Title: ESMOLOL IS NOT ASSOCIATED WITH AN EXAGGERATED SUCCINYLCHOLINE MEDIATED HYPERKALEMIC RESPONSE

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INTRODUCTION. Acute administration of beta blockers in dogs has been associated with an increased hyperkalemic response to succinylcholine(SCh).[1] In light of several studies demonstrating that esmolol is beneficial in attenuating the hypertensive and tachycardic responses to induction of anesthesia and intubation, it is important to determine whether acute administration of esmolol similarly potentiates serum potassium rises due to SCh. This study was undertaken to evaluate this potential drug interaction.

METHODS. After approval from the Institutional Review Board, informed consent was obtained from 10 adults scheduled for elective surgery. Patients with conditions known to exaggerate SCh induced increase in plasma K^+ (massive trauma, widespread neuromuscular disease) were excluded. Diazepam 10 mg was given PO 60 mins prior to induction of anesthesia. Study patients were randomized into 2 groups. Group 1 (n=5) served as control (no esmolol). Patients in group 2 (n=5), received an IV infusion of esmolol, initially at a rate of 500 mcg/kg/min over 2-5 mins prior to induction of anesthesia. After adequate response was noted (20-25% decrease in heart rate) the infusion rate was reduced to 50-300 mcg/kg/min and maintained during the procedure. After application of appropriate monitors, anesthesia was induced in all patients with an IV injection of sodium thiopental, 4-6 mg/kg and SCh, 1.5 mg/kg followed by inhalation of isoflurane 1% in nitrous oxide and oxygen, 60:40. Muscle relaxation was monitored and maintained with vecuronium according to surgical need. Patients were ventilated to maintain $F_{ET}CO_2$ between 28-38 mm Hg. Heart rate and blood pressure were continuously monitored. Arterial blood samples were drawn as follows: prior to esmolol administration (Group 2 only), prior to SCh injection and at 1,3,5,10,15,20,30,45,60, and 90 minutes thereafter. All samples were collected in heparinized syringes and immediately cooled in melting ice. Plasma was separated and analyzed for potassium concentration using ion specific electrodes in a Beckman E4 analyzer. Intergroup differences of plasma K^+ were analyzed using the unpaired t-test. Intragroup comparison was done using the paired t-test. The threshold for statistical significance was taken as p 0.05 in all cases.

RESULTS. Results are summarized in the Table and Figure. Both groups of patients had statistically significant increases in plasma K^+, which were of similar magnitude. The rise in plasma K^+ in the control group was significant at 5 and 10 mins after SCh in the control group, while the response was delayed to 15 and 20 mins in the esmolol group. Group 2 patients had no significant change in plasma K^+ attributable to the esmolol loading prior to succinylcholine injection.

DISCUSSION. Although several groups have looked at the potential for an exagerated hyperkalemic response in beta blocked subjects receiving SCh, results have been conflicting. Studies in dogs[1] have demonstrated a greater increase in serum K^+ in acutely beta blocked animals compared to controls, while in humans[2] there was no difference between those receiving beta blockers compared to controls. These differing experimental results may be attributed to the fact that the animal studies involved acute beta blockade while the human studies focused on patients receiving chronic beta blocker therapy. Our patients received esmolol hydrochloride, a new short acting $beta_1$ (cardioselective) blocker. Based on the previous human beta blockade studies, we suspected that esmolol treated patients would not have a greater rise of plasma K^+ compared to the controls. Brown et al[4] attributed the enhanced potassium rise in beta blocked subjects to the failure of K^+ reuptake by extrarenal tissue, a $beta_2$ receptor mediated effect. Goldhill et.al[3] confirmed this in dogs by comparing the effects of a $beta_1$ blocker (metoprolol) with those of a $beta_2$ blocker (ICI 118551). In our study, esmolol, a metoprolol analog, similiarly did not significantly increase the magnitude of the SCh induced elevation in plasma K^+ when compared to controls but did prolong the time to peak K^+ concentration after SCh, and the duration of the increase. This seems to be due to the very specific $beta_1$ action of esmolol which does not impede potassium reuptake. The development of new $beta_1$ selective adrenergic blocking agents greatly facilitates anesthetic management of patients with complex medical conditions. Beta-adrenergic blockade may be desirable in attenuating the response to the stress of both anesthesia and surgery.[5]. It is reassuring to know that patients with significant medical problems who may benefit from $beta_1$ blockade can be given esmolol, without the risk of precipitating acute hyperkalemia should SCh be indicated for muscle relaxation.

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3. Goldhill DR, et al: Brit J Anaesth 59;611-616, 1987.
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TABLE OF RESULTS (MEAN ± S.D, n=5 in each group)

	CONTROL	ESMOLOL	P
AGE (yr)	47 ± 13	45 ± 15	0.5(NS)
WEIGHT(kg)	87 ± 13	91 ± 10	0.97(NS)
BASE K^+ (mEq/L)	3.82 ±.23	3.92 ±.28	0.56(NS)
K^+ CHANGE (mEq/L)	0.56 ±.32*	0.49 ±.30*	0.75(NS)
K^+ max (mEq/L)	4.38 ±.39*	4.34 ±.31*	0.86(NS)

* significantly different from baseline