

# The Cost of Neuromuscular Blockers in Operations of Variable Length in Turkey

Güvenç Koçkaya<sup>\*1</sup>, Pınar Daylan Koçkaya<sup>2</sup> and Albert Wertheimer<sup>3</sup>

<sup>1</sup>General Directorate of Pharmaceuticals and Pharmacy, Pharmacoeconomy Department, <sup>2</sup>Polatlı Duatepe Government Hospital, Turkey

<sup>3</sup>Temple University, School of Pharmacy, Center for Pharmaceutical Health Services Research, Turkey

**Abstract:** Decision makers develop new strategies to minimize the anesthetic costs and maintain the quality of health care. The aim of our study is to help decision makers, in Turkey, in developing new strategies to minimize anesthetic costs. Three different operational strategies were assumed. The first strategy was for operations under 30 minutes; the second strategy was for operations between 30 and 60 minutes and the third strategy was for operations above 60 minutes. Neuromuscular blocker cost by milligram per kilogram was calculated for each operation strategy. Atracurium had the lowest per milligram cost (US\$0.08), followed by rocuronium (US\$0.09), mivacurium (US\$0.38), vecuronium (US\$0.44) and cisatracurium (US\$0.59). Atracurium and vecuronium had the lowest costs in operations which are under 30 minutes, followed by rocuronium, mivacurium and cisatracurium. Vecuronium had the lowest costs in operations which are 30-60 minutes, followed by atracurium, rocuronium and cisatracurium. Vecuronium which had the lowest costs in operations above 60 minutes, followed by atracurium, rocuronium and cisatracurium. The managements of hospitals or hospital groups which are in Turkey can choose atracurium and vecuronium in operations under 30 minutes, vecuronium in operations 30-60 minutes and above 60 minutes in their neuromuscular blocker (NMB) formularies for making cost reductions from NMBs.

**Keywords:** Neuromuscular blocker agents, economics, hospital costs.

## INTRODUCTION

Fiscal policy is the use of government expenditures and revenue collection to influence the economy [1]. Fiscal policy for health systems has affected health care management and health care workers through efforts to minimize costs in hospitals, including hospital closures and amalgamations. Also the pharmaceutical industry has been affected by these changes too. Although the proportion of hospital operating costs directed to anesthetic pharmaceuticals is small, approximately 0.24% of hospital budget [2], they are a great proportion of variable anesthetic supply costs [3]. Decision makers develop new strategies to minimize anesthetic costs and maintain the quality of health care. Because neuromuscular blocking (NMB) drugs constitute approximately 30% of the total anesthesia drug budget in the United States [4], these drugs are appropriate targets for cost-minimization strategies in anesthesia [3].

Neuromuscular blockers have similar effects and side effects. The main differences are on onset of action and duration of action times. The differences occur from the differences in pharmacokinetics. Anesthesiologists choose the optimum NMB for each operation depending on the operation time, duration of action time and the clinical situation of a patient. In general, NMB drugs are used depending on their drug information leaflet in Turkey and

hospitals use the same inhaled or intravenous anesthetics in all patients except special patients who have special clinical indications.

Atracurium, cisatracurium, mivacurium, rocuronium, and vecuronium are the NMBs in the Turkish pharmaceutical market. Total sales which were taken from Ministry of Health in government hospitals of NMBs is US\$ 2.3 Million in year 2010 in Turkey. The distribution of sales of NMBs which were taken from IMS were mentioned in Fig. (1). The duration of action times were reported as 12-18 minutes, 30 minutes, 30-40 minutes, 45-70 minutes and 60-80 minutes for mivacurium, atracurium, vecuronium, rocuronium and cisatracurium, respectively. Onset of action times were reported as 60 seconds, 75 seconds, 90 seconds, 90 seconds and 90 seconds for vecuronium, rocuronium, mivacurium, atracurium and cisatracurium, respectively [5].

We expected mivacurium and atracurium to be least expensive for brief operations of <30 minutes and vecuronium and rocuronium to be least expensive for brief operations of between 30 and 60 minutes, cisatracurium to be least expensive for operations of greater than 60 minutes because of difference in duration times of action.

In the current analysis we evaluated and compared NMB drug costs of starting dose and maintaining dose in different operation times depending on information leaflets of drugs for helping decision makers, in Turkey, for developing new strategies to minimize the cost of NMBs which is US\$ 2.3 million per year.

