The induction dose of Propofol, while using either Ketamine or Midazolam as co-induction agent

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Abstract

The drug-induced state of general anesthesia prevents patients from being awakened even by painful overstimulation. Depressed spontaneously respiration or drug-induced decrease of muscle control may necessitate the ability to autonomously maintain a patent airway and positive pressure breathing. Aim of study: To compare the induction dose of propofol, while using either ketamine or midazolam as co induction agent. This prospective study was conducted in "Baghdad Teaching Hospital" from 3rd (October) 2020-20th (April) 2021. Forty patients were enrolled in this study. The patients were randomly collected and divided in two groups according to drug combination they received, group A and group B comprising 20 patients for each. The patients of group A were given ketamine (0.5mg/kg) and group B patient's midazolam (0.03 mg/kg) of midazolam were preparedas co-induction agent for propofol. Induction of anesthesia performed with sleeping dose of propofol which were recorded for each patient. After induction of anesthesia intubation done with the aid of non-depolarizing muscle relaxant Intermediate-acting (Atracurium or Rocuronium with different dose). All continuous variables i.e. patient's hemodynamic responses (Pulse rate, systolic and diastolic blood pressure), time of sleepiness and dose of propofol was presented by mean ± standard deviation (SD). P value off <0.05 was considered statistically significant.

In this study we found a minimally dissmilarities in induction dosage of propofol between G.A and G.B was (0.1 mg) with a (p-value 0.5). We encompass patients of male and female and property to ASA-I and ASA-II physical status. They found mean induction dosage of propofol of (1.2 mg/kg) with ketamine propofol group and (1.4 mg/kg) with midazolam propofol group. Only The difference between the two groups only 7%. The difference in this study in the mean induction dosage of propofol not statistically significant (P-value 0.5). Depended on results of study, we can conclude that is not dissmilarities in the mean induction dosage of ketamine-propofol and midazolam-propofol co-induction.

Keywords: *Propofol, Midazolam, ketamine, Hemodynamics.*

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الجرعة البدائية التخديرية للبروبوفول، مع استخدام إما الكيتامين أوالميدازولام كدواء مساعد للبروبوفول

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الخلاصة

التخدير العام هو تثبيط للوعي بسبب الأدوية لا يكون المريض خلاله مستيقظًا ، حتى عن طريق التحفيز المؤلم. قد تكون هناك حاجة إلى القدرة على الحفاظ بشكل مستقل على مسالك الهواء والتهوية بجهاز التهوية الاصطناعي بسبب تثبيط التهوية الذاتية المنخفضة أو بسبب تثبيط الوظيفة العصبية العضلية التي يسببها الدواء. هدفت الدراسة لمقارنة الجرعة البدائية من البروبوفول، أثناء استخدام إما الكيتامين أو الميدازولام كدواء مساعد. أجريت هذه الدراسة في "مستشفى بغداد التعليمي" في الفترة من 3 (أكتوبر) 2020 إلى 20 (أبريل) 2021. تم جمع أربعين مريضًا في هذه الدراسة و بشكل عشوائي وتقسيمهم إلى مجموعتين وفقًا لتركيبة الأدوية التي تلقوها، المجموعة A والمجموعة B تضم 20 مريضًا لكل منهما. تم إعطاء مرضى المجموعة A الكيتامين وبجرعة (0.5 ملجم / كجم) وتم اعطاء الميدازولام للمرضى من المجموعة B وبجرعة (0.03 ملجم / كجم) وكدواء مساعد للبروبوفول. بداية اعطاء التخدير مع جرعة النوم من البروبوفول والتي تم تسجيلها لكل مريض. بعد اعطاء التخدير نقوم بادخال الانبوب الرغامي، يتم هذا الإجراء بمساعدة مرخي عضلي غيرمزيل للاستقطاب متوسط المفعول (أتراكوريوم أو روكورونيوم وبجرعات مختلفة). تم جمع جميع المتغيرات المستمرة أي استجابات الدورة الدموية للمريض (معدل النبض وضغط الدم الانقباضي والانبساطي) ووقت النعاس وجرعة البروبوفول بمتوسط الانحراف المعياري .(SD) قيمة0.05> وكانت النتائج في هذه الدراسة فيها اختلافًا طفيفًا في جرعات بداية اعطاء التخدير مع البروبوفول بين GA و GB والذي كان (0.1 مجم) مع (قيمة p 0.5) قمنا بتضمين المرضى من كلا الجنسين والذين ينتمون إلى الحالة الجسدية ASA-I و ASA-II. وجدوا متوسط جرعة بداية اعطاء التخدير مع البروبوفول (1.2 مجم / كجم) في مجموعة الكيتامين بروبوفول و (1.4 مجم / كجم) في مجموعة ميدازولام بروبوفول. كان هناك فرق 7٪ فقط بين المجموعتين. في هذه الدراسة لم يكن الاختلاف ذوقيمة في متوسط جرعة بداية اعطاء التخديرمع البروبوفول ذات دلالة إحصائية (قيمة.P0.5) اعتمادًا على نتائج هذه الدراسة ، يمكننا أن نستنتج أنه لا يوجد فرق في متوسط جرعة بداية اعطاء التخدير مع كيتامين-بروبوفول وميدازولام-بروبوفول.

