



USE OF ATRACURIUM AND ITS REVERSAL BY ANAESTHESIOLOGISTS AT A TERTIARY CARE HOSPITAL

Salam Asma Abdus, Afshan Gauhar*

Department of Anaesthesiology, Aga Khan University Hospital, Karachi, Pakistan

E-mail: gauhar.afshan@aku.edu

Article Received on: 17/01/13 Revised on: 01/02/13 Approved for publication: 12/03/13

DOI: 10.7897/2230-8407.04315

IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com

© All rights reserved.

ABSTRACT

Atracurium Besylate is a non-depolarizing neuromuscular blocking agent. The aim of this study was to determine the practice trends for the use of reversal agent after atracurium by anaesthesiologists. A structured questionnaire was designed to know the practice of anaesthesiologists using reversal agent in patients who have undergone general anaesthesia and were given the intermediate acting neuromuscular blocker atracurium. Ninety nine percent participants used atracurium as a common neuromuscular blocking agent. 83.6% used the reversal agent after atracurium in every patient whereas 16.4 % used it in selected patients. In our institution most of the anaesthesiologists use reversal agent after atracurium in every patient as it is a general belief that not using reversal will prolong the recovery time, despite the fact that the use of reversal agent is debatable all over the world. Further study should be carried out to know the practice trends of rest of the anaesthesiologists as well as to evaluate the effective recovery following the single dose or infusion of atracurium and the need of reversal agent.

Keywords: atracurium, reversal agent, neuromuscular blockade.

INTRODUCTION

Neuromuscular blocking agents (NMBA) and their antagonists are established components of balanced anaesthesia but it appears that there is a wide range of strategies for handling the clinical situations.¹ Adequate recovery of muscle power is mandatory before discharging a patient to avoid serious complications like residual paralysis. Incomplete neuromuscular recovery is a common problem in patients in post anaesthesia care units and the incidence of residual paralysis after administration of current intermediate-acting neuromuscular blocking agents may be up to 40-60%.^{2,3} The use of anticholinesterases to reverse residual neuromuscular block is efficacious only if recovery is already established.⁴

Atracurium besylate is a non-depolarizing skeletal muscle relaxant and is susceptible to degradation by Hofmann elimination and ester hydrolysis.⁵ Hofmann elimination is the major degradation pathway at physiological pH and temperature. Recovery from neuromuscular block under balanced anaesthesia can be expected to begin approximately 20 to 35 minutes after injection. Under balanced anaesthesia, recovery to 25% of control is achieved approximately 35 to 45 minutes after injection, and recovery is usually 95% complete approximately 60 to 70 minutes after injection.⁶ Repeated administration of maintenance doses of atracurium has no cumulative effect on the duration of neuromuscular block if recovery is allowed to begin prior to repeat dosing. Moreover, the time needed to recover from repeat doses does not change with additional doses. Repeat doses can therefore be administered at relatively regular intervals with predictable results.

Reversal of neuromuscular blockade can be achieved with an anticholinesterase agent such as neostigmine, edrophonium, or pyridostigmine in conjunction with an anticholinergic agent such as atropine or glycopyrrolate. Once the acetylcholinesterase is completely inhibited, any additional increase in the neostigmine dose will not further improve reversal, and therefore higher neostigmine doses are rather unlikely to be beneficial. Reduced doses (10-30 mcg/kg) of neostigmine are effective in antagonizing shallow atracurium

block. For successful reversal within 10 min, as little as 20 mcg/kg neostigmine may be sufficient. These dose recommendations are specific for atracurium and an intravenous anesthetic background.⁷ However, when the criteria for adequate recovery from neuromuscular blockade are not met and the dose of neostigmine cannot be adapted accordingly, then waiting for more spontaneous recovery may be the only thing the clinician may do to improve the efficacy of neostigmine-induced reversal.

It has also been found that the appropriate dose of anticholinesterase for this situation has not yet been determined, as several neostigmine side effects are dose dependent, and overabundance of acetylcholine at the neuromuscular junction has the potential to increase muscle weakness rather than reverse residual neuromuscular block.^{7,8,9,10} Upper airway dilator muscles may be especially vulnerable to this paradoxical effect of neostigmine, showing a decrease in inspiratory upper airway volume caused by neostigmine-evoked weakness of upper airway dilator muscles.¹¹ It also causes nausea, vomiting, bradycardia, prolongation of QT interval over the electrocardiogram (ECG), bronchoconstriction, miosis and increased intestinal tone.⁴

In our institution, a leading tertiary care hospital, the practice of using neostigmine/ glycopyrrolate is common for the reversal of atracurium induced muscle relaxation whether used as a single dose or in multiple doses. However we still need to know the practice trends of the anaesthesiologists working in our institution regarding the reversal of atracurium so that the data can further be extrapolated to evaluate the effective recovery following a single intubating dose of atracurium with or without giving reversal agent.

