

Two Forgotten Induction Agents; Etomidate versus Thiopental Sodium with Rocuronium for Rapid Sequence Induction

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Abstract

Objective: To assess the effect on intubating conditions and haemodynamic response on intubation of two different induction agents etomidate and thiopental sodium with rocuronium during rapid sequence induction.

Methods: This prospective quasi experimental study was conducted in Department Of Anaesthesia, SICU and Pain Management, Dow Medical College, Civil Hospital Karachi and Abbasi Shaheed Hospital Karachi Medical and Dental College over a period of one year. Total 120 American Society of Anaesthesiologists (ASA) physical class I and II, adult patients of either gender, aged between 18 to 60 years, undergoing elective surgery were allocated randomly into two equal groups to receive either intravenous thiopental sodium (Group NTR) or etomidate (Group NER) for rapid sequence induction. Group NER was given nalbuphine 0.1mg/kg, induction agent etomidate 3 mg/kg with muscle relaxant rocuronium 1.0 mg/kg while in group NTR induction agent thiopental sodium was given in the dose of 4 mg/kg with nalbuphine and rocuronium in the same doses. After sixty seconds, laryngoscopy was done. Intubating condition was assessed using the criteria of Cooper and colleagues: ease of intubation, condition of vocal cords and response to intubation. Cardiovascular response on intubation in terms of systolic and diastolic blood pressure and heart rate was evaluated at 0, 1, 3 and 5 minutes.

Results: Demographic data were comparable between the groups. Intubating conditions which were assessed in terms of ease of laryngoscopy, condition of vocal cords at intubation and intubation response coughing, bucking and diaphragmatic movement were significantly better in the group NER ($p < 0.05$). Similarly, arterial blood pressure remained close to base line in NER group but there was significant fall in both systolic and diastolic blood pressure in group NTR. However, there was no significant difference in change in the heart rate in the groups.

Conclusion: Etomidate-rocuronium is better than thiopental-rocuronium in terms of intubating conditions and haemodynamic stability during rapid sequence induction in non-septic surgical patients in emergency department.

Keywords: Etomidate, thiopental sodium, nalbuphine intubation, rocuronium, laryngoscopy. (ASH & KMDC 19(2):79;2014).

Introduction

Rapid sequence induction (RSI) is the standard anaesthetic technique and the depolarizing neuromuscular agent succinylcholine has been the drug of choice for RSI and anticipated difficult intubations for its short and rapid acting

properties. Nothing had yet replaced succinylcholine in the scenarios of difficult intubation before but with advent of rocuronium antagonist (ORG-25969, sugamedax) that chelates the drug and act as the reversal agent, rocuronium can also be used in difficult intubation situations in RSI. However, rocuronium is the suitable alternative, equally rapid acting muscle relaxant in the recommended doses for RSI (2 or 3x ED₉₅) where succinylcholine is relatively contraindicated, like in the patients with hyperkalemia or known family history of abnormal cholinesterase enzyme activity^{1,2}. In addition, rocuronium being monoquaternary amino steroidal

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drug, does not cross placenta therefore can safely be used in obstetrical surgeries where risk of regurgitation requires rapid sequence induction³⁻⁵.

The most popular hypnotic agents for RSI in emergency cases in South Asia have been intravenous thiopental sodium, ketamine, propofol and etomidate. Thiopental sodium, a short acting thiobarbiturate, is considered a gold standard and has been widely used induction agent even for RSI in the past. However, it causes reduction in arterial blood pressure and reflex tachycardia in the presence of hypovolemia by abolishing the sympathetic compensation with rapid induction. Regardless of its side effects thiopental sodium had long been used with pre-induction pharmacological optimization and intravenous fluids resuscitation. It suppresses neuronal activity, making it a useful induction agent in haemodynamically stable patients with conditions that can elevate intracranial pressure including seizures, intracranial bleeding, or trauma. However, its use as induction agent is now limited due to unavailability in western part of world and the advent of newer hypnotics like propofol^{4-7, 9}.