الكلمات المفتاحية: *بروبوفول , ميدازولام, كيتامين, ديناميكية الدم.*

1. Introduction

Propofol may inhibit neurotransmission mediated by Gamma aminobutyric acidreceptor (GABA A) binding. The interaction affinity of GABA for the GABA A receptor is increased allosterically. The neuronal membrane becomes hyperpolarized when this receptor which is connected to a chloride channel is activated. The intravenous (IV) induction anesthetic drug is frequently utilized. In healthy individuals, amount of the induction with propofol ranges from 1.5 to 2.5 mg/kg, depending on concurrent drugs (such as opiate analgesics), the age of patient and condition of physical, surgical excitation degree [1]. It starts working within between 15 and 45

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seconds and lasts for up to 10 minutes [2]. As a result of decreased preload, cardiac contractility, and systemic vascular resistance, it lowers arterial blood pressure [1].

The use of two or more medications to induce anaesthesia has been referred to as "co-induction of anaesthesia." Anaesthetists currently use pharmacological interactions, notably synergism, between midazolam, fentanyl, sufentanil, alfentanil, and propofol to induce deliberate co-induction of anesthesia. All stages of anesthesia, including induction, maintenance, and recovery, can benefit from it A benzodiazepine called midazolam promotes chloride ion conduction through the Gamma aminobutyric acid (GABA) receptor [3]. Premedication sedation, anxiolysis, induction, and anaesthesia co- induction are all things it is used [4]. With propofol, midazolam become utilized as a co-induction agent. Combining midazolam and propofol has benefits, including lowering the amount of propofol and, thus, the risk of adverse reactions and expense [5]. The extreme bradycardia that can occasionally occur when using propofol and opioids together is less likely with a lower propofol dose, but this can be avoided with vagolytic drugs [4].

Ketamine is an antagonist of the N-methyl D-aspartate (NMDA) receptor and causes dissociative anesthesia. Ketamine raises blood pressure, heart rate, and cardiac output more than other anesthetic drugs do. In people complain coronary arteries diseases, unstable hypertensive, congestive heart failure, elevated intracranial pressure (ICP), and aneurysms of arterial, it should be avoided [5]. Its effects frequently combine with those of other medicines [6]. An essential approach, especially in the treatment of seriously ill patients, is the mixing of ketamine with propofol or midazolam with propofol.

2. Patients and Methods

This study was conducted in “Baghdad Teaching Hospital” during 2021-2022. A totaled of forty patients with American Society of Anaesthesiologist (ASA) status of physical I and II, aged from 20-50 years of either sex, who were scheduled for general surgeries, were selected. Patients with a history of narcotic addiction, hepatic or renal disease, convulsions, hypertension, convulsions, or other psychiatric disorders were excluded from the study. Patients with fentanyl, propofol, or ketamine hypersensitivity were also disqualified from the trial. ECG (continuous), heart rate, non invasive blood pressure, and oxygen saturation were all monitored during surgery. Before the suggested time of operation, all patients were instructed to fast for 8 hours.

The patients were randomly collected and divided in two groups according to drug combination they received, group A and group B comprising 20 patients each. The patients of group A were given ketamine (0.5mg/kg) and group B patients midazolam (0.03 mg/kg) of midazolam were prepared as

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Co-induction agent for propofol. Induction of anesthesia performed with sleeping dose of propofol which were recorded for each patient depended on eyelash reflex, corneal reflex, respiratory depression. After induction of anesthesia intubation done with the aid of non-depolarizing muscle relaxant Intermediate-acting (Atracurium or Rocuronium with different dose).

Endotracheal tube inserted with direct laryngoscopy and was maintained with inhalation agent (halothane) in O_2. The parameters recorded were systolic and diastolic blood pressure, pulse rate at pre and post induction. The Endotracheal tube was removed and patient was extubated at completion of surgery and given postoperative oxygenation by the facemask.

3.Result

Table (1): Distribution of patients according to propofol drug given, statistical analysis and relevant data related for dose of propofol (mg/kg), Time of sleepiness (sec.), for both groups (GA) and (GB).

Parameter	G.A (20) Mean ± Std. Deviation	G.B (20) Mean ± Std. Deviation	P-value
Dose of propofol	1.5± 0.2	1.6± 0.23	0.5 NS
Time of sleepiness (sec.)	27.5± 7.52	28.7± 6.94	0.4 NS

*NS=Non significant, P value off <0.05

In table 1 show distribution of dose of propofol (mg/kg), and time of sleepiness (sec.), for both groups (GA) and (GB). The mean induction dosage of propofol was (1.5) mg/kg with group A patients with mean of time of sleepiness was (27.5) in group A, while the induction mean dosage of propofol was (1.6) mg/kg with group B patients with mean of time of sleepiness was (28.7) in group B. The difference between mean inductions doses of propofol were statistically no significant (P-value of 0.5) and for time of sleepiness (0.4) between two groups.