MATERIAL AND METHODS

It was a Cross Sectional Survey, conducted at Aga Khan University Hospital Karachi, a tertiary care hospital. It was completed in six months after approval from Departmental Research Review Committee (DRC). All practicing anaesthesiologists with one year experience working in anaesthesia department at AKUH were included in this study.

The strength of the anaesthesiologists working in the department is 80. Expected response rate was 90% with 7% margin of error, sample size was 74. It was assumed that the study dropout rate will be 10% and therefore all anaesthesiologists were included. Those who denied to participate in the survey were excluded from study. An informed verbal consent was taken from anaesthesiologists involved in patient care. All anaesthesiologists with one year experience were interviewed according to the structured questionnaire which was designed to know the practice of using reversal agent in patients who have undergone general

anaesthesia and were given the intermediate acting neuromuscular blocking agent atracurium. It was conducted in Urdu (national language) and the sequence of the questions were followed strictly according to the structured design of the questionnaire. The questionnaire was submitted to the research assistant of the Department on the same day. Data was entered and analyzed on statistical package for social sciences SPSS version 19. Frequencies and percentages were computed for categorical variables like gender and practice trends.

Table I: Characteristics of Participants of the study (n=74)

Variables	Frequency	Percentage
Gender		
Male	48	64.9%
Female	26	35.1%
Experience of participants		
≤ 2 Years	15	20.3%
3 to 5 Years	15	20.3%
6 to 10 Years	26	35.1%
>10 Years	18	24.3%
Working as		
Consultant	37	50%
Senior Resident (3 -5 years)	22	29.7%
Junior Resident (1 -2 years)	15	20.3%

Table II: Practice trends for the use of reversal agent after atracurium by anaesthesiologists working at Aga Khan University Hospital (n=74)

Questions	Responses	Percentage
What is the commonest neuromuscular agent NMBA you use in operating room? (n=74)	73	98.6%
Atracurium	01	1.4%
Others		
For maintenance you use atracurium as (n=74)		
Bolus, in increments	10	13.5%
Infusion	03	4.1%
Both	61	82.4%
Do you use reversal agent for atracurium? (n=74)		
No:		
Yes	01	1.4%
▪ In every patient	73	98.6%
▪ In selected patients	61	83.6%
	12	16.4%
If you routinely use reversal agent, what is your criterion to use? (n=12)		
▪ Spontaneous recovery	2	16.7%
▪ Surgery lasted for more than 1 hour	1	8.3%
▪ Infusion was used	4	33.3%
▪ Last dose was used 5-10 min ago	1	8.3%
▪ As per the degree of block	5	41.7%
TOF: 0.7 – 0.9	1	
1-2 muscle twitch on NMT	1	
▪ In certain type of surgeries	1	
Neurosurgery	2	16.7%
Obstetrics	1	8.3%
ENT	1	8.3%
All Type of surgery	1	8.3%
▪ Other reasons	1	8.3%
	3	25%

RESULTS

74 anaesthesiologists with working experience ranging from one year to upto forty years participated in this survey. They have been working in the department, either as residents (junior, senior) or consultants (junior, senior) (Table I) Out of 98.6% anaesthesiologists who used atracurium as a common neuromuscular blocking agent, 83.6% (n= 61) used the reversal agent in every patient whereas 16.4 % (n= 12) used it in selected patients. (Table II). 25% (n=3) anaesthesiologists who gave other reasons said they would give reversal agent 1- depending on when the last dose of atracurium was used and patients respiratory efforts 2- TOF 0.7-0.9 along with clinical parameters and 3-if the criteria for

extubation is not met i.e inadequate tidal volume VT, shallow breaths, no eye opening, less dose of the reversal agent is given. Spontaneous recovery, when infusion was used, as per the degree of block (TOF: 0.7 – 0.9 and/or 1-2 muscle twitch on NMT), and certain type of surgeries were the most common answers given as the criteria for the use of reversal agent.