Propofol, a phenol derivative, attenuates intubation response the most as compare to all other induction agents, but it can cause marked hypotension and bradycardia with rapid induction in compromised emergency situations^{4,14}. Ketamine, a dissociative anaesthetic poorly attenuates the intubation response, is favorable in situation where marked cardiovascular decompensation is anticipated after induction, provided the endogenous catecholamine stores are not depleted as in critically ill patients. On the contrary, it can cause hypertension and marked tachycardia that can be deleterious in hypertensive patients with left ventricular dysfunction^{2,4, 11-13}.

Etomidate, an imidazole compound, produces sedation and amnesia through α amino butyric acid (GABA)inhibitory neurotransmitter system. Its onset of action is rapid and comparable to propofol and thiopental sodium that is 15-20 seconds. It has a superior profile in terms of cardiovascular stability even when used in patients with severe left ventricu-

lar dysfunction; it does not cause haemodynamic instability. The circulatory factor that determines the intravenous anaesthetic etomidate proportionally effects the distribution of rapid acting muscle relaxant; hence supporting the better intubating condition in shortest period of time for rapid sequence induction¹³⁻¹⁶.

The aim of this study is to determine the effect on intubating conditions and haemodynamic response on intubation of two almost forgotten but available and well proven different anaesthetic induction agents, etomidate and thiopental sodium, with a rapid acting muscle relaxant rocuronium in emergency department.

Patients and Methods

This study was conducted in department of anaesthesia, Civil Hospital Karachi, Dow University of Health Sciences and Abbasi Shaheed Hospital after approval from concerned ethics committee, departmental permission and informed consents from all the patients, from Nov 2011 to Dec 2012. This was a prospective quasi experimental study, included 120 adult patients of either gender, aged between 18 and 80 years, having American Society of Anaesthesiologists(ASA) physical class I and II, undergoing emergency surgeries, including general, orthopaedic, plastic and neurosurgeries were allocated randomly into two equal groups to receive either intravenous thiopental sodium (Group NTR) or etomidate (Group NER) as induction agent with muscle relaxant rocuronium for rapid sequence induction.

The patient with anticipated difficult laryngoscopy and intubation, allergy to any study medications, receiving any other sedatives, acute upper air way disease causing hyperreactive airway, pharyngeal or laryngeal disease and having any neuromuscular dysfunction, severe sepsis were excluded from the study.

The patients were randomly grouped using odd and even method, patient with odd serial numbers were grouped to receive thiopental sodium with

rocuronium while patient on even serial were grouped in to have etomidate and rocuronium for RSI. The anaesthetists, who intubated and assessed the effect of drugs in terms of intubating condition and haemodynamics, were more than three year in experience and were blinded for the study drugs. The primary investigator prepared the anaesthetic drugs and ensured the blinding with screen from intubating anaesthetist. All patients had standard monitoring including non-invasive blood pressure, SpO₂, ECG, capnography and temperature monitoring. Baseline blood pressure, heart rate were noted in all the patients.

Group NTR was given intravenous analgesia Injection Nalbuphine 0.1 mg/kg, induction agent thiopental sodium 4 mg/kg and muscle relaxant injection rocuronium 0.6mg/kg (2xED 95), while in group NER, induction was done with intravenous etomidate 0.3 mg/kg with same doses of nalbuphine and rocuronium as in group NTR. After sixty seconds of the administration of rocuronium, laryngoscopy was done, trachea intubated. Intubating conditions were assessed using the criteria of Cooper and colleagues; ease of laryngoscopy (0=impossible, 1=difficult, 2=fair, 3=easy), condition of vocal cords (0=closed, 1=closing, 2=moving, 3=open) and response to intubation⁹.

The cardiovascular response on intubation in both the groups was recorded in terms of systolic and diastolic blood pressure and heart rate at baseline 0,1,3,5 minutes. All the data were recorded on proforma.

Statistical analysis of categorical variable was done using chi square test and fisher exact test while continuous data was evaluated by student t-test ($p < 0.05$) was taken as significant.

