Title: ANTITACHYCARDIC EFFECTS OF ALINIDINE IN PATIENTS AFTER OPEN HEART SURGERY

Authors: C.K. Spiss, M.D., Ch. Rosenits, M.D., B. Haslinger, M.D., G. Redl, M.D., W. Haider, M.D.

Affiliation: Study Group of Cardiovascular Anesthesia and Intensive Care. Clinic of Anesthesia and General Intensive Care Medicine and 2nd Surgical Clinic, University of Vienna, A-1090 Vienna, Austria

Alinidine (A), an N-allyl derivative of clonidine, belongs to a new class of specifically bradycardic agents. It reduces the slope of the slow diastolic depolarization in the SA-node and does not interact with the ß-adrenergic receptors (1). Recently, A was used experimentally or clinically in individuals in whom sinus tachycardia occurred due to treatment of vasodilators or catecholamines (2,3). The purpose of this study was to investigate the efficacy of A as a bradycardic drug when used in patients presenting tachycardia after open heart surgery.

Methods. 6 patients ($\bar{x}$=65 a) without severe ventricular function who had undergone CABG (n=4) or aortic valve replacement (n=2) were eligible for the study which had institutional approval and informed consent. All patients had thermodilution pulmonary artery and left atrial catheters. Perioperative digitalis, ß-blocker or calcium antagonist use excluded patients. The study was performed 6-18 h after surgery. All patients had developed sinus tachycardia (>100/min) for at least 30 min. Heart rate (HR), mean arterial pressure (MAP) and left atrial pressure (LAP) were continuously recorded. Thermodilution cardiac output (CO) was determined in triplicate. Using standard formulas, the following hemodynamic data were calculated: CI, SI, LVSWI and SVR. We additionally sampled arterial blood for A, ephinephrine (EPI) and norepinephrine (NOR-EPI) determination by HPLC and plasma renin activity (PRA) by RIA. After control measurements had been taken, a 10 mg A-bolus was given, followed by constant infusion of 20 mg A over 2 h. Measurements were repeated after 15, 30, 60, 120 and 150 min following the bolus injection. Data are presented as mean ± SD. Unpaired t-test with Bonferroni correction (significance level $p < 0.05$) was used for statistical analysis.

Results. (see Table). A given to patients after open heart surgery decreased HR significantly by 18% ($p < 0.01$). CI, LAP and CVP were unchanged during the whole investigation. SI showed a highly significant 20% increase whereas LVSWI rose by 12%. An insignifican 11% drop in MAP and SVR was observed throughout the study. A plasma levels stayed in a therapeutic range above 100 ng/ml. Baseline catecholamine and PRA levels were all above normal ranges but no significant changes occurred during the study.

Discussion. Sinus tachycardia may be detrimental in patients after open heart surgery since it increases myocardial oxygen demand. Therefore, there is a need for a bradycardic agent without untoward hemodynamic effects. In our study, A immediately reduced HR. No arrhythmias were recorded. The reduction of HR was responsible for the observed increase of SI and LVSWI. In our clinical setting A did not interfere with myocardial contractility because filling pressures stayed unchanged and CO was unaltered. The highly elevated EPI, NOR-EPI and PRA levels were certainly due to the previously finished operation and were not further influenced following A application.

Conclusion. The results of the present study suggest that A is effective in treating sinus tachycardia in patients after open heart surgery.

Table. Data are presented as mean ± SD

		ALINIDINE				
	Baseline	15 min	30 min	60 min	120 min	150 min
HR	112.2 (6.1)	100.0	97.8	96.5	93.3*	91.2*
MAP	90.5 (11.9)	84.7	86.2	85.8	80.7	81.0
LAP	14.8 (4.6)	13.5	14.5	12.8	12.5	13.7
CI	2.3 (0.6)	2.2	2.1	2.0	2.2	2.3
SI	20.8 (6.1)	21.8	21.3	21.0	22.8	25.2*
LVSWI	41.0 (11.3)	40.5	40.7	41.5	42.0	46.0
SVR	1455.8 (436)	1472.7	1543.0	1563.5	1378.8	1275.3
A ng/ml	< 2.5	134.3	154.5	145.5	143.5	104.3
EPI pg/ml	460.8 (168)	426.8	358.8	361.2	301.6	261.6
NOR-EPI	1548.5 (641)	1572.2	1835.0	1975.5	1525.7	1455.0
PRA ng/ml/h	4.8 (3.8)	5.5	5.5	7.0	5.2	4.8

* significantly different from baseline ($p < 0.01$)

References. 1) Kobinger W, et al.: Eur J Pharmacol 58: 141-150, 1979.
2) Zimpfer M, et al.: Eur J Clin Invest 12: 9-12, 1982.
3) Benjamin E, et al.: Anesthesiology 63: A 88, 1985.