

TITLE: THE EFFECTS OF HYPOCAPNIC ALKALOSIS (HA) ON THE VASODILATING ACTION OF NICARDIPINE (N)
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HA causes an increase in the systemic vascular resistance index (SVRI) and a decrease in the cardiac index (CI) (1). Vasomotor interactions between HA and calcium antagonists have previously been studied experimentally in the cerebral and coronary circulations (2, 3). The purpose of this work was to study these interactions in the general circulation.

MATERIAL AND METHODS: This study was carried out in 6 patients who were hospitalized for subarachnoid hemorrhage (2 males, 4 females; age=46±10 yrs). All were mechanically ventilated, and had Swan-Ganz catheters in place. Six steps were studied. T0: baseline; T1: HA (3.5 kPa for 30 min); T2: 30µg/kg bolus I.V. of N (peak plasma determination at 3 min); T3: 30 µg/kg/min N by continuous infusion (60 min); T4: determination of the N infusion flow rate which cancelled the vasomotor effects of HA (120 min); T5: reestablishment of normocapnia without modifying N. Statistical analysis was carried out using the repeated measures analysis of variance and the Fischer test. Plasma N levels were determined by GCECD at the end of each step. This protocol was approved by the hospital ethics committee.

RESULTS: Table I shows the posology of N at T4 for each patient. At T1 HA increased the SVRI by 20% (Table II). At T2 the N bolus cancelled the

effects of HA. At T3 HA masked the effects of N infusion, At T4 the plasma levels required to cancel the effects of HA were twice those at T3. At T5 normalization of the PaCO₂ caused a fall in the SVRI and a rise in the CI by 28% in comparison with T0.

CONCLUSION: Since HA antagonizes the effects of N, reestablishment of normocapnia therefore enhanced the vasodilating effects of N. These interactions are important to consider when N is used during general anesthesia.

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2. Proc. West. Pharmacol. Soc. 1983, 26:127-129
3. Am. Heart. J. 1981, 102:206-210

Patient	1	2	3	4	5	6
Dose at T4	60	60	30	240	60	60
TABLE I: Posology of nicardipine (µg/kg/min) at peribds T4 and T5						
Mean ± SD	T0	T1	T2	T3	T4	T5
HR (beats/min)	71±10	76±13	80±13*	79±16*	85±14*,b	85±14*,b
HAP (mmHg)	92±20	96±22	88±17	93±11	91±13	95±05
PCVP (mmHg)	8.6±2.8	9.0±3.2	9.6±3.6	8.6±1.9	9.0±3.0	9.0±3.5
MAP (mmHg)	7.3±2.7	7.6±3.7	7.0±2.0	6.3±2.5	6.5±2.6	7.0±3.4
CI (l/min/m ²)	4.25±0.89	3.88±1.03	4.67±1.26	4.19±1.32	4.17±0.90	5.47±1.09*
SVRI	599±135	720±183*	532±142*b	616±166*	535±089*,b,e	434±062*
PaCO ₂ (kPa)	4.88±0.57	3.35±0.33*	3.48±0.33*	3.38±0.36*	3.46±0.23*	5.15±0.89*
Plasma levels of nicardipine (ng/ml)						
	0	0	108±47	44±20*c	101±78*d	96±66*d

TABLE II: Interaction of HA with nicardipine-induced vasodilation. *: P<0.05, a: T0 vs T1-T5, b: T1 vs T2-T5, c: T2 vs T3-T5, d: T3 vs T4-T5, e: T4 vs T5

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ROUTINE APPLICATION OF HIGH-DOSE APROTININ IN OPEN-HEART SURGERY- A STUDY ON 1,784 PATIENTS.

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 The application of the proteinase inhibitor aprotinin may considerably reduce bleeding in open-heart surgery (1-4). To study the clinical effectiveness and safety of aprotinin we evaluated the data of 1,784 consecutive patients with and without aprotinin treatment prospectively.

Methods: With consent and institutional approval 902 adult cardiac surgical patients were treated with aprotinin (Gr. A) and were compared to 882 cardiac patients without aprotinin (Gr. C) operated on during the same period. The aprotinin dosage was: 2x10⁶ KIU after induction of anesthesia and additionally to the pump prime. A continuous infusion of 5x10⁵/hour was administered during operation. Postop bleeding and intra- and postoperative blood requirement as well as the course of creatinine were recorded. ANOVA and chi-square test were used regarding a p<0,05 as significant.

Results: Patients' demographic data and the distribution of the types of operations were comparable. 10.3% (n=91) of all procedures were reoperations in Gr. C and 12.3% (n=111) in Gr. A. The correlation between duration of operation and blood requirement was significant in Gr. C whereas it was not in Gr. A. Creatinine at the discharge from the ICU was 1.3 mg/dl in both groups. 2.2% of the patients in Gr. C and 2.3% in Gr. A required hemodialysis postoperatively due to renal failure. Two patients in Gr. A showed signs of allergic reactions but finished their

operation uneventfully. In these patients positive IgM and IgG antibodies against aprotinin were detected, which resulted probably from a previous aprotinin challenge.

	operation	n	total blood loss homol. blood	
			[ml]	[ml]
group C	CABG	525	1148±714	1760±1792
	valve replac.	292	1075±809	2132±2810
	CABG+valve	65	1213±906	3324±2687
	total	882	1128±552	1999±2283
group A	CABG	560	739±487*	831±1596*
	Valve replac.	264	710±567*	1005±1722*
	CABG+valve	78	914±962*	1519±1449*
	total	902	746±762*	942±1630*

* p < 0.05 vs control

Discussion: Aprotinin acts in plasma levels >300 KIU/ml as inhibitor of the contact phase of coagulation (1). Thus, the damaging effect of cardiopulmonary bypass on hemostasis may be attenuated with the consequence of a better preserved platelet function post bypass. This study demonstrated in a large group of patients a reduction of 34% in blood loss and of 53% in blood requirement using high-dose aprotinin. This effect was more pronounced in longer lasting operations. Aprotinin is not recommended in patients with previous aprotinin exposure. Clinically relevant negative influences on renal function were not detected. Therefore, the routine use of high-dose aprotinin in open-heart surgery is recommended.

- References**
1. Thorac Cardiovasc Surgéon 1989;37:92-98
 2. J Thorac Cardiovasc Surg 1989;97:364-372
 3. Thorac Cardiovasc Surgéon 1989;37:89-91
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