Table (2): Distribution of Group A according to pulse rate

No.	Pulse Rate	Mean ± Std. Deviation	Range
1	Pre-induction.	99±17.58	(70-130)
2	Post-induction.	109± 17.24	(71-156)

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In table 2 show distribution of Group A according to pulse rate**,** in the pre-induction the pulse rate range (70-130) with Mean ± Std. Deviation (99±17.58) while**,** post-induction the pulse rate range (71-156) with Mean ± Std. Deviation (109± 17.24).

Table (3): Distribution of Group A according to Blood Pressure.

Group A				
No.	**Blood Pressure**		**Mean ± Std. Deviation**	**Range**
1	Pre-induction.	Systolic	117±14.55	(84-147)
		Diastolic	70±14.55	(61-100)
2	Post-induction.	Systolic	129±14.64	(113-158)
		Diastolic	80±10.73	(60-99)

Table 3 observed in group A, that the Blood Pressure in Pre-inductionthe Systolic (84-147) with Mean ± Std. Deviation (117±14.55) while the Diastolic (61-100) with Mean ± Std. Deviation (70±14.55), Blood Pressure Post-Induction Systolic (113-158) with Mean ± Std. Deviation (129±14.64) Diastolic (60-99) with Mean ± Std. Deviation 80±10.7.

Table (**4**)**:** Distribution of Group B according to Pulse Rate.

Group B			
No.	**Pulse Rate**	**Mean ± Std. Deviation**	**Range**
1	Pre-induction.	95±4.82	(88-104)
2	Post-induction.	115±8.23	(112-130)

In table 4 show distribution of Group B according to pulse rate**,** in the pre-induction the pulse rate range (88-104) with Mean ± Std. Deviation (95±4.82) while**,** post-induction the pulse rate range (112-130) with Mean ± Std. Deviation (115±8.23).

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Table(5): Distribution of Group B. according to gender Blood Pressure.

Group B.				
No.	**Blood Pressure**		**Mean ± Std. Deviation**	**Range**
1	Pre-induction.	Systolic	121±6.75	(100-130)
		Diastolic	83±5.08	(76-87)
2	Post-induction.	Systolic	112±4.96	(100-118)
		Diastolic	76±4.37	(70-85)

Table 5 observed in group B, that the Blood Pressure in Pre-inductionthe Systolic (100-130) withMean ± Std. Deviation (121±6.75) while the Diastolic (76-87) with Mean ± Std. Deviation (83±5.08), Blood Pressure Post-induction Systolic (100-118) with Mean ± Std. Deviation (112±4.96) Diastolic (70-85) with Mean ± Std. Deviation (76±4.37).

4. Discussion

The induction dosage of propofol combined with ketamine or midazolam was determined. These substances served as co-inducers. Each of these medications has been applied as a general anesthesia induction agent in accordance with recommended dosages. When used alone at its anesthetic dosages, each of these medications has certain side effects.

Co-induction is the process of bringing on general anesthesia by combining two sedatives or anesthetics. Goal is to utilize a lower dose of the induction agent in order to reduce the possibility of drug- related negative effected. Primary goals method to decrease price the expensive medications like propofol and to increase the ratio of desirable to unwanted effects [7-9]. In our investigation, a specific amount of sedation was achieved and propofol side effects were avoided by administering a mixture of two medications. When administered alone, the median induction dosage of propofol 1.5 – 2.5 mg/kg [10-12]. In one trial, cressey discovered that midazolam 0.025 mg/kg pre-treatment resulted in a significant decrease in the amount of propofol that was needed per kilogram in the older and younger age groups when comparative to placebo ($p < 0.01$ in both cases) [13-15].

Although we did not include the propofol alone group, we discovered that the induction dosage of propofol lower with both the G.A. and G.B. groups compared to the suggested induction dosage.

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With a P-value of 0.5, the variation mean induction dosage of propofol between two groups was statistically insignificant.

Our goal was to compare mean induction dosage propofol were administered with midazolam or ketamine and discover whether co-induction drug was more effective at lowering the induction dose of propofol. Propofol's side effects have been demonstrated to be inversely proportional to the dosage [16-18]. A 0.1 mg difference in induction dosages of propofol between G.A. and G.B. was discovered in our study, a p-value of 0.5. Patients of male and female and with ASA-I and ASA-II physical state were included. When comparing our research with that of Srivastava [8], they discovered that the average induction dosage of propofol was (1.2 mg/kg) for the midazolam propofol groups, (1.4 mg/kg) for the ketamine propofol group. The difference among the two groups was only 7%. In our investigation, no statistically significant differences the average induction propofol dosage (P-value 0.5). The small predicted sample size may be one cause of this negligible discrepancy.Hemodynamic parameters were also contrasted intraoperatively at precise time intervals before and after induction. The mean arterial blood pressure in group A postoperatively increased only slightly, whereas the mean arterial blood pressure in group GB decreased just slightly. The average pulse rate increased in both of the groups.

5. Conclusion

Based on the findings of this study, we conclude that the mean induction doses of ketamine-propofol and midazolam-propofol co-induction are identical.

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