Title: **INOTROPIC AND ELECTROPHYSIOLOGICAL EFFECTS OF PROPOFOL ON ISOLATED VENTRICULAR MYOCARDIUM**

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Introduction: Clinical studies have shown that propofol (P) reduces the systemic blood pressure primarily by decreasing systemic vascular resistance rather than by compromising the pumping function of the heart (1). The aim of the present *in vitro* study was to investigate the direct effects of P on the inotropic, lusitropic, and electrophysiological properties of ventricular myocardium.

Methods: Isolated guinea pig papillary muscle was used to determine the influence of P on the isometric force of contraction (cumulative concentration-response curve, time-response curve, and mechanogram) and on the transmembrane action potential (AP) [1 Hz, 35 °C].

Results: P had a concentration-dependent (0.01-300 µm/l) maximal negative inotropic effect of 76 ± 4% and 65 ± 7% compared with the pre-drug value on the papillary muscles of animals pretreated with reserpin (RES) [7.5 mg/kg b.wt. i.p.,16-18 h prior to the study] and on untreated animals (nRES) respectively. The IC_{25} values were 16 ± 11 µmol/l (6-36; n = 6) for RES and 17 ± 15 µmol/l (6-45; n = 6) for nRES; the IC_{50} values were 70 ± 41 µmol/l (29-130; n = 6) for RES and 78 ± 44 µmol/l (39-140; n = 6) for nRES.These values did not differ significantly in either of the groups. P at a concentration of 45 µmol/l (= 8 µg/ml; equivalent with the maximum plasma level following a P bolus injection of 2,5 mg/kg b.wt. [2]) reduced the developed force of contraction (Fc) by 39.4 ± 3.9%, the maximal rate of rise of Fc ($+dFc/dt_{max}$) by 23.9 ± 3.8%, the maximal rate of fall of Fc ($-dFc/dt_{max}$) by 49.9 ± 3.3%, the time to peak Fc by 19.9 ± 1.5%, and the total period of isometric contraction by 7.0 ± 1.8% as compared to the pre-drug value. The ratio of $+dFc/dt_{max}$ and $-dFc/dt_{max}$ was increased by 37.8 ± 5.2 %, while the halftime for isometric relaxation (RT1/2) remained unaltered. The resting membrane potential, the AP amplitude, and the AP duration at 90% repolarisation showed no significant differences with P (45 µmol/ l, n = 5). However, the AP duration at the plateau level (at 20% repolarisation; phase 2) decreased significantly by 13.5 ± 2.3%.

Discussion: The results show that P has a negative inotropic effect under *in vitro* conditions which are not influenced by systemic vascular resistance or neuro-humoral changes. This effect is dose-dependent, should not interfere with catecholamines stored endogenously and is accompanied with an impairment of relaxation. The mechanical data implicate that the delayed isometric relaxation is caused by an impaired function in the sarcoplasmic reticulum (SR) rather than by a change of the calcium responsiveness of the contractile proteins.The P mediated shift of the AP plateau towards repolarisation may suggest a decrease of transsarcolemmal calcium influx. In conclusion the results suggest that both the depression of the transmembrane calcium influx and the inhibition of the calcium uptake of the SR contribute to the negative inotropic effect of P.

References: (1) Sebel PS, Lowdon JD: Anesthesiology 71:260-277, 1989; (2) Kirckpatrick T et al.: Br J Anaesth 60:146-150, 1988

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TITLE: ESMOLOL ATTENUATES THE INCREASE IN INTRAOCULAR PRESSURE DURING LARYNGOSCOPY AND INTUBATION

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Bolus doses of 100-200mg of esmolol (ES) immediately prior to laryngoscopy and intubation (L&I) will prevent tachycardia and mitigate systolic hypertension. Because of its rapid onset and brief duration of action, ES may be an effective adjunct to use with succinylcholine during a rapid sequence induction procedure to prevent a potentially dangerous increase in intraocular pressure (IOP). The purpose of this study was to test the efficacy of a single-dose bolus of ES in preventing the increase IOP during L&I.

With informed consent and institutional approval, 20 ASA I patients from our Same-Day Admission unit were randomly assigned to receive ES 200mg IV, or saline. Premedication consisted of 1-3mg of midazolam and 10-20mcg of sufentanil IV, 20 min prior to induction, and .06mg of d-tubocurarine (dTC) and 20cc of ES or placebo 3 min prior to a standardized induction with thiopental 5mg/kg and succinylcholine 2mg/kg. A third group of 10 patients did not receive ES, but received 30-40mcg sufentanil premedication instead. IOP was measured 1) prior to premedication; 2) after sufentanil; 3) 3 min after dTC and ES; 4) 15 sec after thiopental; 5) 20 sec; and 6) 40 sec after succinylcholine; and at 7) 15 sec, 8) 1 min, and 9)2-3 min after L&I. Systolic BP and HR were recorded every min during the study. Analysis of variance for repeated measures was used for analysis.

Baseline IOP, BP, and HR were similar for the two groups. IOP increased slightly after midazolam and sufentanil, probably the result of CO_2 retention. Three min after dTC and ES or saline, IOP returned to baseline, but BP and HR decreased with ES. Thiopental decreased IOP and BP below baseline and they remained below baseline after succinylcholine. L&I produced an immediate increase in IOP, HR, and BP in the saline group, and an increase in IOP and SBP in the ES group, although the change was not as great; HR remained constant in the ES group. Covariate analysis revealed a significant association between the increase in BP and IOP. Therefore, ES will attenuate the increase in IOP with L&I, but is not as effective as narcotic agents in preventing the increase in IOP during laryngoscopy and intubation.