TITLE: EFFECT OF INTRAVENOUS ATP ON ENFLURANE-N_2O MAC IN SPONTANEOUSLY BREATHING RABBITS: ASSESSMENT OF CARDIO-RESPIRATORY EFFECTS

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INTRODUCTION: Purine derivatives (Adenosine,ATP) have been shown to reduce MAC requirements for halothane. High doses of enflurane (ENF) with N_2O attenuates responses to noxious stimuli but at the cost of cardio-respiratory depression. We proposed to substitute ATP for ENF,and to assess if sufficient anesthesia could be achieved while avoiding such cost.

METHODS: 6 intubated rabbits (4-5 Kg) spontaneously breathing 60% N_2O in O_2 were studied. Electrical stimulation in increasing voltage,as tolerated, up to 50v was applied. This allowed quantifiable, reproducible stimulation. Measurements were taken every 15 min. Purposeful escape movements were used as end-points. ENF concentrations of 0.5, 1.0, 1.5, 2.0, 2.5% were added to N_2O stepwise; responses and blood gases were recorded; in addition to electrical stimulation, the tail, ear and leg were clamped with a hemostat, and pinprick was applied to reconfirm responses to nociception. When negative response to stimuli was achieved, the dose of ENF was decreased stepwise by 0.5% till positive response was shown; then, ATP infusion was titrated to replace the decreased ENF anesthesia till ATP could totally and effectively replace ENF (ATP initial dose: 5 μg/kg/min).

RESULTS: Under 60% N_2O,increasing doses of ENF up to 1.5% showed an elevated pain-threshold, but still responded positively to tail clamp. ENF, more than 2%, could completely inhibit such responses. At this dose, however,significant cardio-respiratory depression was shown (Table). Addition of increasing doses of ATP (5-70 μg/kg/min) allowed ENF to be replaced without diminishing the pain tolerance. Moreover, SBP and HR returned to control levels but analgesia persisted.

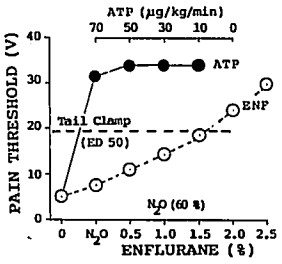
CONCLUSION: Although natural purines (Adenosine, ATP) have extremely short plasma half lives, IV ATP may have intrinsic analgesic activity in the CNS since the selective analgesic effect persisted after the infusion had stopped; this effect may have been due to activation of central purinergic receptor (P_1*, P_2) mechanism, which once activated, has a long duration. This was seen by the observation of sustained analgesia after discontinuation of ATP which was partially reversed by IV aminophylline. This sustained analgesic property without cardio-respiratory depression may have marked clinical significance.

(*P_1 includes Ado A_1 and A_2)

Cardio-Respiratory Data

	O_2 ONLY	CONTROL (N_2O)	ENF (N_2O)	ATP* (N_2O)
SBP (mmHg)	109±11	126±15	69±22*	112±20
DBP (mmHg)	83±5	84±4	49±10*	83±16
HR (bpm)	270±13	267±15	255±33*	278±26
RR (bpm)	76±5	85±5	72±19*	81±14
$PaCO_2$ (mmHg)	25±4	22±2	25±1*	22±3
PaO_2 (mmHg)	443±68	147±11	148±16	145±24

RR: Respiratory Rate, O_2:100%, N_2O:60%, ENF:2.0-2.5%, ATP:70±32*(ug/kg/min), Mean±SD
* p<0.05 vs CONTROL, (n=6)



A402

TITLE: EFFECT OF ANESTHETICS INJECTED INTO THE VERTEBRAL ARTERY BEFORE AND AFTER HEMORRHAGE AND PERICARDIAL TAMPONADE

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To study anesthetic inhibition of central sympathetic outflow (S), the left vertebral artery (VA) was catheterized in 22 dogs. (VA supplies the vasomotor center.) Blood pressure (BP) and perfusion pressure (PP) were measured. One isolated hind limb with intact sympathetic innervation was autoperfused. Blood flow was kept constant, hence PP varied proportionally to arterial resistance. To enhance S, dogs in Group I (GI) were sequentially hemorrhaged (H) 20, 40 and 60% of estimated blood volume. Dogs in Group II (GII) were given a pericardial tampanade (PT) by injection of warm saline (100, 150, 200 cc) into the pericardial sac.

Thiopental (TH) and diazepam (D) were studied in GI, while TH and ketamine (K) were studied in GII. The effect of VA injection of these anesthetics on BP and PP before H and PT was studied. The anesthetic injections were repeated following H and PT. ΔBP and ΔPP were recorded. Data are expressed as mean ± SEM, with $p < 0.05$ considered significant by paired T test. Figs 1 and 2 show the results plotted against the several doses.

Prior to H or PT, anesthetic injection did not alter BP or PP (control). After H and PT, TH produced significant drops in BP and PP in both GI and GII, but D produced no change from control in GI, nor did K in GII. After PT (200 cc), all dogs died after TH injection.

The dose of TH into VA was too small to cause direct cardiac and vascular depression. The fall in BP and PP seen subsequent to H and PT must be due to inhibition of vasomotor centers during sympathetic excitation. Sympathetic stimulation increases with increasing H and PT, indicated by increasing PP. After TH, fall in BP and PP increased with increasing H and PT. During severe H and PT even a minute dose of 6 mg TH caused detrimental hypotension and resulted in a few cardiac arrests in our study.

Fig. 1
Effect of TH & D on BP & PP

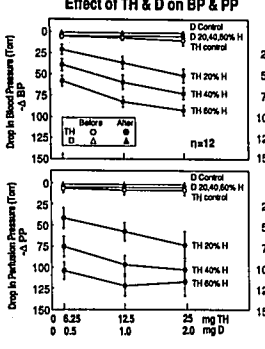

Fig. 2
Effect of TH & K on BP and PP