Title: AORTIC SURGERY: CLONIDINE PREVENTION OF SYMPATHETIC ACTIVATION PRODUCES STABLE VASOMOTOR TONE

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Introduction. Aortic surgery induces major hemodynamic changes, especially in patients with coronary artery disease (CAD) and/or hypertension (HBP). This is associated with very high levels of plasma catecholamines (CA).[1] This increased sympathetic activity has cardiovascular and metabolic consequences which may be detrimental in this subset of patients. Clonidine may suppress the central and peripheral sympathetic and/or cardiovascular hyperactivity occurring during surgery or stress. Thus clonidine could suppress the sustained increase in plasma CA and produce stable vasomotor tone. The present investigation addressed the following questions: 1) whether clonidine would modify the increase in plasma CA levels observed during aortic surgery 2) whether this would affect systemic hemodynamics upon aortic cross clamping or clamp release.

Methods. The study protocol was approved by the Ethics Committee and informed consent was obtained. All the patients treated for hypertension (defined as a blood pressure above 160/90 mmHg for more than 6 months), coronary artery disease or heart failure received all their current medications with the exception of diuretics the morning of surgery. Patients were randomized in a double blind manner to two groups: placebo group (n=14) received flunitrazepam 15 ug kg^{-1} po and placebo 120 min before induction; clonidine group (n=14) received flunitrazepam 15 ug kg^{-1} and clonidine 4.7 ± 1.2 ug kg^{-1} po at the same time. Hemodynamics and arterial plasma samples were measured at the following intervals: 1) baseline (BL): immediately after the end of vascular catheterizations, i.e., immediately before induction, 2) immediately before aortic cross clamping (bX), 3) immediately after aortic cross clamping at peak blood pressure increase (aX), 4) 20 to 30 min after aortic cross clamping (dX), 5) immediately after unilateral unclamping at lowest blood pressure (uUX), 6) immediately after bilateral unclamping (bUX), 7) upon skin closure (SK). All patients were given flunitrazepam (30 ug kg^{-1}), fentanyl (10 ug kg^{-1}) and pancuronium (100 ug kg^{-1}) for induction. Maintenance was provided with N_2O (50%) in O_2 and infusion of fentanyl (4 ug $kg^{-1} h^{-1}$) and pancuronium as required, up to skin closure. Cardiovascular and anesthetic interventions were designed to maintain mean arterial pressure and heart rate within 30% of baseline. ANOVA was applied to hemodynamic data, the Fisher's exact test and the Wilcoxon test were used where appropriate.

Results. The number of anesthetic and cardiovascular interventions necessary to maintain cardiovascular stability was halved in the clonidine group ($p<0.05$ for fentanyl reinjections). Plasma catecholamines were significantly different in the two groups ($p<0.05$) throughout the study period (fig 1A and B). HR and MAP were lower at all intervals in the clonidine group (fig 1B). This achieved statistical significance ($p<0.01$) for MAP at baseline, upon unclamping and skin closure. Systemic vascular resistance index showed similar directional changes after aortic clamping and unclamping in both groups but the absolute values were significantly lower in the clonidine group ($P<0.005$) (fig 1D).

Discussion. The blunting of peripheral catecholamine release during aortic surgery resulted in a stable vasomotor tone. This is likely due to an action of clonidine on the rostral ventrolateral medulla, a site considered to be the final integrative area of the vasomotor control. The prevention of sympathetic activation and the attending hemodynamic stability observed confirm previous results.[2] Thus clonidine appears to be a useful tool to stabilize the sympathetic and the cardiovascular systems during the perioperative period.

References.

1. Normann NA, Taylor AT, Crawford ES, DeBakey ME, Saleh AS: Catecholamine release during and after cross clamping of descending thoracic aorta. J Surg Res 34:97-103, 1983.

2. Flacke JW, et al: Reduced narcotic requirement by clonidine with improved hemodynamic and adrenergic stability in patients undergoing coronary bypass surgery. Anesthesiology 67:11-19, 1987.