DISCUSSION

The use of anticholinesterases to reverse residual neuromuscular block is efficacious only if recovery is already established. Administration of reversal agent at the end of anaesthesia is indicated to avoid the known deleterious

consequences of partial paralysis. However, the administration of reversal does not guarantee the lack of partial paralysis in all patients.³ There is no significant difference in the incidence of postoperative residual block between patients who did or did not have reversal of neuromuscular blockade.¹²

So far very limited studies have evaluated the knowledge and practice trends of anaesthesiologists using reversal agent for neuromuscular blocking agents. Osmer et al had conducted a similar survey among British, French and German anaesthesiologists to evaluate the possible national differences in the peri-operative use of muscle relaxants and their reversal agents.¹

In our study atracurium was the commonest (98.6%) intermediate acting NMBA used in the operation theater despite the availability of other muscle relaxants like rocuronium. This could have been the personal preference of individual anaesthesiologists and also due to easy availability of atracurium in our institution as well as in our part of the world. Osmer et al in their study found out that 76% of French anaesthesiologists, 45% of British and 32% of Germans use atracurium for elective intubation. Peri-operatively the same relaxants atracurium, vecuronium and pancuronium were used in all three countries.¹ In another study, Baillard et al had left the decision and management of neuromuscular block in the operating room at the discretion of primary anaesthesiologists and found out that the main NMBA used was atracurium.¹³

In our study 82.4% anaesthesiologists used atracurium both as bolus and as infusion peri-operatively. 13.5% used it only as bolus in increments. Osmer in his study stated that the timing of the additional doses of the respective relaxant was mainly by clinical judgment of the anaesthetist in all three countries.¹

In our institution, anaesthesiologists are overly conscious about postoperative residual neuromuscular block, delayed recovery and lack of proper recovery facilities which leads to the usage of reversal agent despite being aware of its untowards cardiopulmonary effects. This could be the reason why 98.6% anaesthesiologists routinely used reversal agent and only 1.4% did not use reversal agent at all after atracurium. 83.6% used it in every patient who received NMBA whereas 16.4% (n=12) used it selectively. 5 of those 16.4% were relying on the peripheral nerve stimulator before reversal agent was given. Many studies have demonstrated the use of peripheral nerve stimulator.^{3,14,15} However Osmer et al in their study¹ found out that only in Great Britain a peripheral nerve stimulator was used by a significantly high number (67%) of participating anaesthetists. Anaesthetists of France (48%) and Germany (51%) rarely used this device. They have not analyzed the difference in the use of nerve stimulator between nations and have also stated that the use of cholinesterase inhibitor to reverse possible residual neuromuscular block was handled differently in three countries. 15% of French anaesthesiologists had never given a reversal agent at all. They had also noticed it to be the “departmental policy”.

Our survey represents the current practice trend of anaesthesiologists only at one institution about the use of neuromuscular blocking agent and its reversal but is not an overall representative of the Pakistani anaesthesiologists. We did not specifically ask for reasons from those who did not use reversal at all, neither are there any guidelines available for the decision of administering reversal agent except the

studies and data on clinical parameters like head lift, hand grip, adequate tidal volumes and regular breathing.

The participants of this survey were both trainees as well as consultants who have completed their higher professional education. This could have led to discrepancy between usage and nonuse of reversal agent but as majority used the reversal agent, we did not correlate the experience with the use of reversal agent.

Though very limited data is available on practice trends internationally, this was the first study in Pakistan gathering data of anaesthesiologists working in one of the leading, tertiary care hospital and almost 100% of the sample size participated. In conclusion, atracurium is the commonest NMBA used by the practicing anaesthesiologist of our institution. Almost all anaesthesiologists use reversal agent after atracurium whether used as bolus or infusion despite the fact that the use of reversal agent is debatable all over the world and general belief of our practicing anaesthesiologists is that no reversal will prolong the recovery time. There also seems to be an over-use of reversal and under utilization of nerve stimulator in our institution. On the basis of these results we can emphasize on the use of nerve stimulator after devising guidelines affirmed by Quality Insurance Committee (QIC) of the department. As this was a preliminary survey based at a single institution, a nationwide multi-centered study should be carried out to know the practice trend of rest of the anaesthesiologists as well as to evaluate the effective recovery following single dose or infusion of atracurium and the need of reversal agent.

ACKNOWLEDGEMENT

Dr Azhar Rehman, Senior Instructor, Department of Anaesthesiology, Aga Khan Hospital, Pakistan is acknowledged for general support. Mr. Amir Raza, Research Supervisor, Department of Anaesthesiology, Aga Khan University is acknowledged for his assistance in statistical analysis.

