NEUROMUSCULAR TRANSMISSION II

A792

TITLE: PANCURONIUM POTENTIATES THE EEG EFFECT OF ISOFLURANE IN DOGS

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Forbes *et al* reported that pancuronium (PNC) reduced the MAC of halothane in man by 25%.[1] Subsequent study by Fahey and colleagues failed to replicate this result.[2] In order to clarify the relationship between neuromuscular blockade and the effects of volatile anesthetic on the brain, the present study was designed to determine the effect of pancuronium on steady state electroencephalographic burst suppression produced by isoflurane.

Anesthesia was induced in 5 dogs by mask inhalation of isoflurane and oxygen. Tracheal intubation was accomplished without neuromuscular blockade and ventilation continued with isoflurane and oxygen to maintain end-tidal carbon dioxide tension at 32-36 mm Hg as measured by infrared analysis. Intravenous and arterial catheters were inserted and lactated Ringers solution was infused at 4ml/kg/hr. Constant temperature was maintained with warming blankets.

The analog EEG was recorded from bifrontal platinum subdermal electrodes with a Neurotrac monitor. Isoflurane dose was adjusted to achieve EEG burst suppression (high voltage high frequency activity alternating with periods of electrical silence). The mean end-tidal concentration of isoflurane administered was 3.04 ± 0.4 volume percent. The end-tidal isoflurane concentration was measured by infrared analysis and maintained constant for each animal throughout the experiment. After at least 90 minutes at steady state, pancuronium 0.1 mg/kg was administered iv and the EEG again recorded after documentation of neuromuscular blockade by absence of response to tetanic stimulation. After partial recovery from neuromuscular blockade, as documented by appearance of single twitch to train of four stimulation, neostigmine 0.05mg/kg and glycopyrolate 0.01mg/kg were administered iv and the EEG recorded again.

The raw EEG was analyzed for percent time in isoelectricity and the values before pancuronium, after pancuronium and after neostigmine were compared by repeated measures analysis of variance.

As shown in the table, pancuronium administration resulted in more profound burst suppression characterized by increased time of EEG electrical silence. This effect was reversed by the administration of neostigmine.

Isoflurane in increasing concentrations is known to produce a progressive effect on the EEG, from continuous activity to burst suppression to complete electrical silence. The duration of electrical silence during burst suppression increases with increasing anesthetic dose. The potentiation of isoflurane EEG burst suppression by pancuronium suggests that isoflurane anesthetic action is enhanced either by neuromuscular blockade or by the direct CNS effect of pancuronium.

References

1. Anesth Analg 58:497,1979
2. Anesthesiology 71:53,1989

EFFECT OF PANCURONIUM ON ISOFLURANE EEG

	Isoflurane	Isoflurane + PNC	Neostigmine
% of EEG isoelectric (mean ± SD)	22.5 ± 9.9	35.9 ± 11.7 *	20.2 ± 8.0

* $P < 0.05$ compared to isoflurane alone

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TITLE: REDUCTION IN VECURONIUM INFUSION DOSE REQUIREMENTS BY NICARDIPINE IN HUMANS

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Although potentiation of neuromuscular blockade by calcium antagonists was shown in animals[1,2], it is not clear whether, or to what extent, this potentiation could occur in clinical settings. The present study was designed to analyse quantitatively the interaction of nicardipine with vecuronium using a constant infusion technique[3].

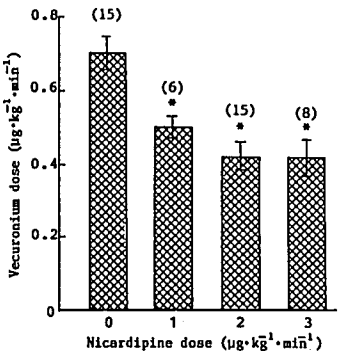
The subjects were 44 ASA PS I-II patients who were to undergo elective surgery. The protocol was approved by the institutional human investigation committee, and informed consent was obtained. Anesthesia was induced with thiopental and N_2O by face mask. Neuromuscular blockade was assessed with a Relaxograph®(Datex), which measured adductor pollicis electromyography in response to supramaximal stimulation of the ulner nerve. Tracheal intubation was facilitated with 0.1 mg/kg iv vecuronium. Anesthesia was maintained with N_2O (67%) and isoflurane (1% end-tidal). Patients were randomly assigned to receive one of four doses of nicardipine (0, 1, 2, 3 μg/kg/min). Nicardipine infusion was started after tracheal intubation and 2 hr was allowed to reach steady state plasma level. When muscle twitch tension returned to 10% of control, the infusion rate of vecuronium was continually adjusted to maintain a stable 90% of control twich tension. After 1 hr of 90% depression at a constant infusion rate, blood samples were drawn to determine plasma vecuronium and nicardipine concentrations. Mean values for groups were compared by analysis of variance and the Student's t test. A p value < 0.05 was considered to be significant.

The vecuronium infusion rate required to maintain 90% depression of control twitch tension in each group was shown in the figure. Nicardipine significantly decreased the vecuronium infusion requirement in a dose dependent manner. Total plasma clearance for vecuronium did not differ among the groups.

It is concluded that clinical doses of nicardipine markedly potentiate the action of vecuronium and that the vecuronium infusion requirement is reduced by as much as 40% by clinical doses of nicardipine.

References

1. Anesthesiology 60:298-303, 1984
2. Anesth Analg 67:1-8, 1988
3. Anesthesiology 67:503-506, 1987



Effect of nicardipine on the vecuronium infusion dose required to maintain 90% depression of control twitch tension (mean ± SE). The number of experiments is indicated by the figure in parenthesis. *p < 0.05