\*Address correspondence to this author at the Sogutozu M. 2176. Sok. N:5 K:9 Cankaya, Ankara, Turkey; Tel: + 90 544 795 0880; E-mail: guvenckockaya@yahoo.com

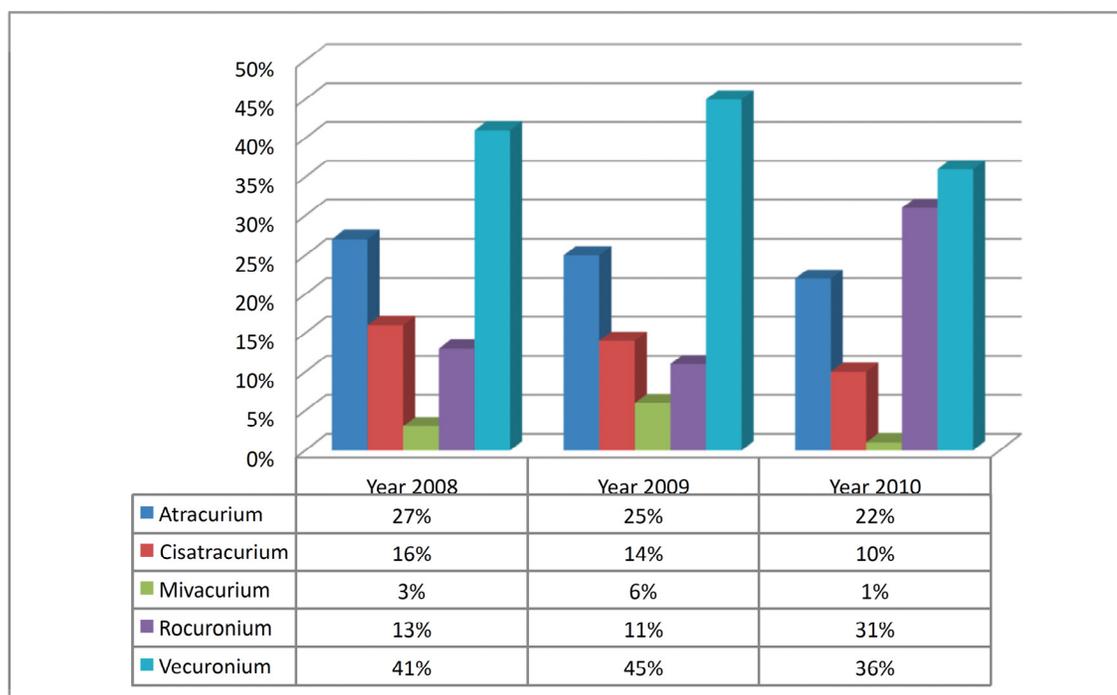


Fig. (1). Distribution of Sales of Neuromuscular Blockers in Unit (IMS Data).

## METHODS

Three different operation strategies were assumed. The first strategy was for operations under 30 minutes. Second strategy was for operations between 30 and 60 minutes (Mean 45 minutes). A third strategy was for operations above 60 minutes (Mean 90 minutes).

It was assumed that there were not any differences in other anesthetics which could be used in pre/per/post-operations or in other procedures (inhaled anesthetics, anesthesia antagonists like neostigmine, etc.). *For example, if a anesthesiologist wants to choose a NMB in a same operation type, the only difference between NMBs is cost of drugs.* Because of this, in this investigation only the cost of NMB drugs were compared for different operation times.

Costs of the drugs were taken from the Republic of Turkey Drug Pharmacy General Management Drug List [6] which was published on 16.04.2010. In Turkey, some neuromuscular blockers have original and generic brands. The cost per milligram of each of the drugs which were used in analysis were pooled by using original and generics costs per milligram. All costs were changed into US Dollars with TL/USD rate as 1.50, and calculated in USD (Table 1).

Table 1. Milligram Cost of Neuromuscular Blockers

Neuromuscular Blockers	Range Costs of 1 Miligram	Mean Costs of 1 Miligram
Atracurium	\$ 0.085 – 0.089	\$ 0.08
Cisatracurium	\$ 0.45 – 0.70	\$ 0.59
Mivacurium	\$ 0.37 – 0.40	\$ 0.38
Rocuronium	\$ 0.09 – 0.10	\$ 0.09
Vecuronium	\$ 0.38 – 0.50	\$ 0.44

Intubation and maintaining dosages of NMB drugs were taken from drug information leaflets of each drug. Drug dosages for intubation and maintaining for each kilogram were calculated depending on the leaflets since intubation and maintaining of all neuromuscular blockers are the same for adults and children (Table 2).

