TITLE: **VECURONIUM OR ATRACURIUM FOR ORTHOTOPIC LIVER TRANSPLANTATION**

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Vecuronium elimination is considered to be predominantly hepatic and plasma clearance has been shown to be decreased markedly in patients with cirrhosis (1). To further elucidate the role of the liver in its metabolism, we compared the requirements of vecuronium during the anhepatic phase of orthotopic liver transplantation (OLT) with the requirements during the other two phases. Atracurium, which does not depend on the liver for elimination (2) was given to a control group.

Two groups of patients undergoing OLT were studied after approval by our Ethics Committee. Group 1 (n = 10), aged 42 ± 8 yr (mean ± SD), weighing 63 ± 6 kg received vecuronium while group 2 (n = 7), aged 50 ± 8 yr, weighing 61 ± 14 kg received atracurium for neuromuscular blockade. The patients were premedicated with hydroxyzine 100 mg orally and anesthesia was induced by thiopental 5 mg.kg-1. Vecuronium 0.1 mg.kg-1 or atracurium 0.6 mg.kg-1 was given for intubation. Anesthesia was maintained with a continuous infusion of midazolam (50 µg.kg-1.h-1) and fentanyl (10 - 12 µg.kg-1.h-1), and neuromuscular blockade with an infusion of veruronium (initial rate 0.1 mg.kg-1.h-1) or atracurium (initial rate of 0.6 mg.kg-1.h-1). Mechanical ventilation was performed with an oxygen-air mixture. End-tidal CO2 tension was maintained between 30 and 36 mmHg. The ulnar nerve was stimulated supramaximally and the evoked compound action potential of the hypothenar muscles was recorded (RELAXOGRAPH, DATEX corp. Finland)) continuously (3). The rate of infusion of vecuronium and atracurium was adjusted by an increase or decrease of 25% of the infusion rate every 15 min to maintain a single twitch depression (T1/TC) (the height of the first twitch of the train-of-four with respect to the control twitch height) at less than 10%. The amount of muscle relaxants were calculated during the 3 stages of OLT (mg.kg-1.h-1). Preoperative and postoperative (day 7) liver function tests were recorded in order to investigate the possibility that the requirements of vecuronium after reperfusion of the transplanted liver might be used as a predictor of graft function. Results are expressed as mean ± SD. Statistical analysis was performed using repeated measures ANOVA followed by appropriate post-hoc tests ($p < 0.05$ considered was significant).

The results are summarized in the table. Requirements of vecuronium are signficantly reduced during anhepatic phase, whereas requirements of atracurium did not change during the 3 phases of OLT. No correlation was found between the clotting factor V and the transaminases level postoperatively and the requirement of vecuronium in postreperfusion phase.

This study shows that during the anhepatic phase metabolism of vecuronium is dramatically reduced, whereas atracurium metabolism is unchanged. In conclusion, continuous atracurium administration provides a stable muscular relaxation during OLT.

References: 1) Anesthesiology, 62: 601- 605, 1985
2) Br.J. Anaesth. 58: 96S-102S, 1986
3) Br.J. Anaesth. 58: 1447-1452, 1986

Table mg.kg-1.h-1	Dissection phase	Anhepatic phase	Reperfusion phase
Vecuronium	0.072 ± 0.022*	0.036 ± 0.012	0.065 ± 0.018*
Atracurium	0.87 ± 0.40	0.62 ± 0.13	0.75 ± 0.28

* $p < 0.05$ vs Anhepatic phase, mean ± SD.

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TITLE: EFFECTS OF 3 INTUBATING DOSES OF ORG 9426 IN HUMANS

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ORG 9426, a nondepolarizing steroidal muscle relaxant, has an onset time twice as fast as vecuronium in cats(1)and its ED95 in humans is 285 mcg/kg.(2)After institutional approval, 2.0, 2.5 or 3.0 ED95 doses of ORG 9426 (570, 710 or 850 mcg/kg) were randomly administered to 30 ASA 1 or 2 consenting patients, age 18-65, having general surgery, to determine the drug pharmacodynamics.

After premedication, anesthesia was induced with thiopental and fentanyl and maintained with 60% N20, 02 and narcotic. The ulnar nerve was stimulated with supramaximal 2 Hz Train-Of-Four (TOF) every 10 sec. Contraction of the thumb was quantitated with a force transducer and recorded. When anesthesia and TOF were stable, patient received ORG 9426 and intubation was carried out at maximal depression of the first TOF response (T_1). The following parameters were measured = time intervals from the injection of ORG 9426 to :1) 90% depression of T_1 (T_1 90% block), 2) maximal T_1 depression (onset time), intubating conditions, clinical duration (time for T_1 to reach 25% of control), heart rate, blood pressure and any adverse clinical experience.(See Table 1)

ORG 9426 provided adequate intubating conditions with all doses. Its onset time was rapid (60% of 2xED$_{95}$ vecuronium) but increasing doses did not shorten the onset. T_1 90% block was reached even faster (about 1 minute) when intubation may have been possible. Clinical duration of ORG 9426 was short (60% of 2x ED$_{95}$ vecuronium) and increased with increasing doses. No clinically significant changes in heart rate and blood pressure and no adverse clinical experience was noticed.

These findings fully warrant further clinical evaluation of ORG 9426 for endotracheal intubation.

References: 1) Br J Anaesth, 63,400-10,1989
2) Anesthesiology,71,A773;1989

TABLE I (Means + Standard Error of Mean)

9426 Groups	2xED95 n=10	2.5xED95 n=10	3xED95 n=10
T_1 90% Block (sec)	75±6	73±8	77±11
Onset times (sec) (T_1=100% block)	111±11	109±13	110±18
Intubation Conditions	6 exc. 4 good	9 exc. 1 good	8 exc. 2 fair
Clinical duration (min)	27±5*	39±3*	45±4*

*Significantly different at p level ≤ 0.01(ANOVA)