Title: DESFLURANE (I-653) POTENTIATION OF PANCURONIUM BROMIDE: A COMPARISON WITH ISOFLURANE

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Introduction Inhalational agents have been shown to reduce the required dosage of relaxant. This study compares equivalent MAC concentrations of desflurane and isoflurane on pancuronium dose response.

Methods Patients who were ASA Class I-II gave informed consent to participate in this IRB approved study. Patients received midazolam 0.02-0.08 mg/kg intravenously 15-30 min. prior to surgery. Anesthesia was induced with sodium thiopental 4-8 mg/kg, nitrous oxide 60%, and isoflurane 2.1% or desflurane 9.0%. Intubation was performed without muscle relaxant. Following intubation a stable concentration of inhaled agent of 0.65 (low dose) or 1.3 MAC (high dose) was confirmed by infrared gas analysis (Datex-PB). This concentration was maintained for 15 minutes. Pancuronium bromide in 0.005 mg/kg doses was administered incrementally until T1 depression of greater than 90% occurred.

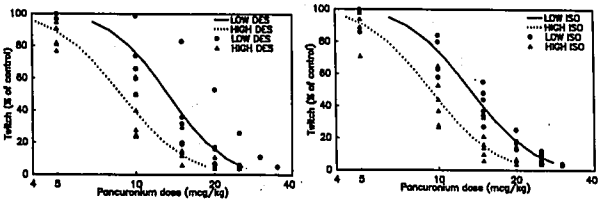
The ulnar nerve was stimulated by surface electrodes at the wrist every 12 seconds. Train of four was measured with a Grass FT-10 Transducer.

ED50 and ED95 for pancuronium bromide under isoflurane and desflurane anesthesia in low and high dose were calculated by probit analysis of the total dose vs. blockade. Values were compared by analysis of variance. $P<0.05$ was considered significant.

Results Twenty-three patients were studied. Analysis of ED50 and ED95 values reveals no difference between desflurane and isoflurane at either low or high concentrations. Both inhaled agents significantly reduced ED50 and ED95 when the high dose was compared to low dose ($p<0.02$).

Discussion Both desflurane and isoflurane decrease the ED50 of pancuronium below that of balanced anesthetic (29.5 mcg/kg). The neuromuscular potentiation of desflurane is remarkably similar to isoflurane at both high and low doses. Desflurane should therefore be easy to incorporate into practice.

Figure 1,2 Effect of low and high dose inhaled agent concentration on pancuronium dose.



	Des Low (n=5)	Des High (n=6)	Iso Low (n=6)	Iso High (n=6)
ED50 (mcg/kg)	13.3±4.0	8.8±1.7	13.4±1.7	9.3±1.8
ED95 (mcg/kg)	25.8±6.3	18.7±3.6	27.9±3.4	19.8±3.7

1. Anesthesiology 65:1-5, 1986

A904

TITLE: PHARMACOKINETICS OF ATRACURIUM DURING CONTINUOUS INFUSION UNDER FENTANYL ANESTHESIA.

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Introduction Pharmacokinetic data for muscle relaxants are traditionally determined following a single dose. Such data can be used to design infusion regimens, although its accuracy in describing the pharmacokinetics during continuous infusion is unknown. This study was undertaken to determine the pharmacokinetics of atracurium during continuous infusion by a model-independent method.

Method After institutional approval and informed consent, 20 patients were studied. The age of the patients was 57±8 yr, weight 74±14 kg, with 13 male and 7 female. Anesthesia was induced with thiopentone and fentanyl and maintained with nitrous oxide and incremental doses of fentanyl. Atracurium was infused for 60min according to a predetermined profile to maintain stable muscle paralysis. The infusion maintained a constant plasma concentration (Cpss) after 20-30min with the infusion rate becoming constant after 39min. Arterial blood samples were taken with the atracurium concentration determined by an HPLC assay.

The clearance of atracurium (Cl) was estimated after 50-60min by the constant infusion rate (Ia) required to maintain the Cpss, such that: $Cl = Ia/Cpss$

The volume of distribution of atracurium (Vd) was estimated after 60min using a method described by Gibaldi and Perrier (ref 1), by: $Vd = Xss/Cpss$ $Xss = Xd - Cl.AUC$

where Xss is the amount of drug in the body at 60min, Xd is the total dose administered and AUC is the area under the plasma concentration time curve to 60min. Data presented as mean±SD.

Results A constant plasma concentration during 50-60min was confirmed in all patients by a less than 5% drift in plasma concentration. The estimated Cl of atracurium was 3.4±0.8 ml/kg/min and Vd was 119±35 ml/kg (n=20).

Discussion With a single dose method, the estimated Cl of atracurium under fentanyl anesthesia is 5.8±1.1 ml/kg/min and Vd is 152±39 ml/kg (n=4, ref 2). The 41% lower estimate of Cl found in this study is unlikely to be due to errors with our method. A constant rate infusion maintaining a steady-state plasma concentration is an accurate method for estimating Cl.(ref 1) The method tends to overestimate Cl if measurments were not made under steady-state conditions, which is the only assumption with this method. Single dose pharmacokinetic data may be inaccurate for atracurium due to modelling the drug as a single entity when it is a mixture of 10 isomers with varying pharmacokinetic parameters.(ref 3).

This study was supported by the Faculty of Anaesthetists, Royal Australasian College of Surgeons and Wellcome Australia Limited.

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