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ALFENTANIL DOES NOT POTENTIATE THE NEGATIVE INOTROPIC EFFECTS OF PROPOFOL AND MIDAZOLAM IN PERFUSED ISOLATED RAT HEARTS.

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Propofol(P) and midazolam (M) in combination with alfentanil (AF) are now largely used for total intravenous anesthesia. These anesthetic agents variably cause cardiovascular depression in vivo (1), but their direct cardiac effects have not been compared. Therefore, we examined their comparative effects on myocardial contractility assessed by left ventricular (LV) dp/dt_{max} in isolated rats hearts.
After IP heparinisation (500 IU) 48 Wistar rats were decapitated and their hearts quickly removed and perfused retrogradely through the aorta according to a constant flow perfusion technique The perfusate is a modified Krebs-Henseleit solution (37°C) oxygenated and equilibrated to achieve a normal acid-base balance with a membrane oxygenator supplied by O2 et CO2. The O2 partial pressure amounts to 500±30 mmHg in the aortic cannula with a pH value of 7,4±0,05. A thin filled fluid latex balloon was placed in the LV in order to monitor LV pressures. This balloon was inflated to maintain a constant LV volume and to produce a LVEDP of 10 mmHg.The hearts were paced at a constant rate of 300 beats.mn^{-1}.
After a 30 min period of stabilisation and baseline measurements, four (C_{1-4}) increasing concentrations of AF [0.57,0.74,0.92,1.1 μgml^{-1}],M[11.2 14.9,18.4,21.9 μgml^{-1}],P[5.4,7.2,8.9,10.5 μgml^{-1}] or combination with the same dosages were perfused intracoronarily to a given heart for 10 min periods. After the last dilution (C_4) the hearts were perfused with the normal perfusate for 10 min and recovery readings were obtained.
Data on dp/dt_{max} are expressed as per cent of the average of the control and recovery values(table)

mean ± sem	C1	C2	C3	C4
AF (n=8)	98±2	105±6	100±3	101±2
P (n=10)	86±1,8*	81±1,8*	76±1,7*	71±1,7*
M (n=10)	83±2,1*	66±2,8*¶	51±5,5*¶	40±3*¶
P+AF(n=10)	80±1,9*	82±2,1*	78±1,9*	74±2,3*
M+AF(n=10)	86±4,1*	62±5,2*	43±2,9*	36±2,9*

(* P<0,05 vs controls - ¶ P<0,05 P vs M)
(ANOVA and appropriate post-hoc tests)

In this model,and at clinically relevant dosages, our results show that: 1) AF alone caused no change in the myocardial performance of isolated rats hearts. 2) P and M caused a dose related decrease in LV dp/dt_{max}. M is a more potent depressor than P.The slopes of the dose-effect curves are significantly different (P<0,001). 3) AF does not potentiate the negative inotropic effects of P and M.

References
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INOTROPIC EFFECT OF ALFENTANIL, FENTANYL, AND SUFENTANIL

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Narcotics are widely used for induction and maintenance of general anesthesia. In clinical doses alfentanil, fentanyl, and sufentanil are considered to have minimal,if any, myocardial depressant activity [1,2]. We examined and compaired the effect of these drugs on the denervated rabbit myocardium.

The protocol was approved by the institutional animal investigation committee. Each New Zealand white rabbit (n=6), 2-3 kg, was anesthetized with halothane. The heart was immediately removed and the septum was perfused via the first septal perforator artery with Kreb-Ringer-Bicarbonate buffer solution equilibrated with 95% O_2 and 5% CO_2. Each septum was stimulated supramaximally, 5 volts 5 msec, at 1.7 Hz with a pair of field electrodes and the isometric contraction was stabilized for 30 min. before the experiment began. The baseline peak tension was more than 2 times the resting tension in each preparation. The perfusates were alfentanil 0.5, 5.0, 50.0 mcg/ml, fentanyl 0.1, 1.0, 10.0 mcg/ml, and sufentanil 0.05, 0.5, 5.0 mcg/ml, individually given for 3 min. at random sequences. The peak developed tension (T) and its maximal acceleration (+dT/dt) and deceleration (-dT/dt) were recorded and calculated as % of baseline response. The time from stimulation to beginning of contraction (latency), the time from beginning of contraction to peak tension (TPT), and the time duration of isometric relaxation to half tension ($RT_{½}$) were measured. The cycle of measurements were repeated for each perfusate. Data (mean ± SD) were analyzed with repeated measures ANOVA and Dunnett's contrast for $p < 0.05$.

At the highest concentration of alfentanil, fentanyl, and sufentanil, a decrease in T (Fig. 1), +dT/dt, and -dT/dt was seen. There was no change in latency, TPT, and $RT_{½}$ from baseline at any concentration. A complete recovery of the myocardium occured within 2 minutes during each perfusate washout.

The results suggest that alfentanil, fentanyl, and sufentanil cause minimal direct myocardial depression. Only in concentrations 2 orders of magnitude greater than their respective blood concentration is there a statistically significant negative inotropic effect. The decrease in T at high concentration may suggest that calcium influx is inhibited, calcium release from the saroplasmic reticulum is decreased and/or the sensitivity of the contractile proteins is decreased.

References:
1. Anesth Analg 58:390-5, 1979
2. Br J Anaesth 55:1835, 1983