

# Clinical Experience with Nondepolarizing Neuromuscular Blocking Agent Atracurium in Adults

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## Summary

*The new relaxant drug Atracurium was tested in clinical practice and the results revealed. 40 patients of the age of 25–62 years undergoing abdominal surgery were given the drug, monitored and clinically investigated in order to evaluate the properties of the drug. It can be concluded that atracurium can be successfully used for endotracheal intubation. The rate of recovery after single or repeated bolus is fast and predictable and can be accomplished without the need for neostigmine. Nevertheless paralysis can be rapidly antagonised by neostigmine. It has no cardiovascular side effects, none or only slight cumulation, and causes probably very slight release of histamine. Its inactivation is likely to be independent of renal and hepatic function.*

Muscle relaxants are widely used drugs, extremely important for everyday anesthetic practice. In spite of this there has not yet been found a drug, which could be labelled "ideal relaxant drug". All those in current use possess important side effects potentially dangerous for anesthetized patients. This situation led to wide research in the last two decades and as well to the formulation of features of so called "ideal relaxant drug". Those characteristic features first formulated by Karis and Gissen in 1971 are the following:

Such a drug should possess:

1. nondepolarizing way of action
2. suspension of action should not depend on function of liver or/and kidney
3. products of degradation should not possess relaxant properties
4. the drug should be short acting and there should not be cumulation after repeated doses of drug
5. the specificity for muscle end-plate should be high
6. there should not be negative side effects to the other systems
7. reversal of the block should be easy.

After this had been postulated, people researching in this field started to work on hundreds of promising drugs. One of the best, we had the possibility to work within clinical practice, is atra-

curium dibesylate, which is distributed under the name "Tracrium" by the firm Wellcome, UK. This drug possesses the special way of elimination, so called "Hoffmann's elimination", very useful for anesthetic practice. This elimination is performed only by the influence of body temperature and pH of blood and because of that does not depend on renal and hepatic functions.

Our clinical research in adult patients at University Teaching Hospital in Motol, Prague 5 Czechoslovakia was finished in March 84.

We investigated 40 patients undergoing abdominal surgery of age 25-62 and body weight of 45–116 kg. 32 were women and the age group of 40–60 years was the biggest one.

According to general conditions of patients, the group could be divided into two. The group we started our research with were healthy adults. But in the last period of research we worked also with patients suffering from important cardiovascular and other diseases.

Since we wanted to obtain as precise information as possible according to the action of drug we chose the kind of operations demanding very good relaxation.

The patients were premedicated by pethidine 1 mg/kg, atropine 0,01 mg/kg and diazepam 0,2 mg/kg. This was used as a standard way of

premedication to achieve as equal general condition of all the patients as possible. After preoxygenation of the patient we induced anesthesia by the thiopentone 5 mg/kg b.w. and then the relaxant atracurium in the initial bolus of 0,5 mg/kg b.w. was administered.

Monitoring of the patients blood pressure, heart rate and ECG was provided by Kardiomonitor Tesla LKM 200. The values were measured in two minutes intervals for six minutes before and 10 minutes after the administration of atracurium, then in intervals of 5 – 10 minutes.

We observed that there was certain time interval from the administration of the relaxant drug to the achievement of the best conditions for tracheal intubation. Most of the patients were intubated within 60 – 90 sec after the administration of the drug as recommended in the literature. But we noticed, that there were patients in sufficiently relaxed conditions to be intubated even sooner and some patients where we had to wait up to 120 sec. from administration of atracurium.