Atracurium's intubation and maintaining dosages were reported as 0.3-0.6 mg/kg and 0.1-0.2 mg/kg, respectively. The mean of the dosages were included for the calculations as 0.45 mg/kg and 0.15 mg/kg, respectively. First maintaining dosage was reported as in 20-45 minutes after the intubation dosage depending on clinical duration. Following maintaining dosages were reported as in every 15-25 minutes after the first maintaining dosage. The mean of the minutes were included for the calculations as 30 minutes and 20 minutes, respectively [7].

Cisatracurium's intubation and maintaining dosages were reported as 0.15 mg/kg and 0.03 mg/kg, respectively. Maintaining dosages were reported as in every 20 minutes after intubation dosage [8].

Mivacurium's intubation and maintaining dosages were reported as 0.07 – 0.25 mg/kg and 0.15 mg/kg, respectively. The mean dosage of intubation dosages were included for the calculation as 0.15 mg/kg. Maintaining dosages were reported as in every 15 minutes after intubation dosage [9].

Rocuronium's intubation and maintaining dosages were reported as 0.6 mg/kg and 0.15 mg/kg, respectively [10]. Although maintaining dosages were not reported directly in drug information, the duration of action time was reported as 45-70 minutes [5] in trials depending on clinical duration. It could be said that the time limit of duration of action of rocuronium is nearly the same as cisatracurium (60-80 minutes [8]). So rocuronium maintaining dosage times were

**Table 2. Neuromuscular Dosages, Application Times & Costs**

Neuromuscular Blocker Drug	Intubation Dosage	Maintaining Dosage	Maintaing Dosage Time	Cost of Milligram	Cost of Dosages (1 kg)	
					Begin.	Maint.
Atracurium	0.45 mg/kg (0.3-0.6 mg/kg)	0.15 mg/kg (0.1-0.2 mg/kg)	First 30 minutes (20-45 minutes) Following 20 minutes (15-25 minutes)	\$ 0.087	\$ 0.039	\$ 0.013
Cisatracurium	0.15 mg/kg	0.03 mg/kg	Every 20 minutes	\$ 0.59	\$ 0.088	\$ 0.017
Mivacurium	0.15 mg/kg (0.07-0.25 mg/kg)	0.15 mg/kg	Every 15 minutes	\$ 0.38	\$ 0.057	\$ 0.057
Rocuronium	0.6 mg/kg	0.15 mg/kg	Every 20 minutes (estimated from cisatracurium time)	\$ 0.09	\$ 0.054	\$ 0.013
Vecuronium	0.09 mg/kg (0.08-0.10 mg/kg)	0.0125 mg/kg (0.010-0.015 mg/kg)	Every 30 minutes	\$ 0.44	\$ 0.039	\$ 0.005

Numbers were rounded.

included as every 20 minutes after intubation dosage as with cisatracurium [10].

Vecuronium’s intubation and maintaining dosages were reported as 0.08-0.10 mg/kg and 0.010-0.015 mg/kg, respectively. The mean dosage of intubation dosages were included for the calculation as 0.09 mg/kg and 0.0125 mg/kg, respectively. Maintaining dosages were reported as in every 25-40 minutes after intubation dosage depending on clinical duration. The mean time of maintaing dosages were included for the calculation as 30 minutes [11].

NMB drug costs were approximated as follows: NMB drug usage for per kilogram X acquisition cost for per milligram amounts.

The cost of each drugs intubation, maitaining and total usages for each operation times were calculated for each operation strategy (Tables 2-5). Cost of mivacurium was calculated for only the first strategy because the duration of action time of mivacurium is 12-18 minutes [2]. Also in general, mivacurium is used for only short term operations like operations under 30 minutes. A cost-minimization analysis was performed depending on these results.

**RESULTS**

Atracurium had the lowest cost in milligram cost (\$0.08), followed by rocuronium (\$0.09), mivacurium (\$0.38), vecuronium (\$0.44) and cisatracurium (\$0.59) (Table 1). This ranking is not useful and was changed in operation cost rankings. Because the included dosages were chanced in different operation strategies. Only the cost of intubation dosages were included in operations under 30 minutes for all neuromuscular blockers. Cost of one intubation and one maintaining dosage were included in operations 30-60 minutes for all neuromuscular blockers. The main differences were in operations above 60 minutes because the duration of action times of neuromuscular blockers were different. So one intubation dosage and two maintaining dosages were included for atracurium, one intubation and three maintaining dosages were included for vecuronium, one intubation and four maintaining dosages were included for rocuronium and cisatracurium. The cost of mivacurium for operations 30-60 minutes and above 60 minutes were not calculated.

