A Comparative Study of Ketofol and Thiopental Sodium in Patients undergoing Dilation and Curettage by General Anesthesia

Un estudio comparativo de Ketofol y sodio tiopental en pacientes sometidos a dilatación y curetaje por anestesia general

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Abstract

Considering that the combined drug, Ketofol has been used and its efficacy observed in patients, we have aimed to compare the effects of ketofol and thiopental sodium on patients who are undergoing dilatation and curettage. This study was conducted as a randomized controlled clinical trial. In this study, 150 patients undergoing dilatation and curettage after classification were randomly selected and enrolled. The first group received ketofol, while thiopental sodium was administered to the second group. Any change in hemodynamics or respiratory distress, including the occurrence of apnea or hypotension, desaturation and the need for respiratory support were recorded in both groups. Finally, after the completion of the surgery and transfer to the recovery room, the recovery rate of each group was recorded, and once they were conscious and alert, were questioned about their satisfaction. All of the patient information was entered into the SPSS v18 software, and the data were analyzed. This study was conducted on 150 patients undergoing curettage; the mean ages in the first and second groups were 31.82 ± 9.18 and 33.64 ± 11.39 years, respectively. Ninety two percent of patients in the ketofol group and 100% of the patients in the thiopental sodium group experienced apnea and needed respiratory support. About 25.3% of patients in the ketofol group and 44% of patients in the thiopental group required a re-dose of the drug for the anesthetic process. The duration of recovery in the ketofol group was lower than the other group. About 2.7% of the patients in the ketofol group and 12% of the patients in the thiopental group had hallucinations and delusions at the end of the operation Six patients in the thiopental group also had hiccups. The results of the present study showed that ketofol is a better drug than thiopental because of the duration of anesthesia, reducing the need for medication, the incidence of apnea, and the complications of anesthesia

Keywords: General anesthesia, Ketofol, Thiopental sodium, Dilatation, Curettage

Resumen

Teniendo en cuenta que el fármaco combinado, Ketofol se ha utilizado y su eficacia se ha observado en pacientes, el objetivo fue comparar los efectos del ketofol y el sodio tiopental en pacientes que están en proceso de dilatación y legrado. Este estudio se realizó como un ensayo clínico aleatorizado controlado. En este estudio, 150 pacientes sometidos a dilatación y legrado después de la clasificación fueron seleccionados al azar y se inscribieron. El primer grupo recibió ketofol, mientras que el tiopental sódico se administró al segundo grupo. Cualquier cambio en la hemodinámica o dificultad respiratoria, incluida la aparición de apnea o hipotensión, la desaturación y la necesidad de asistencia respiratoria se registraron en ambos grupos. Finalmente, después de la finalización de la cirugía y el traslado a la sala de recuperación, se registró la tasa de recuperación de cada grupo, y una vez que estuvieron conscientes y alertas, se les preguntó acerca de su satisfacción. Toda la información del paciente se ingresó en el software SPSS v18 y los datos se analizaron. Este estudio se realizó en 150 pacientes sometidos a curetaje; Las edades medias en el primer y segundo grupo fueron 31.82 ± 9.18 y 33.64 ± 11.39 años, respectivamente. Noventa y dos por ciento de los pacientes en el grupo de ketofol y el 100% de los pacientes en el grupo de sodio tiopental experimentaron apnea y necesitaron asistencia respiratoria. Alrededor del 25,3% de los pacientes en el grupo de ketofol y el 44% de los pacientes en el grupo de tiopental requirieron una nueva dosis del fármaco para el proceso anestésico. La duración de la recuperación en el grupo de ketofol fue menor que en el otro grupo. Alrededor del 2,7% de los pacientes en el grupo de ketofol y el 12% de los pacientes en el grupo de tiopental tuvieron alucinaciones y delirios al final de la operación Seis pacientes en el grupo de tiopental también tuvieron hipo. Los resultados del presente estudio mostraron que el ketofol es un fármaco mejor que el tiopental debido a la duración de la anestesia, lo que reduce la necesidad de medicación, la incidencia de apnea y las complicaciones de la anestesia.