Results

Demographic characteristics were comparable between the groups except the ASA status (Table. 1). In group NTR 44 patient were ASA1 while 48 in Group NER. Laryngoscopy was found easier in 56 patients in those induced by etomidate NER versus

18 patients which had thiopental sodium as the induction agent NTR ($p=0.002$), shown in Fig 1. The vocal cords seen open in statistically significant patients on laryngoscopy, were 56 patients in NER versus 38 patients in the other group ($p=0.036$) whereas in group NTR 8 and 12 patients had closing and moving vocal cords respectively at the time of intubation (Fig. 2). No patient from either group had severe coughing and bucking. However 12 patients in group NTR showed mild coughing versus 4 patients in the group NER. Slight diaphragmatic movement was also noticed in 26 patients which was higher than found in group NER ($p=0.007$), (Table 2.). There was statistically significant difference in the mean of addition of all the scores i.e. 6.84 ± 1.41 in group NTR compared to 8.44 ± 1.04 in group NER ($p=0.0001$).

For haemodynamic changes, there was no statistically significant difference in terms of baseline heart rate, systolic and diastolic blood pressures between the groups. Also, there was no significant change in heart rates from baseline after 1, 3, and 5 minute in both groups. However, the systolic and diastolic blood pressure were significantly higher in group NER recorded on the given intervals ($p < 0.05$), (Table 3).

Discussion

The ease in performing endotracheal intubation depends on the type and degree of muscle relaxation, depth of anaesthesia and the skill of the anaesthesiologist. In this study we used the steroidal non depolarizing muscle relaxant rocuronium for facilitation of intubation with two different intravenous induction agents: etomidate and thiopental sodium. We found it suitable alternative for historically used depolarizing muscle relaxant succinylcholine, in situations where its use is relatively or absolutely contraindicated. The rapid onset of adequate paralysis for endotracheal intubation was achieved with intravenous bolus of rocuronium bromide after one minute.

Table 1. Demographic Data

	NTR n=60	NER n=60	P-value
Age	30.48 ±12.28	29.52 ±13.38	0.944
Gender♂	38	35	0.233
Weight	42.6 ±10.16	40.88 ±16.48	0.342
ASA 1	44	48	0.052
ASA 11	16	12	0.012

Table 2. Response of Intubation in NTR and NER group

Response of Intubation	Group NTR n=60	Group NER n=60	P-value
0 (severe coughing and bucking)	0	0	0.007
1 (mild coughing)	12	4	
2 (slight diaphragmatic movement)	26	12	
3 (none)	22	44	

Fig. 1 : Ease of Laryngoscope in NTR and NER patients

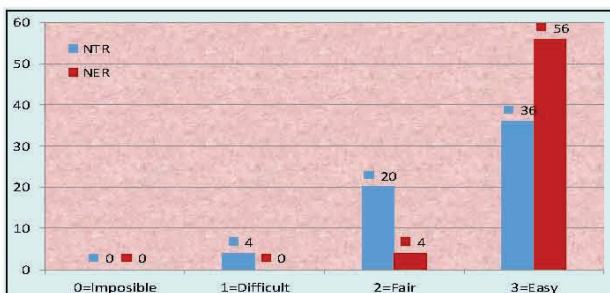
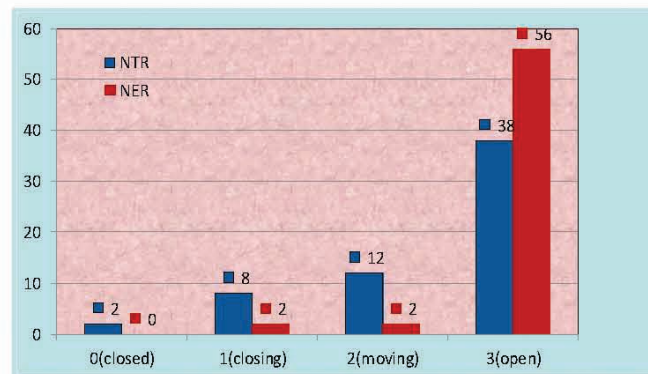


