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석사학위 논문

소아에서 rocuronium 의 작용발현 및 지속 시간에 대한 thiopental sodium, ketamine, 그리고 propofol 의 효과

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Comparison of the effects of thiopental sodium, ketamine, and propofol on the onset time and clinical duration of rocuronium in children

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소아에서 rocuronium 의 작용발현 및 지속 시간에 대한 thiopental sodium, ketamine, 그리고 propofol 의 효과

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배경: 응급상황에서, 기도 확보의 실패는 소아 사망의 일반적이고 중대한 이유이다 특히, 소아기도 확보의 실패로 인한 생리적인 합병증을 최소화하기 위해 신속한 기관내삽관이 요구된다. 신속한 의식 소실과 신속한 신경근 차단제의 작용발현은 빠른 연속 삽관에 있어서 필수적인 조건이다. 본 연구에서는, rocuronium의 작용발현시간 및 지속 시간에 소아 마취의 유도에 빈번하게 사용되는 thiopental sodium, ketamine 및 propofol의 효과를 비교하였다.

방법: 다양한 정규수술을 받는 총 89명의 환자를 대상으로 하였다. 환자들은 마취 유도 약물에 따라 3군으로 할당되었다 (T군, thiopental sodium; P군, propofol; K군, ketamine). 의식 소실 후 신경근 모니터링을 적용하고 rocuronium 0.6 mg/kg을 투여한 후 발현 시간과 rocuronium 임상 지속 기간을 측정하였다. 기관내삽관 조건은 기관삽관점수 시스템에 의해 측정되었다. 혈역학적 변화는 마취유도 전부터 기관내삽관 5분 후까지 관찰하였다.

결과: 발현시간은 K 군(39.9 초)에서 T 군(61.7 초)와 P 군(50.7 초)보다 훨씬 빠르게 나타났다. 임상적인 작용시간과 기관내삽관의 상태는 군간에 유의한 차이가 없었다. 삽관 후 평균혈압 및 심박수는 다른 군보다 K 군에서 높았다.

결론: ketamine은 thiopental sodium, propofol보다 rocuronium의 발현시간을 단축할 수 있는 것으로 보인다.

Introduction

Airway management is the first priority in the emergency care of pediatric patients. Endotracheal intubation is definite procedure in the optimal management of the airway [1]. Rapid sequence intubation (RSI) is commonly used in the emergency situation to facilitate the securement of an airway. It has two basic technical components such as tracheal intubation with direct laryngoscopy and the induction of general anesthesia.

Although, succinylcholine remains the preferred neuromuscular blocking agent (NMBA) for RSI, there are arguments because of its side effects such as cardiac arrest or malignant hyperthermia that occur in relatively predictable circumstances [2]. Recently, rocuronium is widely used for the RSI because of its rapid onset [2]. However, the onset time of rocuronium can changed by the changes of cardiac output [3]. And, the prolonged duration of action compared to the succinylcholine can be the considerable problems during emergency situation [2]. Intravenous induction agents can produce hemodynamic changes [4], therefore, the onset time and clinical duration of rocuronium can be changed according to the induction drugs .

Rapid loss of consciousness and rapid onset of neuromuscular blocking agent is a necessary condition for the rapid sequence intubation. Thiopental sodium, ketamine, and propofol are frequently used for the induction of anesthesia in children. Thus, we carried out the study to compare the effects of thiopental sodium, ketamine, and propofol on the onset time and clinical duration of rocuronium.

Materials and Methods

The study was conducted after approval by the Institutional Review Board. A total of 90 patients who were scheduled for elective surgery, aged 3 to 10 years, and American Society of Anesthesiologists class I or II were enrolled. Exclusion criteria were as follows: patients with difficult airway, neuromuscular diseases, allergies to anesthetics and NMBA, and neurologic deficit. Informed consent was obtained from all patients' parents after full explanation of aim and method of the study. Patients were randomized into 3 groups according to anesthetic induction drugs through a computerized randomization. Patients in group T received thiopental sodium 5 mg/kg for the induction of anesthesia. Those in group P received propofol 2.5 mg/kg and in group K received ketamine 2.0 mg/kg for the induction of anesthesia .

No drug has used before the induction of anesthesia. After arrival at the operating room, standard monitoring devices such as electrocardiogram, pulse oximetry, and non-invasive blood pressure were attached to the patients. Preoxygenation with a facemask was applied for 3 min before the induction of anesthesia. Induction drug as above was injected for the loss of consciousness, and then ventilation with face mask was started.

Neuromuscular function was assessed with signle twitch for the assessment of the onset time and Train-of-four (TOF) stimuli for assessment of clinical duration. The neuromuscular module performed an automatic searched for the optimal stimulus current for the maximal response of the adductor pollicis muscle and the corresponding electromyographic (EMG) amplitudes were measured and displayed on an anesthetic monitoring system (Anesthetic Monitoring System S/5TM, Datex-Ohmeda Inc., Helsinki, Finland.).

