex, types and numbers of the operations.

Table (2) showed the intraoperative parameters with significant changes in heart rate in group A (120 ± 8 beats per minute) compared with group B (98 ± 5 beats per minute) and group C (96 ± 7 beats per minute).

Systolic blood pressure was higher in group A (130 ± 15 mmHg) compared with group B (110 ± 15 mmHg) and group C (110 ± 12 mmHg).

Also, diastolic blood pressure was higher in group A receiving ketamine only (78 ± 8 mmHg) compared with group B (60 ± 10 mmHg) and group C (60 ± 8 mmHg).

The number of patients having airway obstruction during operation was higher in group B (8 patients receiving ketamine and midazolam, 16%) compared to the other two groups.

Group A had higher patients suffering intraoperative vomiting (8 patients, 16%) compared with 3 patients (6%) in group B and only two patients (4%) in group C.

Table (3) showed the postoperative hallucinations which were significantly higher in group A (16 patients, 32%) compared with groups B and C. Also, hallucination was significantly higher in group B (7 patients, 14%) compared to group C (3 patients, 6%).

Recovery time for sedation was longer in patients receiving ketamine with midazolam (group B) (22 ± 2.5 minutes) and patients receiving ketamine with pethedine (group C) (21 ± 3.5 minutes) compared with group A patients who received only ketamine (15 ± 2 minutes).

The incidence of postoperative vomiting showed no significant difference between patients in all groups.

Table (1): Patient characteristics and demographic data

Character	Group A	Group B	Group C
Age	35 ± 12	34 ± 10	34 ± 11
Sex (M/F)	35/15	34/16	36/14
Types of operations	35 ± 6	34 ± 8	
Appendectomy	20	20	20
Abscesses	15	14	15
Dependent	6	7	7
Suturing	9	9	8

Table (2): Intraoperative monitoring

	Group A	Group B	Group C
H.R	120 ± 8	98 ± 5	96 ± 7
Systolic blood pressure	130 ± 15	110 ± 15	110 ± 12
Diastolic blood pressure	78 ± 8	60 ± 10	60 ± 8
O_2 saturation	98 ± 2	97 ± 1	97 ± 2
Obstructed patients	0 (0%)	8 (16%)	2 (4%)
Intra operative vomiting	8 (16%)	3 (6%)	2 (4%)

Table (3): Postoperative monitoring

	Group A	Group B	Group C
Hallucination	16 (32%)	7 (14%)	3 (6%)
Recovery time (minutes)	15 ± 2	22 ± 2.5	21 ± 3.5
Vomiting	2 (4%)	3 (6%)	3 (6%)

DISCUSSION

Ketamine is a potent analgesic and sedative and its analgesic effect persists after its sedation effect[(2)], but still there is controversy about using ketamine as analgesic due to its psychomimetic adverse effects like hallucinations or nightmares. So, the need for combination with midazolam or pethedine[(3)].

In our study, there was high statistically difference in intraperative monitoring including heart rate which was higher in patients receiving ketamine along without combination (120 ± 8 beats/minute) compared to patients receiving ketamine with midazolam (98 ± 5 minutes) and with pethedine (96 ± 7). Also, systolic blood pressure was higher in the first group (130 ± 15 mmHg) compared with midazolam and pethedine groups (110 ± 15 minutes, and 110 ± 12 mmHg) respectively.

Also, diastolic blood pressure was higher in ketamine group (98 ± 2 mmHg) compared with midazolam (60 ± 10 mmHg) and pethedine group (60 ± 8 mmHg). 8 patients (16%) in patients receiving midazolam suffering airway obstruction and were in need for anesthetic support by jaw thrust and insertion of oral airway which was

statistically higher compared to 0 in ketamine and 2 patients in pethedine groups.

2 patients (4%) in patients who received pethedine with ketamine suffered intraoperative nausea and vomiting and received metoclopramide, compared to 3 patients in midazolam with ketamine patients which were less compared to 8 patients (16%) in patients receiving ketamine only.

The incidence of postoperative hallucinations was statistically lower in patients receiving ketamine with pethedine (3, 6%) compared to patients receiving ketamine and midazolam and ketamine alone (7 "14%" and 16 "32%" respectively).

Recovery time was short in patients receiving ketamine without combination (15 ± 2 min) compared to 22 ± 2.5 min in patients receiving midazolam with ketamine and 21 ± 3.5 min in patients receiving ketamine with pethedine.

Robert et al.[11] supported the use of intravenous midazolam with ketamine as sedation for therapeutic and diagnostic procedures in children to produce dissociative sedation, and all patients were effectively sedated with his regimen, and four patients experienced transient decrease in oxygen saturation (< 85%) requiring interruption of the surgical procedure.

Wathern et al.[5] in the double randomized study questioned, if midazolam alters the clinical effects of intravenous ketamine sedation in children. They said that midazolam by a dose of 0.1 mg/kg is the lower limit of the general anesthetic induction dose, no doubt accounting for the respiratory depression, also they concluded that in the absence of clear benefit, a lower dose of midazolam or none at all seems to be appropriate for sedation in children with ketamine.

Yeung et al.[10] supported the use of pethedine by a dose of 0.52 mg/kg alone or in combination with midazolam or ketamine for sedation for renal biopsies in children.

CONCLUSION

Pethedine can be used safely in combination with ketamine to produce sedation for minor operations and was better than midazolam to control postoperative hallucination of ketamine.

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استخدام البيتيدين مع الكيتامين في الغاء الهلوسة التي تحدث بعد العملية

الخلفية: يعتبر الكيتامين مخدر ومسكن قوي وتاثيرة كمسكن يبقي بعد زوال تاثيرة كمخدر ولكن مازال هناك جدل حول استخدام الكيتامين كمسكن نتيجة لاعراضة مثل الهلوسة والكوابيس.

الهدف: تقييم تاثير البيتدين عند استخدامة مع الكيتامين في السيطرة علي اعراضة الجانبية بعد التخدير مثل الهلوسة والكوابيس.

المرضي والطرق: ١٥٠ مريضا مقسمة الي ثلاث مجموعات:مجموعة أ مكونة من ٥٠ مريض وتم اعطاؤهم كيتامين بجرعة ١مجم لكل كجم. ومجموعة ب مكونة من ٥٠ مريض وتم اعطاؤهم كيتامين بنفس الجرعة بالاضافة الي ميدازولام بجرعة ٥.،مجم لكل كجم.

ومجموعة ج مكونة من ٥٠ مريض تم اعطاؤهم كيتامين بنفس الجرعة بالاضافة الي بيتيدين

بجرعة ٥،مجم لكل كجم.

النتائج: الهلوسة بعد العملية كانت اعلي في مجموعة أ ١٦ مريض بنسبة ٣٢% مقارنة بمجموعة ب و مجموعة ج.وفى مجموعة ب كانت ٧ مرضي بنسبة ١٤% وهي اعلي من مجموعة ج ٣ مرضي بنسبة ٦%.

الخلاصة:يعتبر البيتيدين افضل من الميدازولام في الغاء الهلوسة التي تحدث بعد العملية الجراحية عند استخدام الكيتامين.