Palabras clave: Anestesia general, Ketofol, Thiopental sodium, Dilatación, Curetaje.

Introduction

About 211 million pregnancies occur annually all over the world, of which, 46 million lead to abortion[1]. Common abortion therapies include pharmaceutical and mechanical therapies.

Dilatation and curettage (D & C) is one of the mechanical methods used for abortion. In this operation, opening the cervix or dilatation is far more painful than curettage[2].The anesthetic method for this operation can be general (GA) or regional, GA is the most common anesthetic approach based on the surgeon and patients' wish. Because bleeding is common in this operation, maintaining the hemodynamic during anesthesia is very important. The duration of the stay in the hospital is often short, and the patient can be discharged if they do not develop any complications[3]. So, it's best to use a method to get the patient to wake up and recover faster. Therefore, the choice type of drug in the general anesthesia should be carefully investigated and the best medicine be chosen[4]. Thiopental induces anesthesia by bonding to the position of ionophore chloride in the Gaba aminobutiric acid receptor (GABA) and inhibiting this receptor about 30 seconds after injection. It has no analgesic effect, but its effect on the cardiovascular system and the reduction of vascular resistance leads to hypotension and sometimes, reflex tachycardia[5]. Propofol is a drug with rapid onset and hepatic clearance after intravenous administration. It has direct antinociceptive effects but no analgesic effect. On the other hand, Ketamine acts on the NMDA via antagonistic effects, which increases the systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). Ketamine has dose-dependent effects of inaccuracy and analgesia[6]. Ketofol is a combination of two drugs (propofol and ketamine) and is used in anesthesia.

Considering that ketofol and its efficacy has been observed among patients, we have aimed to compare the effects of ketofol and thiopental sodium on the patients undergoing dilation and curettage.

Materials and methods

This study was approved by ethical committee of Ardabil University of medical sciences (1395.88) and written informed consent was obtained from all subjects, a legal surrogate, or the requirement for written informed consent was waived by ethical committee. The clinical trial with the IRCT2017031923559N9 code (Somaiyeh Matin, 2017.4.24) was registered before patient enrollment authors. This randomized controlled clinical trial was conducted before on patients with missed or incomplete abortion undergoing dilatation and curettage. In this study, 150 patients aged over 16 years and candidates for dilation and curettage with ASA class 1 and 2 were enrolled after obtaining informed consent. Patients with a history of susceptibility to propofol and other intravenous anesthetic drugs, patients with substance abuse, alcohol and psychotropic drugs, as well as patients with gastrointestinal ulcers, kidney disease or hypertension, and hypertension, osteopenia and osteoporosis, and uncontrolled hypertension were excluded. The patients were randomly classified into two groups and placed in two blocks.

A and B. Group A or Group 1 were the ketofol group and group B or Group 2 were the thiopental sodium group. The preparation of the drugs was carried out by the anesthesia nurses, and after delivery of the syringes, they were covered with a white label. The drugs were administered by an anesthesiologist who did not know the drug content. In both groups, the patients in the operating room underwent cardiopulmonary monitoring. Then, the appropriate intravenous route was established, and the patients were hydrated, and received oxygen by facemask. Midazolam 0.05 mg / kg, fentanyl 1 µg / kg, and lidocaine 1 mg / kg for each patient were administered.

Subsequently, the first group received ketofol (which was mixed with 2: 1 propofol and ketamine in a syringe), and the second group received thiopental sodium 3 mg / kg body weight. The medication injection rate was 10 mg / sec. Any change in the hemodynamics or respiratory distress including the occurrence of apnea or hypotension, desaturation and the need for respiratory support were recorded in both groups. Eventually, after completion of surgery and transfer to the recovery room, the patients were questioned about satisfaction and anesthesia. All patient information was completed by the anesthesiologist. Finally, all the data was entered into the SPSS v18 statistical program and the data was analyzed. In this study, the t-test and chi-square test were used and P value less than 0.05 was considered significant.

Results

In this study, 150 patients were evaluated in two groups (the first group receiving the ketofol and the second group receiving the thiopental sodium). The mean age of the patients in the first group was 31.82 ± 9.18 years and in the second group was 33.64 ± 11.36 years (P = 0.258).

