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Title : ADENOSINE AND ATP AS HYPOTENSIVE AGENTS COMPARED TO NITROPRUSSIDE

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Introduction. Although sodium nitroprusside (SNP) is widely used as a hypotensive agent during anesthesia, it is not free of adverse effects such as reflex tachycardia, rebound hypertension, tachyphylaxis, and cyanide toxicity. Thus a search for a safer and more effective substitute seems indicated. Adenosine (Ad) and adenosine triphosphate (ATP) are known to cause potent vasodilation. When given exogenously, these compounds can produce profound hypotension with negative chronotropism. The present study was planned to examine systematically the hypotensive effects of Ad and ATP in comparison with SNP in experimental animals.

Methods. Fifteen male rabbits (2.5±0.01 SE kg) were induced with halothane; the trachea was intubated, and the ventilation was controlled to keep $PaCO_2$ 30±2 torr. Anesthesia was maintained with 1% halothane in oxygen. Arterial blood pressure (BP) and heart rate (HR) were monitored from a femoral artery. Two ear veins were cannulated for administration of fluids and drugs. After establishment of a steady state of anesthesia (mean BP 104 ±6 and HR 252±7), the three agents were administered intravenously in random order as a single injection or by infusion.

Results. Tables I and II summarize the results. On a weight basis, the hypotensive potency of Ad and ATP was about 1/6 (single injection) and 1/40 (infusion) that of SNP, but they had a more rapid onset of action and shorter recovery time. When the agents were given by constant infusion for 30 minutes at a rate producing a similar magnitude of hypotension (-43 to -46% from control), responses to all agents were rapid in onset (< 30 sec). However, the effects of SNP became maximal only after 2-3 minutes and thereafter showed a progressive recovery throughout the course of the infusion. With Ad and ATP, on the other hand, BP remained remarkably stable and no tachyphylaxis was observed(Fig.1). Another important difference was the effect on HR: administration of SNP invariably caused an increase in HR, both with single injection and with infusion. In contrast, the adenine compounds caused a dose-related concommitant decline in HR. After abrupt termination of the infusion, BP returned quickly to preinfusion levels with both Ad and ATP; there was no rebound hypertension. With SNP however, although systolic pressure had returned to near control levels during infusion, another 20-30 minutes was required for BP to recover completely after termination, and overshoot was frequent (Fig.1).

Discussion. ATP has been used successfully as a hypotensive drug during surgical anesthesia in Japan.[1] Ad is released from the heart,brain, and skeletal muscles, and has been proposed as physiological mediator of metabolic flow regulation in these important organs in both normal and ischemic states. When exogenously given, Ad or ATP dilate systemic vasculature, and decrease HR, thus producing profound hypotension. During light halothane anesthesia, compared to SNP both adenine compounds caused a dose-related, well maintained hypotension unaccompanied by tachycardia or rebound hypotension. The compounds proved to be effective and potent hypotensive agents with an immediate onset, and faster recovery than SNP. Ad and ATP appear to offer a possible advantage over SNP as these compounds are physiological agents and may be devoid of tachycardia and tachyphylaxis.

Reference. Maruyama M, Sato K, Sato Y, et al: Hypotensive anesthesia using ATP. Jap J Anesthesiology 27: 1533-1540, 1978.

Table I. Effects of single i.v. injections.

	N	Dose µg/kg	ΔBP %	ΔHR %	Onset sec	Recov.(80%) sec
SNP	13	43±9	-35±3	+5±0	39±3	153±18
Ad	13	257±36	-38±3	-15±3†	22±1†	24±4†
ATP	13	257±36	-41±3*	-14±3†	24±1†	52±9†

Table II. Effects of constant infusions.

	N	Dose µg/kg min	ΔBP %	ΔHR %	Onset min	Recov.(80%) min
SNP	7	24±5	-43±5	+8±1	2.8±0.3	16±1
Ad	7	984±225	-45±4	-11±3†	2.1±0.6	5±1†
ATP	7	984±225	-46±3	-8±2†	2.4±0.8	5±1†

Values are mean ± S.E., Paired t-test when compared to SNP: *p < 0.05, §p < 0.01, †p < 0.001

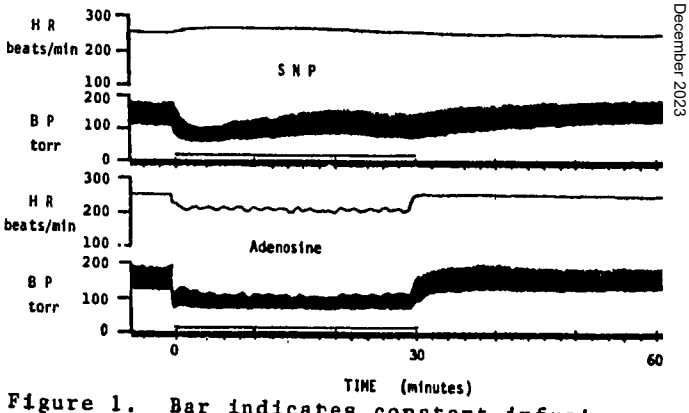

Figure 1. Bar indicates constant infusions: SNP 10 µg/kg/min, Adenosine 400 µg/kg/min