TITLE: SUFENTANIL REDUCES ALL COMPONENTS OF HEART RATE VARIABILITY

AUTHORS: TW Latson, MD, DC Martin, MD, CW Whitten, MD, KW Klein, MD, J Elmore, MD
AFFILIATION: UT Southwestern Medical School, Dept of Anesthesiology, Dallas, Texas 75235

INTRODUCTION: Analysis of heart rate variability (HRV) has been used as a non-invasive measure of autonomic nervous system (ANS) function in both awake and anesthetized subjects. This analysis measures the amplitude of small oscillations in HR associated with homeostatic sympathetic (SY) and parasympathetic (PS) reflexes.[1] Sufentanil (SU) is an anesthetic that decreases SY tone and increases PS tone. The purpose of this study was to examine the effect of SU on these SY and PS HR oscillations. HR oscillations occurring with a cycle time of less than 8 sec are mediated exclusively by the PS system, whereas oscillations of longer cycle times are mediated primarily by the SY system. In awake subjects, changes in SY or PS activity cause corresponding changes in the amplitude of these HR oscillations. If these results from awake subjects can be extrapolated to anesthetized subjects, then SU should cause a decrease in SY oscillations and an increase in PS oscillations.

METHODS: After institutional approval and informed consent, continuous digital recordings of the EKG (250 Hz) were obtained in 9 patients anesthetized for elective cardiac surgery. Anesthesia was induced with a loading dose of SU 0.5 µg/kg IV, followed by infusion of 0.5 µg/kg/min (total dose: 3.0 ± 0.8 µg/kg). After loss of consciousness, patients were given vecuronium 10 mg IV and ventilated by mask with 100% O_2 for the 3 min post-drug study period.

A continuous HR signal was derived from the EKG. The amplitude of the oscillations in this HR signal were quantified by power spectral analysis[2] of representative 105 sec epochs from the pre-drug and post-drug study periods. Summation of the spectral power in appropriate frequency ranges provides an index of the drug effects on both SY (HRVsy: 0-0.125 Hz) and PS oscillations (HRVps: 0.126-0.4 HZ).

RESULTS: As shown in Fig 1, SU administration ("SU") caused significant reductions in both the SY (large, slow HR oscillations) and PS (smaller, more rapid HR oscillations) components of HRV. The relative effects on SY and PS oscillations were quantified by the reductions in HRVsy and HRVps. HRVsy was reduced by 87% ±5% (mean ±SEM; p<.01, paired Student's t test). HRVps was reduced by 75% ±6% (p<.02).

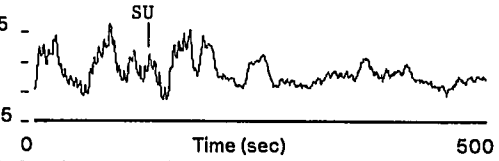

Figure 1.

DISCUSSION: These results show a consistent reduction in both HRVsy and HRVps during induction of anesthesia with SU. The reduction in HRVsy is consistent with the known "sympatholytic" effects of this drug. However, the reduction in HRVps caused by an anesthetic drug known to increase PS activity suggests that the direct relationship between PS tone and HRVps demonstrated in awake subjects may not be valid in anesthetized subjects. Since all prior studies with anesthetics (isoflurane, desflurane, ethrane, and pentothal) have shown a decrease in HRVps, this may represent a non-specific effect of general anesthesia. Alternatively, one previous animal study using vagal stimulation did suggest that large increases in vagal tone might reduce HRVps by reducing the relative influence of the respiratory reflexes mediating HRVps on total vagal activity.[3] This study may be the first evidence of this phenomenon in man.

REFERENCES: 1)Circ Res 59:178-93, 1986. 2)Anesth Analg 70:S226,1990. 3)Am J Physiol 256:H142-H152, 1989.

A374

Title: A CHANGE IN THE EFFECTIVENESS OF ESMOLOL WHEN USED IN REPEATED DOSES IN ELECTROCONVULSIVE THERAPY.

Authors: MB Howie, MD, TD McSweeney, BS, DA Zvara, MD, JA Coffman, MD, HA Black, MD.

Affiliation: Department of Anesthesiology, Ohio State University Hospitals, Columbus, Ohio 43210

Introduction: Previous work has shown that esmolol effectively blunts the hemodynamic response to electroconvulsive therapy (ECT). In this randomized double blind study we determined any loss of effect of esmolol in controlling maximum heart rate (MHR) when used repetitively on alternate days with the patients acting as their own control.

Methods: 20 ASA III adults requiring ECT were studied (160 cases) with 4 esmolol and 4 placebo trials. An infusion of placebo (P) or esmolol (E) 500 ug/kg/min was administered for 4 mins with preoxygenation, followed by 1 mg/kg of methohexitol and 0.5 mg/kg of succinylcholine. Electroshock (ES) was applied after muscle relaxation was confirmed. The infused solution was decreased to 300 ug/kg/min for 3 mins after ES, and then discontinued.

Results: Baseline heart rates were not different at any time. The MHR response in the placebo group always rose to clinically and statistically significant higher levels. Esmolol controlled MHR compared to placebo. However by the fourth treatment day the Esmolol's MHR was significantly greater (p<0.05) than the previous 3 E treatments, even though the E group MHR was still significantly less than placebo.

Conclusion: Though relatively large doses of Esmolol were given to these patients with good evidence of control some decreasing effectiveness could be detected.

This trial of 160 infusions clearly indicates that repeated doses of esmolol and adrenergic stimulation may cause a change in the status of the cardiac beta receptor [up regulation] compared to the earlier administration.

Table 1. Demographics (N=20)

	Mean+SD
Age (yr.)	42 ± 16
Height (inch)	67.2 ± 3.4
Weight (kg)	75.0 ± 16.8
Body Surface Area (M^2)	1.86 ± 0.21

Table 2. Comparison of Baseline and Maximum Heart Rates (N=160)

	Trial 1 Mean+SD	Trial 2 Mean+SD	Trial 3 Mean+SD	Trial 4 Mean+SD
E base	83±15	87±19	83±15	82± 7
P base	83±15	83±13	86±17	84±15
E MHR	109±24[AB]	111±26[AB]	113±21[AB]	129±23[B]
P MHR	144±24[B]	153±19[B]	154±26[B]	156±23[B]

Note. [A]Indicates p<0.05 difference between trial 4 and trials 1,2, and 3. [B]Indicates p<0.05 difference between P and E trials. SD indicates standard deviation. Base indicates baseline measurement.