We decided to evaluate conditions for tracheal intubation into four groups. As the first group – *excellent* conditions – we evaluated situation, when tracheal tube went into the trachea without any effort and there was no cough after that, as *satisfactory* conditions – second – group we considered the situation, when tracheal tube got the trachea without any problem but there was some cough after that, as *bad conditions* – third group – we evaluated the situation, where we were not sure that we could provide atraumatic intubation inspite of vocal cords being a bit open. We then used another relaxant for tracheal intubation. And in the last group – in only one patient – there was no abduction of vocal cords at all, inspite of our waiting for 4 minutes from administration of the drug. We tried to give another bolus of atracurium 0,25 mg/kg b.w. but there was no change in situation at all. Because of that we decided to use minimum dose of suxamethonium 40mg/kg after which intubation was performed in an excellent way. It is extremely interesting that in this patient we decided to continue with atracurium during the operation and relaxation was evaluated by the surgeons – usually quite hard to please – as very good. The dosage and the time intervals for application were the same as in other patients.

The monitoring of blood pressure, heart rate and ECG was carried out to inform us if there is any influence of atracurium to the other systems, especially cardiovascular one. We concluded, that there is no important influence neither in group of

healthy patients nor in the sick ones.

After the administration of atracurium bolus for tracheal intubation we used neuroleptanalgesia. Controlling ventilation by Narkosespiromat Dräger tidal volume 550 – 750 ml, frequency 14 – 16/min.

The first bolus of atracurium 0,5 mg/kg b.w. provided good relaxation for most of the patients for 30 – 40 minutes. Because of precise evaluation of exact time of relaxation we always waited until there was some sign of clinical reversal of block – for example changing tone of muscles, starting to fight the ventilator, or slight movement of head and so on.

We observed that although the anesthetist noticed these signs, there never was any complaint by the surgeons – therefore we concluded that surgical relaxation was still good. The fact, that we were waiting till those signs appeared is probably the reason for our times of relaxation being a bit longer than those mentioned in the literature. After the second, third and other doses of atracurium we noticed, that the time of relaxation remained standard and predictable. It means that the drug possesses minimum cumulation. Side effects, we observed during and after administration of atracurium are summarized (table No. 1). We

TABLE 1 *Side effects of atracurium*

	%	
Bronchospasm	0	0
Hypotension	2	5
Exanthema	5	12,5
Cough	1	2,5
Hiccup	1	2,5

focused mainly on the signs of manifestation of histamine – release exanthema, hypotension and bronchospasm and signs of unsatisfactory relaxation, cough, hiccup. Bronchospasm was never observed. Slight hypotension occurred in two cases but not necessarily in connection with atracurium since they were suffering from hypertension. Relatively often exanthema was observed but we were not sure if it was not due to thiopentone. Once cough was observed, we solved the problem by administering atracurium in shorter intervals. In one case the hiccup was observed about 15 minutes after the administration of atracurium and the problem was again solved by application of another bolus. And, of course, we were interested in reversal of block at the end of the operation. The

results are shown in table 2. When it was possible to predict the time for the operation to be finished the atracurium was administered in such a way that there was no need to use antidote. That situation occurred in 876.5% of cases (table No. 2). Of the

TABLE 2 *Suspension of action of atracurium*

Reversal	%	
Spontaneous	35	87,5
With antidotes /Neostigmine 1,0 – 1,5 mg i.v./	512,5	

12,5% of the patients, needing the application of reversal-drugs two groups are clearly definable: The first group were those in whom the operation finished in a very short time after its beginning, in the second group the surgeons needed complete relaxation till the last stitch of the skin.

In the very end I would like to summarize our first experience with the new relaxant drug "Tracrium" – Welcome – and at the same time to compare its properties with those for "ideal relaxant drug".

Atracurium, although from the group of competitive relaxant drugs, is excellent for tracheal intubation. It has no negative adverse effects to other – especially cardiovascular – systems. After the bolus which is satisfactory for tracheal intubation, the time of relaxation is shorter and better to predict than with the other relaxant drugs available. The suspension of action does not depend

on renal and hepatic functions. The products of degradation have no curarimimetic effects. And at last, reversal, if necessary, can be perfectly made by neostigmine. If we are to compare the claims for properties of "ideal relaxant drug" and the drug "atracurium" we could conclude that atracurium fulfils almost all of them. If one point was to be assigned to each of the claimed properties – atracurium fully gains six out of the seven possible.

#### Literature

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