Atracurium and vecuronium had the lowest costs (US\$ 0.039) in operations which are under 30 minutes, followed by rocuronium (US\$ 0.054 ), mivacurium (US\$ 0.057) and cisatracurium (US\$ 0.088) (Table 3). Vecuronium had the lowest costs (US\$ 0.045) in operations which are 30-60 minutes, followed by atracurium (US\$ 0.052), rocuronium (US\$ 0.067) and cisatracurium (US\$ 0.10) (Table 4). Vecuronium had the lowest costs (US\$ 0.056) in operations which are 30-60 minutes, followed by atracurium (US\$ 0.078), rocuronium (US\$ 0.10) and cisatracurium (US\$ 0.15) (Table 5).

**DISCUSSION**

Many adults and children undergo anesthesia each year and receive muscle relaxants. The proportion of hospital operating costs directed to anesthetic pharmaceuticals is small, approximately 0.24% of hospital budget [2], however they are a great proportion of variable anesthetic supply costs [3]. Desicion makers develop new strategies to minimize anesthetic costs and maintain the quailty of health care. Because neuromuscular blocking (NMB) drugs constitute approximately 30% of the total anesthesia drug budget in the United States [4], these drugs are appropriate targets for cost-minimization strategies in anesthesia [3].

**Table 3. Cost-Minimization Analysis of Neuromuscular Blockers in Operations Below 30 Minutes**

Neuromuscular Blocker Drug	Operations Under 30 Minutes (Calculation: Only Int. Dsg.)
Atracurium	\$0.039
Vecuronium	\$0.039
Rocuronium	\$0.054
Mivacurium	\$0.057
Cisatracurium	\$0.088

Int.: Intubation, Dsg.: Dosages, Numbers were rounded.

A cost comparison of mivacurium and rocuronium for adult ambulatory surgery concluded that mivacurium was less expensive than rocuronium for ambulatory surgery of 1–2 hours duration, i.e., \$26.00 vs \$42.00 (US)[2].

**Table 4. Cost-Minimization Analysis of Neuromuscular Blockers in Operations 30-60 Minutes**

Neuromuscular Blocker Drug	Operations 30-60 (Mean 45) Minutes (Calculation: 1 Int.Dsg. + 1 Mtn. Dsg.)
Vecuronium	\$0.045
Atracurium	\$0.052
Rocuronium	\$0.067
Cisatracurium	\$0.106
Mivacurium	NA

Int.: Intubation, Dsg.: Dosages, Mtn.: Maintaining, Numbers were rounded.

**Table 5. Cost-Minimization Analysis of Neuromuscular Blockers in Operations Less than 60 Minutes**

Neuromuscular Blocker Drug	Operations Above 60 (Mean 90 minutes)	
	Calculation	
Vecuronium	\$0.056	(1 Int. Dsg + 3 Mtn Dsg.)
Atracurium	\$0.078	(1 Int.Dsg. + 3 Mtn. Dsg.)
Rocuronium	\$0.108	(1 Int. Dsg. + 4 Mtn. Dsg.)
Cisatracurium	\$0.159	(1 Int. Dsg.+ 4 Mtn. Dsg.)
Mivacurium	NA	NA

Int.: Intubation, Dsg.: Dosages, Mtn.: Maintaining, NA: Not available, Numbers were rounded.

A cost-minimization analysis was performed to compare the direct costs of various neuromuscular blocking agents (NMBAs) in procedures of specific durations in the USA. Secondary objectives were to review the role of the NMBAs studied with respect to their place on the hospital formulary, and to develop a pharmacoeconomic methodology to be applied to other formulary decisions. Patients were stratified according to estimated length of surgical procedure; group 1 (55 patients) included surgeries estimated to take less than 2 hours, and group 2 (55 patients) included those estimated to be 2-4 hours long. Patients were then randomized to one of three intermediate-acting NMBAs: atracurium, vecuronium, or rocuronium. Anesthesia records were used to obtain all anesthetic agents administered in the operating room, and drug costs were calculated from hospital drug acquisition costs. Postanesthesia care unit (PACU) costs were estimated from patient charges and converted to costs using the hospital's cost-to-charge ratio. Costs that were common to all study treatments or unrelated to the use of NMBAs were excluded from the analysis. Two time-adjusted costs were calculated to determine the cost of neuromuscular blockade/hour and the total anesthesia drug costs/hour. Atracurium was also significantly more costly than either vecuronium or rocuronium/hour (\$21.95 vs \$14.39 and \$16.07) and anesthesia cost/hour (\$28.77 vs \$22.82 and \$23.32). It was reported that vecuronium or rocuronium is preferred over atracurium in procedures with an estimated duration of 2-4 hours. In the patient population evaluated, there were no significant cost differences among the three NMBAs in surgeries with an estimated duration of less than 2 hours [12].