After measurement of baseline value of single twitch, patients received rocuronium 0.6 mg/kg. After induction, no more rocuronium was administered until the end of surgery. The time from the end of rocuronium injection to loss of single twitch was measured as an onset time (OT). After then, TOF was measured and clinical duration (CD) was defined as the time from the end of rocuronium injection until T1 of the TOF had recovered to 25% of the control T1 value. When the single twitch has disappeared, endotracheal intubation was done and the intubation condition was measured by intubation scoring system (ISS) according to Viby-Mogensen [5] (Table 1).

Mean arterial pressure (MAP) and heart rate (HR) were measured according to the time sequence. (T1: baseline before induction, T2: 1 min after injection of anesthetics for induction, T3: just before endotracheal intubation, T4: 1 min after endotracheal intubation, T5: 2 mins after endotracheal intubation, T6: 3 mins after endotracheal intubation, T7: 4 mins after endotracheal intubation, T8: 5 mins after endotracheal intubation.)

Sample size was calculated using "G*Power3" free software (available at: http://www.psycho.uni-duesseldorf.de/abteilungen/aap/gpower3). . Effect size was estimated as 0.4 using standardized effect size of Cohen because there is no previous reports as current study[6]. Using $\alpha = 0.05$ with a power of 80%, the total sample size was calculated at 66. Considering with drop out, 30 patients were allocated to each group.

Statistical analysis was done with SPSS 12.0 (SPSS, Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD). ASA class and gender were compared among the three groups using Chi-Square test. Age, weight, height, onset time, clinical duration, and ISS were analyzed by one-way ANOVA. Hemodynamic changes were analyzed by repeat measures ANOVA, and when between-group differences were observed, Mann-Whitney U

test was used to analyze between pairs of group. Post hoc tests were done with Turkey's HSD. $P < 0.05$ was considered statistically significant.

Results

A total of 90 patients has enrolled and 89 patients were assessed. One patient in the group K has dropped out because of refusal. There were no significant differences among the groups in demographic data (Table 2).

The onset time was significantly faster in group K than group T and group P (42.7 sec vs. 61.7, and 50.7 sec, p= 0.001). There were no significant differences in clinical duration and intubation condition among the groups (clinical duration, p=0.646; intubation condition, p=0.949). MAP and HR were higher in group K than other groups after intubation ($p<0.001$, Fig.1 and Fig.2).

Discussion

In the current study, we compared the effects of thiopental sodium, ketamine, and propofol on rocuronium onset time and clinical duration. We showed ketamine significantly decreased the onset time of rocuronium.

Although the effect of cardiovascular factors on the onset time of NMBA has not been completely defined, it is partly determined by the time which the drug reaches to the neuromuscular junction, and cardiac output and blood flow of muscle are the contributing factors [7]. Previous study showed a close relation between the circulation time and the onset time of succinylcholine [8]. Munoz et al. have reported that a single dose of ephedrine administered during induction reduced the onset time of rocuronium, and the authors thought that ephedrine might increase the cardiac output and muscle blood flow [9]. Gill et al. also have reported that the onset time of vecuronium was shorter when etomidate has used for the induction compared to the thiopental sodium because of the lesser hemodynamic depression of etomidate than the thiopental sodium [10]. Thus, we compared the onset time according to the induction drugs in the current study.

According to the comparison of cardiovascular effects between propofol and thiopental sodium, MAP decreased greater after propofol administration than after thiopental sodium administration [11]. However, the reduction in cardiac index showed no significant differences between propofol and thiopental sodium [11]. In the current study, reduction of MAP was greater after administration of propofol compared to the thiopental sodium after administration, but there were no significant differences. The reduction of MAP showed significance only after intubation between thiopental sodium and propofol. In case of ketamine, less pediatric patients experienced significant

MAP decreases (> 20% compared to baseline) during induction when used ketamine, not propofol [12]. It is well known that ketamine can override its negative inotropic effects and tend to cause an increase in blood pressure and HR because of its sympathomimetic properties [13]. In this study, MAP has increase after injection of ketamine, and the MAP in the patients who administered ketamine were significantly higher than those who administered thiopental sodium or propofol. However, there were no significant changes among the groups in the HR until 1 min after endotracheal intubation.

According to these hemodynamic results, a difference in cardiac output among the groups is suspected. With these results, we can suggest the hypothesis that increased cardiac output in the patients who administered ketamine increased muscle blood flow, and this is the reason of reduction of the onset time after use of ketamine compared to the thiopental sodium or propofol .

Although, there is a limitation to the current study that we did not measured cardiac output or muscle blood flow directly, we speculated the differences of hemodynamic variables after use of ketamine and hypothesized these are the mechanism for the reduction of the onset time. However, further evaluation with direct measurement of cardiac output is needed.

In conclusion, we found that the use of ketamine for the induction agents could decrease the onset time of rocuronium than thiopental sodium or propofol.

