TITLE: DIRECT AND INDIRECT EFFECTS OF KETAMINE ON MAMMALIAN VENTRICULAR MYOCARDIUM

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Ketamine is a cardiovascular stimulant through its sympathomimetic effects. Yet, its direct inotropic effect has been reported as positive in rat (1) and negative in rabbit (2) ventricular myocardium. This study re-examines the effect of ketamine on the contractile properties of mammalian ventricular myocardium in the presence and absence of beta-adrenergic blockade.

Methods. Each of eight ferret right ventricular papillary muscles was exposed to ketamine HCl (10^{-6}M to $3x10^{-4}$M in 0.5 log M increments) while contracting isometrically at 30°C at 4 second stimulus intervals. This protocol was repeated for nine muscles pre-exposed to the beta-adrenoceptor antagonist bupranolol HCl (10^{-7}M). Values of developed force (DF, mean± SE) were compared within groups to corresponding control values and between groups at each ketamine concentration with Student's paired t-tests with Bonferroni correction.

Results. Ketamine exerted a concentration-dependent positive inotropic effect that was maximal at 10^{-4}M (Fig. 1); at $3x10^{-4}$M ketamine's inotropic effect decreased. Bupranolol abolished ketamine's positive inotropic effect and unmasked a marked impairment of contractility at ketamine 10^{-4}M (Fig. 2).

Discussion. Ketamine's effects on the myocardium are in part mediated by a direct or indirect activation of the beta-adrenoceptor; ketamine may impair catecholamine uptake by sympathetic post-ganglionic nerve terminals or by myocardial cells (3). In addition, ketamine exerts an intrinsic depressant effect on the contractile apparatus, the mechanism of which is yet to be defined.

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References:

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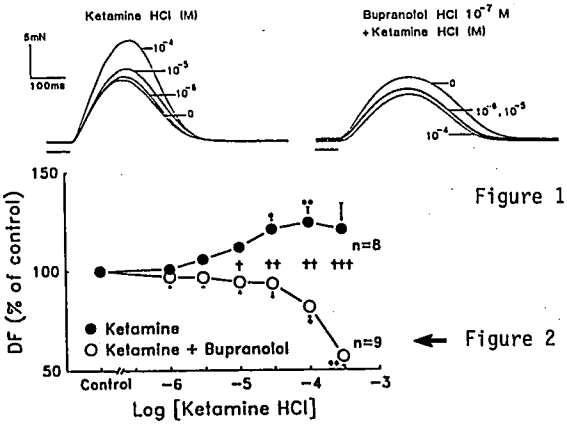

Figure 1

← Figure 2

TITLE: IDEAL MIXTURE OF SODIUM NITROPUSSIDE AND TRIMETHAPHAN

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A Mixture of sodium nitroprusside (SNP) and trimethaphan (TM), empirical 1:10 weight ratio[1], has been advocated to counteract their mutual untoward effects. The purpose of this study was to investigate the effect of various ratios of a SNP and TM mixture on heart rate (HR), renal sympathetic nerve activity (RSNA), and renal artery blood flow (RBF) in order to find the ideal ratio of SNP and TM for induced hypotension.

Seven mongrel dogs were anesthetized with α-chloralose and the lungs were mechanically ventilated. The left kidney was exposed retroperitoneally by a left flank incision. Renal sympathetic nerves along the renal artery were isolated and placed on a bipolar silver electrode for recording RSNA. An ultrasonic transit-time blood flowmeter was placed around the renal artery. After a steady state was established, various ratios of a SNP and TM mixture were infused in a randomized fashion for 10 min at one hour intervals to obtain a steady mean arterial blood pressure of 75±5 mmHg while measuring HR, RSNA, RBF.

Percent changes of HR and RSNA as compared with control values (before initiating induced hypotension) are shown in Figs.1 and 2. There were significant positive correlations between SNP/TM ratio and % change of HR (r=0.630, p<0.01), and % change of RSNA (r=0.844, p<0.01). Percent change of RBF and calculated renal artery resistance (RAR) are shown in the Table. SNP to TM ratio, 1:2.5 resulted in the most stable RSNA(108±17%), but caused a moderate increase in HR (138±11%).

The untoward effects of SNP include reflex tachycardia and reflex activation of the sympathetic nervous system since SNP does not attenuate the baroreflex. The untoward effects of TM stem from its ganglionic blocking property and include bradycardia and diminished efferent sympathetic nerve activity . TM alone depressed RSNA the most significantly but increased HR slightly(110±12%). It has been reported [2] that HR may either increase or decrease, depending on the sympathetic and parasympathetic balance during TM infusion. Nevertheless, TM seems to counteract the reflex tachycardia caused by SNP. RBF was well maintained with various mixture of SNP and TM because of a reduction of renal artery resistance. Our results indicate that a mixture of SNP and TM, approximately 1:2.5 ratio, may provide stable sympathetic nerve activity and therefore catecholamine release would not be enhanced.

References: 1. Anaesthesia 36:312-315, 1982
2. J Anaesth 44:523-527, 1972

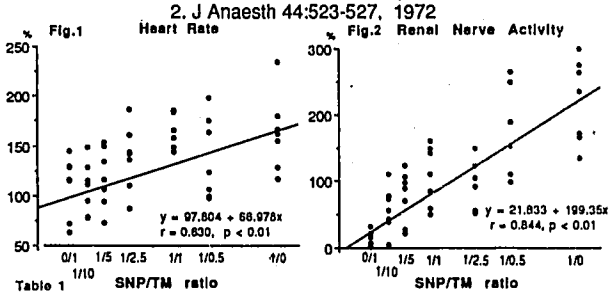

Table 1

SNP/TM ratio	control	0/1	1/10	1/5	1/2.5	1/1	1/0.5	1/0
RBF(%)	100	98±9	90±11	105±6	109±8	120±10	111±7	150 ±25
RAR(%)	100	67* ±9	67* ±60	58* ±2	55* ±4	53* ±4	53* ±5	47* ±9

Values are mean±SE. RBF: renal blood flow, RAR: renal artery resistance
*p < 0.01 compared with control values

Statistical analysis : ANOVA followed by the Newman-Keuls' test