The costs of intermediate-acting neuromuscular blocking drugs in children during routine ambulatory surgery were compared for Canada. Two hundred subjects were enrolled in the study. The costs of NMB drugs at the time of the study in CND \$ /mg were: atracurium \$0.356/mg, cisatracurium \$0.9975/mg, mivacurium \$0.512/mg, rocuronium \$0.255/mg, and vecuronium \$1.874/mg. The cost of NMB drugs at 30 minutes for 10 kilogram patients in \$CDN were: atracurium \$1.45-1.83, cisatracurium \$0.87-1.11, mivacurium \$2.01-2.69, rocuronium \$1.64-2.05, and vecuronium \$1.98-2.43. The cost of NMB drugs at 60 minutes for 10 kilogram patients in \$CDN were: atracurium \$2.05-2.67, cisatracurium \$1.34-1.67, mivacurium \$3.51-4.68, rocuronium \$2.24-2.95, and vecuronium \$2.73-3.32[13]. Cisatracurium had the lowest cost for all durations.

The recommended doses of NMB drugs used in the OR are calculated by performing dose-response studies which include least-squares linear regression of the log-probit transformation of the administered doses. With these curves, both ED<sub>50</sub> and ED<sub>95</sub> are determined [13-16]. The dose of NMB drug administered to a patient is primarily based on the patient's age, the anesthetic being used, and ED<sub>95</sub> for the drug to be used. It is important to note that the ED<sub>95</sub> used in calculating the dose of NMB drug to be administered to the patient must have been calculated during similar clinical conditions. That is, an ED<sub>95</sub> calculated during balanced anesthesia is only applicable to other patients receiving a balanced anesthetic [13]. For the current study, we used published ED<sub>95</sub> values obtained during balanced anesthesia or inhaled anesthesia in information leaflets for each NMB.

Turkey uses reference pricing system. Spain is the one of reference countries for reference pricing system of Turkey [17]. Due this looking to the cost analysis of reference countries for evaluating a cost analysis for Turkey will be helpful. It was reported that atracurium had the lowest neuromuscular cost compared with cisatracurium, vecuronium and rocuronium in four groups of patients in age, weight or surgery duration in Spain [18].

There are some limitations in the analysis. Some costs such as anesthesia cost/hour, adverse reactions or post-anesthesia care unit costs were not included. It is necessary to perform another analysis by including these costs to obtain greater accuracy. Drug costs used were retail selling costs. But hospitals or hospital groups bought their drugs through auctions. So, the selling price of each drug will be different depending on the actual acquisition price. It is important to perform the analysis for different hospitals or hospital groups. There was not performed any budget impact analysis to hospital budgets. It is necessary to calculate the budget impact of chosen NMBs to hospital budgets. Although we estimated that the anesthesia procedures are the same in each patient, anesthesiologists perform different procedures for different patients. So it is necessary to perform the analysis in the light of clinical data which includes different patients and different procedures.

## CONCLUSION

If the limitations were disregarded, in our analysis: Atracurium and vecuronium had the lowest costs (US\$ 0.039) in operations which are under 30 minutes, followed by rocuronium (US\$ 0.054), mivacurium (US\$ 0.057) and

cisatracurium (US\$ 0.088). These results are similar as Spain which is Turkey's one of reference country for pricing pharmaceuticals. Vecuronium had the lowest costs (US\$ 0.045) in operation which are 30-60 minutes, followed by atracurium (US\$ 0.052), rocuronium (US\$ 0.067) and cisatracurium (US\$ 0.10). Vecuronium had the lowest costs (US\$ 0.056) in operation which are above 60 minutes, followed by atracurium (US\$ 0.078), rocuronium (US\$ 0.10) and cisatracurium (US\$ 0.15).

This means that the managements of hospitals or hospital groups which are in Turkey can choose atracurium and vecuronium in operations under 30 minutes, vecuronium in operations 30-60 minutes and above 60 minutes in their NMB formularies for making cost reduction from NMBs which comprise 30% of the total anesthesia drug budgets. On the other hand, there is little difference in the apparent costs of the intermediate acting drugs, and that factors such as aggressive purchasing negotiations, rational inventory control, minimization of waste, and decreasing use and doses of relaxants will have much more impact on cost than whether one relaxant or another is used. Further analysis is needed to be performed with new clinical and cost data.

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