Title : THE EFFECTS OF EPINEPHRINE AS AN ADJUVANT TO EPIDURAL MORPHINE

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Introduction. Vascular uptake of local anesthetics from the epidural space is reduced by addition of epinephrine 1/200,000, and the intensity and duration of neural blockade is enhanced (1). This study was undertaken to see if the effects of epidural morphine are modified in a similar fashion.

Methods. Three healthy male volunteers, aged 20-33, gave informed consent to this study protocol, which had received internal institutional approval. They received 10 mg preservative-free morphine sulfate in 10 ml epidurally (L2-L3) at two sessions several weeks apart. Plain morphine was given at one session and morphine with 1/200,000 epinephrine at the other. One subject returned for a third session to receive epidural epinephrine 1/200,000 without morphine. Subjects were studied for 24-26 hours and the following observations were made at intervals. 1. Serum concentrations of morphine. 2. Cold pressor response test (CPRT) by ice-water immersion of hand and foot. 3. Segmental level of hypalgesia to ice and pin-prick. 4. Resting end-tidal PCO2 (PetCO2) and ventilation at PetCO2 = 55 torr ($\dot{V}55$) from serial CO2-response curves. 5. Onset and duration of non-respiratory side effects (pruritus, nausea, vomiting and urinary retention).

Results. Blood levels of Morphine: Vascular absorption was reduced by epinephrine. Peak concentrations 30 minutes after injection were (means ± SD), 44 ± 12 ng/ml after plain morphine and 13.7 ± 6.7 ng/ml after epinephrine. Analgesia: Epinephrine increased the speed of onset of cutaneous hypalgesia and the duration of analgesia to ice water immersion of hand or foot (Table I and Figures 1 and 2).

Table I. (Means ± SD)		(n = 3) Plain MSO4	(n = 3) MSO4 + Epi.
Time for Cutaneous Hypalgesia to V3 (hr)		6.5	4
Duration: Regression of CPRT to 20% of Control (hr)		10	22
Pruritus:	Incidence	2/3	3/3
	Onset (hr)	3.0	2.6 ± 0.2
	Duration (hr)	4.4	12.7 ± 3.6
Nausea:	Incidence	2/3	2/3
	Onset (hr)	4.9	5.1
	Duration (hr)	4.5	13.8
Vomiting:	Incidence	1/3	2/3
	Onset (hr)	8.75	8.25
	Duration (hr)	0.5	8.25
Respiration:			
Resting PetCO2 at 10th hr (torr)		40.7	47.2
% change of $\dot{V}55$ at 10th hr		-26.3 ± 8.7 *	-68.2 ± 7.7
Incidence of apneic spells lasting 20-50 sec at 6 - 16th hr		0/3	2/3
Urinary Retention			
Mean duration (hr)		11.3	18.8
Naloxone reversal required for micturition		1/3	2/3

* p<0.05

Discussion: The effects of epinephrine on epidural morphine were qualitatively similar to effects on epidural local anesthetics. Epinephrine reduced vascular uptake of morphine and enhanced all effects attributable to neuraxial action. Speed and extent of segmental hypalgesic spread were increased and duration was prolonged. All side effects due to cord and brainstem action were consistently prolonged and intensified and were more distressing, to the point where we decided not to extend the study beyond 3 subjects at this dose of epinephrine-morphine. Respiratory depression was particularly alarming in the 6 -16th hour period, and required close supervision. Epidural epinephrine alone caused limited and tenuous segmental hypalgesia and pilo-erection from T10 to L1 lasting for 6 hours. We conclude that epinephrine probably exerts these effects by permitting increased uptake of morphine into the csf and neuraxis. In additon, epinephrine may have a direct but limited effect on the spinal cord. We recommend that epidural morphine dosage should be reduced if epinephrine is used as an adjuvant.

Reference:

1. Burfoot MF, Bromage PR: The effects of epinephrine on mepivacaine absorption from the spinal epidural space. Anesthesiology, 35:488-492, 1971.

EPIDURAL MORPHINE : ROSTRAL SPREAD OF HYPALGESIA, INFLUENCE OF EPINEPHRINE IN 3 VOLUNTEERS

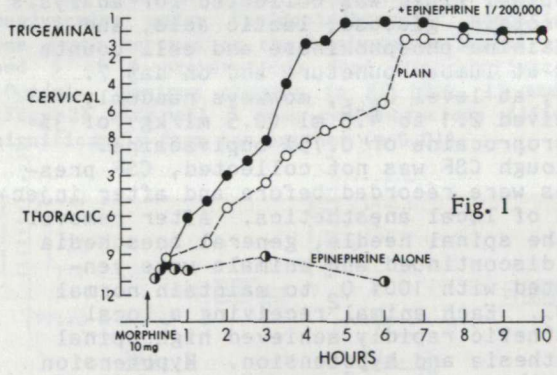

Fig. 1

EPIDURAL MORPHINE : COLD PRESSOR RESPONSE TEST IN 3 VOLUNTEERS PLAIN vs EPINEPHRINE 1/200,000 (MEAN ± SD)

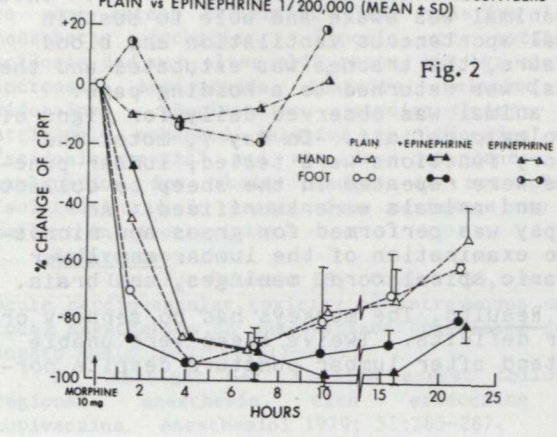

Fig. 2