REFERENCES

- Osmer C, Vogele C, Zickmann B, Hempelmann G. Comparative use of muscle relaxants and their reversal in three European countries: a survey in France, Germany and Great Britain. *Eur J Anaesthesiol.* 1996 Jul;13(4):389-99. <http://dx.doi.org/10.1046/j.1365-2346.1996.00993.x> PMID:8842663
- Baillard C, Gehan G, Reboul-Marty J, Larmignat P, Samama CM, Cupa M. Residual curarization in the recovery room after vecuronium. *Br J Anaesth.* 2000 Mar;84(3):394-5. <http://dx.doi.org/10.1093/oxfordjournals.bja.a013445> PMID:10793602
- Debaene B, Plaud B, Dilly MP, Donati F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *Anesthesiology* 2003;98:1042-8. <http://dx.doi.org/10.1097/0000542-200305000-00004> PMID:12717123
- Srivastava A, Hunter JM. Reversal of neuromuscular block. *Br J Anaesth.* 2009 Jul;103(1):115-29. 5-5-Nigrovic V, Fox JL. Atracurium decay and the formation of laudanosine in humans. *Anesthesiology.* 1991 Mar;74(3):446-54.
- Daily med current medication information. [Online].2010[05/2010]; Available from: URL:<http://dailymed.nlm.nih.gov/dailymed/druginfo.cfm>
- Fuchs-Buder T, Meistelman C, Alla F, Grandjean A, Wuthrich Y, Donati F. Antagonism of low degrees of atracurium-induced neuromuscular blockade: dose-effect relationship for neostigmine. *Anesthesiology.* 2010 Jan;112(1):34-40. <http://dx.doi.org/10.1097/ALN.0b013e3181c53863> PMID:19952724
- Payne JP, Hughes R, Al Azawi S. Neuromuscular blockade by neostigmine in anaesthetized man. *Br J Anaesth.* 1980 Jan;52(1):69-76. <http://dx.doi.org/10.1093/bja/52.10.1056-a> PMID:7378232
- Bartkowski RR. Incomplete reversal of pancuronium neuromuscular blockade by neostigmine, pyridostigmine, and edrophonium. *Anesth Analg.* 1987 Jul;66(7):594-8. <http://dx.doi.org/10.1213/00005539-198707000-00002> PMID:3605668
- Goldhill DR, Wainwright AP, Stuart CS, Flynn PJ. Neostigmine after spontaneous recovery from neuromuscular blockade. Effect on depth of blockade monitored with train-of-four and tetanic stimuli. *Anaesthesia.* 1989Apr;44(4):293-9. <http://dx.doi.org/10.1111/j.1365-2044.1989.tb11280.x> PMID:2719200

10. Eikermann M, Fassbender P, Malhotra A, Takahashi M, Kubo S, Jordan AS, et al. Unwarranted administration of acetylcholinesterase inhibitors can impair genioglossus and diaphragm muscle function. *Anesthesiology*. 2007 Oct;107(4):621-9. <http://dx.doi.org/10.1097/01.anes.0000281928.88997.95> PMID:17893459 PMCID:3473079
11. Hayes AH, Mirakhur RK, Breslin DS, ReidJE, McCourt KC. Postoperative residual block after intermediate-acting neuromuscular blocking drugs. *Anaesthesia* 2001; 56 : 312-8. <http://dx.doi.org/10.1046/j.1365-2044.2001.01921.x> PMID:11284816
12. Baillard C, Clec'h C, Catineau J, Salhi F, Gehan G, Cupa M, Samama CM. Postoperative residual neuromuscular block: a survey of management. *Br J Anaesth* 2005 (5); 95: 622–6 <http://dx.doi.org/10.1093/bja/aei240> PMID:16183681
13. Kim KS, Lew SH, Cho HY, Cheong MA. Residual paralysis induced by either vecuronium or rocuronium after reversal with pyridostigmine. *Anesth Analg* 2002;95:1656–603. <http://dx.doi.org/10.1097/0000539-200212000-00033> PMID:12456433
14. Berg H, Roed J, Viby-Mogensen J, Mortensen CR, Engbaek J, Skovgaard LT, et al. Residual neuromuscular block is a risk factor for postoperative pulmonary complications. A prospective, randomized, and blinded study of postoperative pulmonary complications after atracurium, vecuronium and pancuronium. *Acta Anaesthesiol Scand* 1997;41:1095–103. <http://dx.doi.org/10.1111/j.13996576.1997.tb05541.x> PMID:9366929

Cite this article as:

Salam Asma Abdus, Afshan Gauhar. Use of Atracurium and its reversal by anaesthesiologists at a tertiary care hospital. *Int. Res. J. Pharm.* 2013; 4(3):90-93

Source of support: Nil, Conflict of interest: None Declared