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Table 1. Intubation scoring system according to Viby-Mogensen [5]

Score	Vocal cord	Jaw relaxation	Coughing or bucking
3	Fully abducted	Fully relaxed	Nil
2	Slightly abducted	Slightly stiff	Slight
1	Partially abducted	Stiff	Moderate
0	Closed	Impossible to open	Severe

Table 2. Demographic Data

	Group T (n = 30)	Group P (n = 30)	Group K (n = 29)
Age (yrs)	7.0 ± 2.1	5.8 ± 1.9	6.7 ± 2.6
Gender (M/F)	17/13	20/10	13/16
Weight (kg)	27.6 ± 9.9	25.6 ± 9.9	25.5 ± 8.9
Height (cm)	124.1 ± 14.4	118.1 ± 14.2	121.3 ± 15.4
ASA class (I/II)	30/0	29/1	28/1

Values are mean ± SD. No significant difference among the groups.

Group T: thiopental sodium, Group P: propofol, Group K: ketamine.

Table 3. Onset Time, Clinical duration , and Intubation Condition

	Group T (n = 30)	Group P (n = 30)	Group K (n = 29)
Onset time (sec)	61.7 ± 19.5	50.7 ± 14.0	39.9 ± 11.8*†
Clinical duration (min)	30.8 ± 8.8	30.5 ± 7.7	32.3 ± 7.4
ISS	8.9 ± 0.6	8.8 ± 0.5	8.8 ± 0.4

Values are mean ± SD. *P < 0.05 compared with group T. †P<0.05 compared with group P. Group T: thiopental sodium, Groups P: propofol, Group K: ketamine. ISS: Intuabtion scoring system.

Legend for figures

Figure 1. Sequential changes of mean arterial pressure. MAP was higher in group K than other groups after injection of anesthetics. Group T: thiopental sodium, Groups P: propofol, Group K: ketamine. T1: baseline before induction, T2: 1 min after injection of anesthetics for induction, T3: just before endotracheal intubation, T4: 1 min after endotracheal intubation, T5: 2 mins after endotracheal intubation, T6: 3 mins after endotracheal intubation, T7: 4 mins after endotracheal intubation, T8: 5 mins after endotracheal intubation. *P < 0.05 compared with group T. †P<0.05 compared with group P.

Figure 2. Sequential changes of heart rate. Heart rate was higher in group K than other groups 2 min after endotracheal intubation. Group T: thiopental sodium, Groups P: propofol, Group K: ketamine. T1: baseline before induction, T2: 1 min after injection of anesthetics for induction, T3: just before endotracheal intubation, T4: 1 min after endotracheal intubation, T5: 2 mins after endotracheal intubation, T6: 3 mins after endotracheal intubation, T7: 4 mins after endotracheal intubation, T8: 5 mins after endotracheal intubation. *P < 0.05 compared with group T. †P<0.05 compared with group P.

Figure 1.

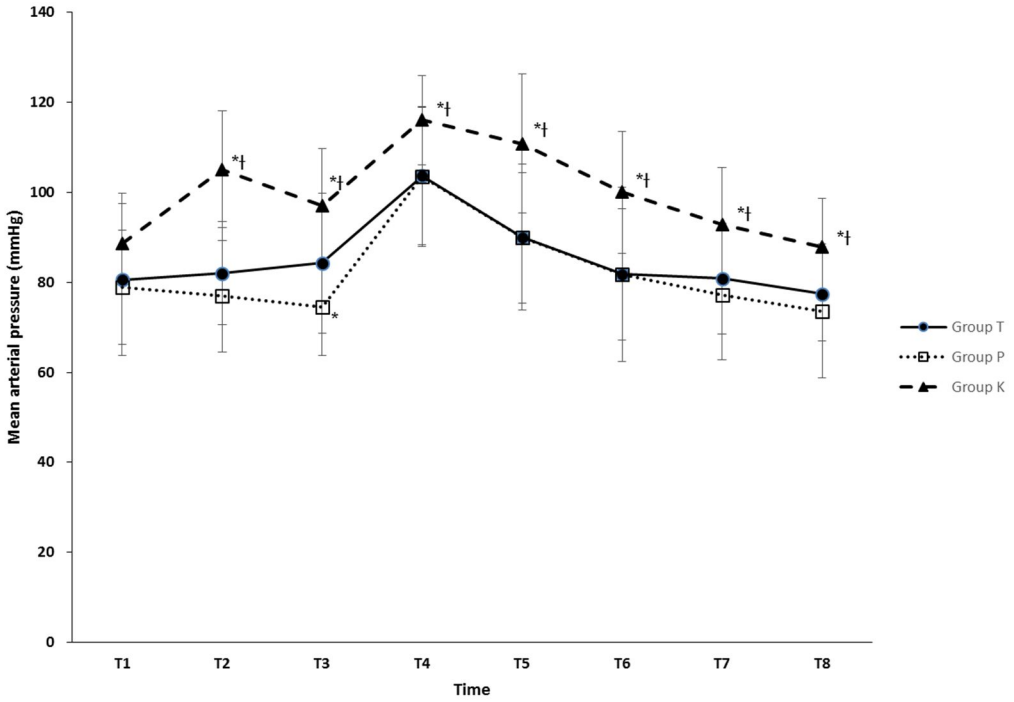

Figure 2.