TITLE: NOREPINEPHRINE PLASMA CONCENTRATIONS AND CARDIOVASCULAR EFFECTS

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Norepinephrine (NOR) is used as a vasopressor and not regarded as a positive inotropic agent at dosages above 0.03µg/kg min[1], but there are no reports on the relationship between plasma levels during infusion of NOR and the cardiovascular effects.

After approval of the ethics committee of the university and informed consent a cumulative dose-response curve was performed in 7 healthy volunteers. In an ascending order NOR was infused in 5 dosages (0.01, 0.06,0.1,0.14 and 0.2 µg/kg min) each infusion lasting 30 min. During the last 10 min of each infusion rate M-mode echocardiography (Diasonics R3400, 2.25 MHz transducer) was performed and the M-mode echo, blood pressure (from a radial artery cannula) and ECG simultaneously recorded on paper. From the enddiastolic dimension (DD,mm) and the end-systolic dimension (DS,mm) the fractional shortening was calculated (FS=(DD-DS)/DD, %). Heart rate (HR, b/min) was derived from the ECG, systolic blood pressure (PS, mmHg) from the paper record. Additionally the quotient PS/DS (ESQ, mmHg/mm) was calculated as an index of the positive inotropic state. The arterial NOR plasma concentrations were measured by HPLC/ECD. For statistical evaluation analysis of variance and linear least square regression analysis were performed using the SAS statistic program.

The NOR plasma concentration increased from 199±75 ng/l before infusion to 7475±1071 ng/l during the 0.2 µg/kg min infusion rate. The increases in PS and ESQ were correlated to the logarithm of the NOR plasma concentrations ($p < 0.05$).

Table 1: Values before infusion and during the highest infusion rate

	PS	HR	DD	DS	FS	ESQ
base line	123 ±14	64 ±9	54 ±3	36 ±2	32.5 ±1.9	3.4 ±0.3
0.2µg/kg min	178* ±17	50* ±9	54 ±3	35 ±2	35 ±2.5	5.0* ±0.5

* indicates $p < 0.05$, analysis of variance.

The changes of the cardiovascular parameters show a positive inotropic effect of NOR. The ESQ as an index of the positive inotropic state is dependent on afterload. But the combination of an increase in the ESQ with an unchanged DD, DS and FS clearly demonstrates a positive inotropic effect despite the increase in vagal activity shown by the decrease in heart rate.

Reference
1. Crit. Care Med. 6:409-416, 1982

TITLE: **HEMODYNAMIC RESPONSE TO INDUCTION OF INTRAVENOUS ANESTHESIA SUPPLEMENTED WITH PENTAMORPHONE OR FENTANYL**

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Pentamorphone (A-4492-10) is a new potent morphinan derivative that has a duration of action similar to that of fentanyl. We compared the hemodynamic response to induction of anesthesia and tracheal intubation after an intravenous infusion of pentamorphone or fentanyl.

After Institutional Review Board approval, 24 consenting ASA class I to III patients who were 18 to 70 years old and scheduled for elective operations were part of a multicenter study. Patients were randomly assigned to receive an intravenous infusion of pentamorphone (1.0 µg/kg [n=16]) or fentanyl (7.5 µg/kg [n=8]). Patients received no premedication. A 5 ml/kg intravenous infusion of balanced salt solution was given before induction of general anesthesia. After recording blood pressure and heart rate, patients received an infusion of one of the study drugs. All patients received thiopental in a dose sufficient to induce loss of eyelash reflex (3 to 5 mg/kg), and succinylcholine (1.5 mg/kg), followed by tracheal intubation. After intravenous induction of anesthesia, blood pressure and heart rate were measured again. Data are summarized as mean ± SD. Student's t test for the paired samples was used to determine the significance of the difference.

Data are summarized in the table. Five patients who received pentamorphone compared to one who received fentanyl experienced an increase in blood pressure.

Table: Hemodynamics before and after induction.

	Pentamorphone		Fentanyl	
	Before	After	Before	After
MAP	95±19	90±20	92±14	73±5*
HR	73±13	61±16*	70±14	54±5*

* p<.05

Narcotic administration during intravenous induction of general anesthesia is used to blunt the sympathoadrenal response to laryngoscopy and intubation. We found that fentanyl effected a consistent fall in heart rate and blood pressure. On the average, pentamorphone appeared to maintain better control of blood pressure. However, the response in blood pressure was inconsistent. It appears that pentamorphone offers no advantage compared to an equipotent dose of fentanyl in supplementing intravenous induction of anesthesia.

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