Title: ANTIANALGESIC EFFECT OF ETOMIDATE

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Introduction. Etomidate is gaining popularity as the hypnotic component of a totally intravenous technique consisting of combinations of etomidate with a narcotic. It is known that etomidate, like barbiturates, does not produce analgesia. However, there is no information in the literature on whether etomidate has an antianalgesic effect which is typical for barbiturates.[1,2]

The aim of the present study was to investigate how etomidate affects an analgesic-induced increase in the pain threshold, and analgesic-induced suppression of cardiac acceleration response to noxious stimulation.

Methods. Two series of experiments were performed in Sprague-Dawley rats. In one series (50 rats), etomidate-morphine interaction was studied in relation to motor reaction threshold to pressure on the tail; in another series (50 rats), etomidate-morphine interaction was investigated with regard to cardiac acceleration response to the tail clamp.

Reaction threshold was determined with an "Analgesy-meter" (Ugo Basile), which provided pressure on the tail increasing at a constant rate until the animal responded with a coordinated struggle.[3] The effect of morphine was designated as positive if the individual reaction threshold to pressure exceeded the mean threshold of control group by two standard deviations of the mean. In one subseries of experiments, the morphine dose-effect curve was determined (probit analysis) without etomidate; in another, with etomidate. Morphine (doses from 0.1 mg/kg to 2 mg/kg) and etomidate (1 mg/kg) were injected intravenously. Morphine ED_{50} doses for both subseries of experiments were compared with Student's t-test.

Cardiac acceleration response was induced by placement of a hemostat in the middle of the tail for 60 sec.[4] The heart rate (HR) was obtained from an electrocardiogram. A microcomputer based cardiotachometer counted the number of beats during a 15 sec interval with the output updated every 5 sec. In one subseries of experiments, animals received morphine; in another subseries, morphine was administered in combination with etomidate (doses in the table). Morphine and etomidate (or saline) were injected intravenously, 15 and 2 min, respectively before tail clamping. After injection of morphine, the animals received tubocurarine 1 mg/kg, followed by endotracheal intubation. Controlled ventilation was provided with a Rodent Respirator.

Results. It was found that etomidate (1 mg/kg) increased morphine ED_{50} for reaction threshold to pressure from 0.2 mg/kg to 1.0 mg/kg ($p < 0.001$). Etomidate also weakened the inhibitory effect of morphine on the cardiac acceleration response to noxious stimulation (table).

Conclusion. Etomidate in rat experiments demonstrated a pronounced antianalgesic effect. The antianalgesic effect of etomidate is qualitatively similar to the well-known effect of pentobarbital. This finding may be explained by the suggestion that the morphine-induced increase in motor response threshold and suppression of cardiac acceleration response result primarily from activation of central nervous system inhibitory control mechanisms; etomidate depresses these mechanisms, and therefore antagonizes the effect of morphine.

MORPHINE-ETOMIDATE INTERACTION IN RELATION TO CARDIAC ACCELERATION RESPONSE

Series	Doses of Morphine	N	Baseline** HR (bpm)	↑ HR (bpm)
Morphine	3	5	391 ± 23+	33 ± 11+
	4	5	404 ± 17	25 ± 11
	6	5	379 ± 14	8 ± 6
	10	5	405 ± 28	6 ± 4
	15	5	387 ± 27	0 ± 0
Morphine-Etomidate*	3	5	405 ± 26	59 ± 15
	10	5	409 ± 16	42 ± 6
	30	5	406 ± 19	59 ± 11
	100	5	402 ± 17	49 ± 12
	300	5	436 ± 16	24 ± 8

*Dose of etomidate in all groups was 1 mg/kg;
**baseline before the noxious stimulation; + mean ± SEM.

References:

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