Title: Effects of isoflurane anesthesia residual levels on the reversal of a vecuronium induced neuromuscular blockade.

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Introduction.
In clinical conditions, the neuromuscular transmission impairment produced by nondepolarizing blocking agents are enhanced by various halogenated anesthetics -including isoflurane- when sustained anesthetic concentrations are maintained. These alterations are clearly anesthetic concentration dependent. Furthermore, the maintenance of enflurane or isoflurane anesthetics can impede the antagonism by anticholinesterases of various nondepolarizing neuromuscular blocking drugs.[1,2] This study was undertaken to document the consequences of isoflurane discontinuation -about 15 min- upon the reversal of a vecuronium paralysis obtained by a fixed atropine/neostigmine dosis given at a precise prereversal twitch height. The final degree of neuromuscular blockade antagonism was assessed by recording the twitch height, train-of-four recoveries, as well the tetanic stimulations, to document the relative sensitivity of these tests for the detection of the residual impairment of the neuromuscular transmission.

Methods and materials.
Thirty-six anesthetized patients, ASA class I-II, (with informed consent and approval by the Research Committee, Brussels Free University, ULB, Brussels, Belgium) undergoing elective surgery were monitored (isometric adductor pollicis mechanical activity) to detect the effects of isoflurane anesthesia discontinuation upon the reversal of a vecuronium paralysis. Neuromuscular block was produced by vecuronium 100 microg/kg and additional doses of 20 microg/kg until termination of surgery. The patients were randomly divided into three groups: CONTROL group (n=12) whose patients received only fentanyl/N_2O; ISOSTABLE group (n=12), where isoflurane at end-tidal concentration of 1.25% was maintained until the end of anesthesia and ISOSTOP group (n=12), for which isoflurane 1.25% was terminated 2 min before neostigmine administration. In all groups, paralysis was reversed with 15 microg/kg atropine and 40 microg/kg neostigmine I.v. when the twitch height regained spontaneously 25% of its control value. To determine isoflurane blood concentrations, heparinized blood samples were taken simultaneously from ipsilateral arterial and peripheral venous sites, and from the superior vena cava 3 min before and 16 min after neostigmine administration. Twitch height was measured every 10 seconds and train-of-four (2 Hz) every 3 min for a 15 min period after antagowere sequentially assessed in a random fashion.

Statistical analysis of the data was performed with the one-way analysis of variance test, according to SPSS package program. The statistical comparisons were considered significant at $p < 0.05$.

Results.
No significant differences were found between the three groups considering the final twitch heights and tetanic fades at 50 Hz. In the ISOSTABLE group, final mean train-of-four was significantly lower : 75% vs 88%. Mean tetanic fades 100 Hz were significantly lower in the ISOSTABLE group (31%) than in the ISOSTOP group (57%) and in the CONTROL group (84%). All results are summarized in the table.

Conclusions.
Our conclusions are : first, 15 min isoflurane discontinuation partially enhances the reversal of a vecuronium paralysis. Second, after the antagonism of a vecuronium paralysis, tetanic fade 100 HZ is useful to detect the slight impairments of the neuromuscular transmission induced by residual isoflurane concentrations.

References.
1. Deslisle S, Bevan DR : Impaired antagonism of pancuronium during enflurane anesthesia in man. Br J Anesth 54 : 441-445, 1982.
2. Dernovoi B, Agoston S, Barvais L, Baurain M, et al : Neostigmine antagonism of vecuronium paralysis during fentanyl, halothane, isoflurane and enflurane anesthesia. Anesthesiology 68 : 698-701, 1987.

Table.
VALUES (%) OF TOF, TF50, TF100 AT THE 15th MIN (MEAN +/- SEM)

	TOF	T.F. 50 Hz	T.F.100 Hz
CONTROL	88+/-2	94+/-1	84+/-4
ISOSTABLE	75+/-2	86+/-3	31+/-5
ISOSTOP	88+/-2	88+/-4	57+/-4

**: STATISTICALLY SIGNIFICANT DIFFERENCES ($p < 0.01$)

Title : Effects of different dosages of atropine, mixed with a fixed dose of neostigmine, on the reversal of a vecuronium induced neuromuscular blockade.