The incidence of apnea and the need for respiratory support in the thiopental sodium group were higher than the ketofol group (Table 1). Also, the mean duration of apnea in the first and second groups were 50.75 ± 27.77 and 99.22 ± 58.17 seconds, respectively (P <0.001). After recording the systolic, diastolic blood pressure and heart rate before and after induction did not show significant differences in the two groups (Table 2), but in each group, there were significant differences in the vital signs (Table 3). In this study, no cases of hypotension and bradycardia were reported. Awakening during anesthesia showed no significant difference in the two groups, but the amount of drug re-administration during anesthesia was significantly lower in the ketofol group than in the other group (P = 0.016) (Table 1). The mean arrival time of the Aldrete score was 9 and recovery in the ketofol, and thiopental sodium groups were 13.21 ± 3.13 and 19.12 ± 21.5 minutes, respectively (P <0.001). Drug complications in Group A were higher than Group B, but the satisfaction of patient and surgeon for the anesthetic level did not show any significant difference in the two groups (Table 1).

Table 1. Different variables in both groups before and after induction

	Thiopental sodium group		Ketofol group			
P Value	Percentage	Frequency	Percentage	Frequency	Variables	
.216	10.7	8	8	6	30y>	Age
	30.7	23	46.7	35	40 to 31	
	32	24	28	21	50to 41	
	26.7	20	17.3	13	<y 50	
.001<	93.3	70	43.7	32	yes	Apnea
	6.7	5	57.3	43	No	
.012	100	75	92	69	Yes	Respiratory support
	0	0	8	6	No	
.191	57.7	43	46.7	35	Yes	Intraoperative awaking
	42.7	32	53.3	40	No	
.016	44	33	25.3	19	Yes	Need to additional drug
	56	42	74.7	56	No	
.028	12	9	2.6	2	Yes	Postoperative hallucination
	88	66	97.4	73	No	
.012	8	6	0	0	Yes	Hiccups
	92	69	100	75	No	
.531	20	15	16	12	score 1	Satisfaction of patient
	12	9	8	6	Score2	
	68	51	76	57	Score3	
.124	13.3	10	16	12	Score1	Surgeon satisfaction score
	21.3	16	9.3	7	Score2	
	65.3	49	.7	56	Score3	

Table 2. Signs of vital signs in both groups before and after induction

	Time	Group	Mean	Standard Deviation	P Value
Heart rate	Before induction	Ketofol	86.36	11.49	0.158
		Thiopental soduim	89.84	17.83	
	After induction	Ketofol	81.81	11	0.162
		Thiopental soduim	84.56	12.87	
Systolic Pressure	Before induction	Ketofol	126.89	15.76	0.213
		Thiopental soduim	131.25	25.76	
	After induction	Ketofol	115.36	15.08	0.554
		Thiopental soduim	116.92	17.03	
Diastolic pressure	Before induction	Ketofol	78.2	9.39	0.296
		Thiopental soduim	80.4	15.54	
	After induction	Ketofol	70.62	9.71	0.093
		Thiopental soduim	73.62	11.9	

Table 3. Signs of vital signs of patients before and after the induction by the prescribed medication

	Drug	Group	Mean	Standard Deviation	
Heart rate	Ketofol	Before induction	86.36	11.49	0.014
		After induction	81.81	11	
	Thiopental soduim	Before induction	89.84	17.83	0.039
		After induction	84.56	12.87	
Systolic Pressure	Ketofol	Before induction	126.89	15.76	< 0.001
		After induction	115.36	15.08	
	Thiopental soduim	Before induction	131.25	25.76	<0.001
		After induction	116.92	17.03	
Diastolic pressure	Ketofol	Before induction	78.2	9.39	<0.001
		After induction	70.62	9.71	
	Thiopental soduim	Before induction	80.4	15.54	0.003
		After induction	73.62	11.9	

Discussion

Various studies have demonstrated that the effect of the combination of propofol and ketamine for the induction of anesthesia is different when injected by a syringe due to different kinetic effects on each other, and the combined drug (Ketofol) produces more effective sedative effects[7].