Fig. 2 : Comparison of Condition of Vocal Cords



In a Cochrane meta analysis of 58 clinical trials, 0.6 mg/kg (2xED) to 1.2 mg/kg (3xED95) doses of rocuronium have been compared with succinylcholine and found comparable intubating conditions with 1 mg/kg dose of rocuronium with 1 mg/kg of depolarizing muscle relaxant¹. Patanwala AE, after a retrospective evaluation of 327 patients also concluded that succinylcholine and rocuronium are comparable in regard to first-attempt intubation success in the emergency department using equivalent doses of both the drugs². However, we used 0.6 mg/kg, a lowest dose and achieved good intubation conditions with etomidate. If a higher dose is chosen i.e. 1 mg/kg, it may further improve the intubation condition in terms of ease of laryngoscopy, vocal cords conditions and response on intubation¹⁻⁴.

In addition to a neuromuscular blocking agent, to achieve optimal intubating conditions, choice of the anaesthetic induction agent and dose most appropriate for the clinical situation is an important component of RSI for haemodynamic stability^{1,5,8,9}.

The induction agent may influence the rate of onset of advocate relaxation required for satisfactory intubating conditions^{3,6,13}. The haemodynamic stability related to the induction anaesthetics proportionally effect the time of the distribution of muscle relaxant. We compared etomidate with thiopental sodium and had more haemodynamic stability in terms of diastolic and systolic blood pressures ($p=0.0001$). Different trials have evaluated the relation between the onset of block and the change in mean arterial pressure; onset of block was shortest when anaesthesia was induced with Etomidate compared with thiopental and propofol⁹. The induction agent also effect intubating condition by attenuating laryngeal and pharyngeal response of laryngoscopy and intubation, among all propofol attenuates these responses better than the two we used, but when muscle relaxant is used this property of propofol does not outweigh the cardiodepressent effect like bradycardia and hypotension which is the major concern with the use of propofol⁴. However, between the two we compared, etomidate was associated with more sustained diastolic and systolic blood pressures while

changes in hearts where comparable that is increased from baseline in after intubation (Table 3).

Our results of the study are consistent with the previous trials that compared induction agent etomidate for intubating condition and cardiovascular stability in emergency situations where risk of aspiration hypoxia and emergency surgeries were the indications for intubation in rapid sequence induction. The controversy with etomidate regarding its use in septic patients has always been there but some researcher found it safe when it is as a single bolus in septic or trauma patients. The researchers concluded that a bolus dose of etomidate for RSI was not associated with increased morbidity and mortality compared to ketamine in critically ill patients but suggested that ketamine is a safe alternative¹⁸⁻²³.

As there is no randomized control trial in our population regarding the use of etomidate in severe sepsis and we did not evaluated serum cortisol levels to determine the adrenal insufficiency in any patient, we recommend cautious administration in patients with evolving or established septic shock, etomidate should be deferred for other options like thiopental sodium and ketamine²¹. However, in patients where haemodynamic instability is not an issue, use of thiopental sodium has been a gold standard and in the presence of hypotension, it should be preferred over commonly used induction agent propofol that is known to be associated with hypotension and bradycardia. Moreover, in our part of the world where thiopental and etomidate are easily available for use, we should not limit our choices of induction agents that compromise patient's safety in terms of hemodynamic stability⁶. American society has shown great concerns over the unavailability of thiopental and its absence is being considered as a risk to their patients' safety in USA and other European countries²⁵.

So, we recommend that the two forgotten anaesthetic induction agents, etomidate and thiopental should be brought in current anaesthesia practice for the safety of our patients especially in emergency situations where haemodynamic instabilities are frequently encountered. We also recommend that rocuronium is equally effective muscle

relaxant in situation where succinylcholine is considered unsafe and contraindicated.

Conclusion

Induction agents etomidate and thiopental are safe for rapid sequence induction in emergency surgeries and etomidate provides better intubating conditions and haemodynamic stability than thiopental. Moreover, nondepolarizing muscle relaxant rocuronium can be an acceptable alternative whenever succinylcholine is contraindicated, provided intubation is not anticipated difficult.

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