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Introduction.
Atropine is an antimuscarinic drug, clinically used to block adverse muscarinic effects of anticholinesterase agents, when the latter are used to reverse residual neuromuscular blockade produced by muscle relaxants. The results observed in man[1] and cats[2] seem indicate that atropine may well influence the neuromuscular junction. This study investigates this possible role in human clinical anesthesia, when atropine is given simultaneously with neostigmine to reverse a vecuronium induced paralysis.

Methods and materials.
Thirthy-six patients, ASA class I-II (with informed consent and approval by the Research Committee, Brussels Free University, ULB, Brussels, Belgium) undergoing elective surgery were monitored (isometric adductor pollicis mechanical activity). Diazepam 0.2 mg/kg was given orally one hour prior surgery. Anesthesia was induced with thiopental 3-5 mg/kg, fentanyl 5 microg/kg and dehydrobenzperidol 100 microg/kg I.v. For maintenance of anesthesia, all patients received only fentanyl and N_2O. Neuromuscular block was produced by vecuronium 100 microg/kg and additional doses of 20 microg/kg until completion of surgery. Intubation was performed when twitch tension was abolished, ventilation was controlled mechanically (semi-closed circuit, 33% O_2 in N_2O) and was adjusted to produce normocapnia. For reversal of paralysis, the patients were randomly divided into three groups of 12 patients each and received a fixed dose of 40 microg/kg neostigmine, mixed with atropine, 10 microg/kg in the first group (A10), 15 microg/kg in the second group (A15), and 20 microg/kg in the third group (A20), when twitch tension spontaneously regained 25% of its control value. After the administration of the neostigmine/atropine mixtures, the following variables were observed during a 15 min period: twitch height was measured every 10 s and train-of-four (2 Hz), every 3 min. Immediately thereafter, tetanic fades -50 and 100 Hz, 5 s duration, 1 min apart- were assessed sequentially in a random fashion. Statistical analysis of the data was performed with the one-way analysis of variance test, according to SPSS package programs. The comparisons were considered significant at $p<0.05$.

Results: All results are summarized in table 1. There are no significant differences between the three groups, except for the 100 Hz, tetanic fades: the mean value of the A10 group (70%) is significantly lower than the values of 84% and 81% recorded respectively in the A15 and in the A20 groups.

Conclusions: Mixed with a fixed dose of 40 microg/kg of neostigmine, the best dosage of atropine, to reverse a vecuronium induced paralysis in the anesthetized patient, and in the conditions described in this study, is higher than 10 microg/kg. The results confirm that atropine, in the clinical dosages usually used, seems well play a role -even if this role is not of major importance- at the neuromuscular junction. Moreover, 100 Hz tetanic fade is the only test able to detect the slight differences of residual neuromuscular blockade between the three groups, after antagonism of a vecuronium induced paralysis. The extent of its clinical significance remains to be investigated.

References:
1. Wall FA, Bradshaw EG, Suer AH, Dark CH: Atropine enhances neuromuscular transmission in humans. Fundam Clin Pharmacol, 1: 59-66, 1987.
2. Alves-do-Prado W, Corrado AP, Prado WA: Reversal by atropine of tetanic fade induced by antinicotinic and anticholinesterase agents. Anesth Analg, 66: 492-496, 1987.

Table 1
Values of TOF, TF 50, TF 100 at the 15th min (MEAN +/- SEM)

GROUP	T.O.F.%	T.F.50 %	T.F.100 %
A10	87+/-1	90+/-1	70+/-3
A15	88+/-2	94+/-1	84+/-4
A20	89+/-1	93+/-1	81+/-2

* Statistically significant differences ($p<0.05$)