In the study by Sawas et al., 52% of the recipients of ketofol and 73% of the propofol recipients experienced respiratory supplements (P = 0.035) [8]. In a study by Goh et al., the incidence of apnea in propofol (3.3%) was lower than ketofol, and in ketofol (6.3%) was less than fentanyl + propofol (23.1%)[9]. Frey et al. reported respiratory suppression in propofol recipients more than cofactor recipients[10]. Jalili, in his meta-analysis study also stated that ketofol can significantly reduce respiratory complications, including depression of the respiratory system[11]. However, in the study by David and colleagues, there was no significant difference in the incidence of apnea in propofol and ketofol[12]. In this study, it was found that the incidence of apnea and the need for respiratory support in the thiopental sodium recipients was higher than that of ketofol. Its incidence in this study was more than other studies, which is probably due to the definition of apnea (respiratory discontinuation of 10 seconds) in this study and its difference with other studies. In their study, Ustun et al. studied the effects of ketofol (0.5 mg/kg) and thiopental (3 mg / kg) on MRI candidates; they observed that the heart rate decreased in both groups. However, there was no significant difference between the two groups in relation to each other[13]. Gholipour et al. also stated that ketofol produces a more stable hemodynamic than the other two groups (etomidated, thiopental + ketamine)[14]. Also, Garg et al. reported the ketamine and propofol combination as the best combination for the hemodynamic stability of patients during anesthesia[15]. Saleem et al. reported the hemodynamic stability in ketofol as more than in propofol and thiopental[16]. The combination of propofol and ketamine has a high degree of hemodynamic stability in other studies by Furuya et al., Ghatak et al., Goh et al., and Ozgul et al. In this study, despite the fact that there was a decrease in blood pressure and heart rate in both groups, no hemodynamic instability was reported, and all patients had stable hemodynamic parameters[9,17,18,19]. Like the previous studies, the two drugs, ketofol and thiopental, showed decreased but stable vital signs.

In a study by Ustun et al., the duration of sedation was 36.2 minutes for ketofol recipients and 24.24 minutes for the thiopental sodium patients, which was statistically significant[13]. The duration of hospital stay was 20.4 minutes in the ketofol group and 4.9 minutes in the thiopental

group, respectively. In a study by Del Pizzo et al., the duration of sedation was 20 minutes in the propofol group (propofol + ketamine with separate infusion) and recovery time was 18 minutes. In the ketamine group, it was 19 minutes (P = 0.469) and the recovery time was 11, 9, and 12 minutes (P = 0.704)[20]. A study by Coulter et al. compared proportions of ketamine and propofol in the ketofol drug and reported that a ratio of 1 to 3 ketamine to propofol was appropriate in short procedures (5 to 20 minutes), and by administration of this drug can be prevented from multiple injections with a ratio of 1 to 4. But the injection of ketofol with a ratio of 1 to 4 can increase recovery time to over 20 minutes[21]. In a study by Frey et al., the sedation time in recipients of ketofol and propofol was 164 and 235 seconds, respectively. In this study as in other studies, the need for re-administration of ketofol was less than thiopental. On the other hand, the ketofol recipients had a shorter duration of recovery[10].

Regarding side effects, Sawas et al. reported that ketofol has fewer side effects than propofol, and it is generally accepted as a better anesthetic drug[8]. Gholipur et al. also reported that 15% of recipients had muscle contractions, and 27.5% had nausea and vomiting while receiving ketamine + thiopental (with separate infusion), 20% had muscle contractions, and 7.5% had nausea and vomiting during surgery, while the patients receiving ketofol did not have any side effects[14]. Jalili et al. reported that ketofol had significantly fewer complications than other anesthetic drugs, including hallucinations, muscle rigidity, nausea, and vomiting[11]. A review of other studies has found that propofol in patients reduces nausea and vomiting; the mechanism of this event is not well understood[22], but its adjuvant effects or its weak antagonistic effects on the subcortical route can be considered[23].

Conclusions

The results of this study showed that ketofol is a better drug than thiopental for the induction of anesthesia, reducing the need for medication, the incidence of apnea, and the complications of anesthesia.

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