PIII-4

DIFFERENT EFFECTS OF PROPRANOLOL, BISOPROLOL, CARVEDILOL AND DOXAZOSIN. G. Koshucharova, MD, K. Stoschitzky, MD, R. Zweiker, MD, P. Lercher, MD, R. Maier, MD, N. Watzinger, MD, W. Klein, MD, Division of Cardiology, Universitätsklinik Graz, Graz, Austria.

Purpose: Beta-blockers usually decrease heart rate and nocturnal melatonin release. However, the alpha- and beta-blocker carvedilol was shown to have no influence on resting heart rate and nocturnal melatonin release in healthy subjects.

Methods: We compared the effects of two beta-blockers (80mg propranolol and 5mg bisoprolol) and an alpha-blocker (4mg doxazosin) on heart rate and blood pressure at rest and exercise 3 hours after intake of single oral doses to those of 50mg carvedilol in 12 males.

Results: At rest, propranolol (-21%) and bisoprolol (-21%) decreased heart rate, whereas doxazosin (+30%) increased heart rate, and carvedilol had no effect. During exercise, propranolol (-26%), bisoprolol (-19%) and carvedilol (-18%) decreased heart rate, whereas doxazosin (+6%) increased heart rate. The only effects of the drugs on blood pressure were those on systolic blood pressure during exercise (-11%, -10%, -11%, -12%, respectively). All the given effects were $p < 0.05$.

Conclusion: We conclude that alpha-blockers may increase heart rate, presumably caused by a reflex increase of sympathetic drive secondary to vasodilation resulting from alpha-blockade, an effect that appears to be strong enough to abolish the beta-blocking effect of carvedilol on resting heart rate in healthy subjects. This might be the reason for the weak side-effects of carvedilol resulting from beta-blockade, and why it does not influence nocturnal melatonin release.

PIII-5

THE DIFFERENTIAL EFFECTS OF ORBOFIBAN AND ABCIXIMAB ON PLATELET RELEASE OF NITRIC OXIDE AND SUPEROXIDE. S. Chakrabarti, PhD, D. Cox, PhD, S. Varghese, S. Sarkar, PhD, M. Mascelli, PhD, J. E. Freedman, MD, Boston University School of Medicine, Royal College of Surgeons, Centocor, Boston, MA.

Unstable coronary syndromes are caused by plaque rupture leading to platelet activation and thrombosis. Platelet aggregates form by fibrinogen binding to glycoprotein IIb/IIIa (GPIIb/IIIa). Although trials have shown that parental GPIIb/IIIa inhibitors decrease morbidity, studies of oral IIb/IIIa inhibitors have failed to show benefit. While GPIIb/IIIa inhibitors block fibrinogen binding, they may not prevent stimulation of select signaling pathways. As activated platelets release reactive oxygen species that may alter platelet function, we compared the effect of the active metabolite of an oral (orbafiban) and a parental (abciximab) GPIIb/IIIa inhibitor on the platelet release of nitric oxide (NO) and superoxide.

Incubation with orbofiban did not significantly change release of platelet-derived NO. However, incubation with abciximab increased platelet-derived NO release by 10.1 ± 3.2 pmol/10^8 platelets ($p<0.01$). Superoxide release was markedly decreased by incubation with abciximab and orbofiban ($80 \pm 6\%$ and $62 \pm 5\%$, respectively; $P<0.05$). Blockade of the platelet GPIIb/IIIa receptor altered stimulation-dependent NADPH oxidase translocation but did not inhibit translocation of eNOS.

In summary, these observations suggest that the pharmacological effects of GPIIb/IIIa antagonists on platelet function, apart from inhibition of aggregation, may contribute to their efficacy.

PIII-6

QT MEASUREMENTS FOLLOWING ACE THERAPY. J. Somberg, MD, A. Agarwal, MD, J. Molnar, MD, V. Ranade, PhD, Rush University, Lake Bluff, IL.

Objective: To evaluate the effects of ACE therapy on the EKG measurement of repolarization, QT dispersion (QTd).

Background: Patients with CHF have cardiac enlargement that could lead to electrical instability, and sudden death (SCD). ACE inhibitors leads to a reduction in cardiac size and SCD.

Methods: Ninety-seven patients with CHF were evaluated with 12-lead EKG before and six weeks after ACE therapy. QTd (the difference between the maximum and minimum QT divided by the minimum QT) was measured by a blinded observer in duplicate.

Results: The mean ACE level (u/ml) was 11 ± 1.1 and the mean inhibited ACE activity was 70 ± 0.9. The QT decreased from 452 ± 83 to 425 ± 64 ms $p < 0.001$ and QTd from 59 ± 13 to 46 ± 11, $p < 0.001$ after ACE for 6 weeks.

Conclusion: These results show a decreased QTd following ACE therapy. It appears that ACE decreases electrical dispersion, possibly explaining the reduced risk for SCD.

PIII-7

NESIRITIDE IN THE MANAGEMENT OF CONGESTIVE HEART FAILURE: A RETROSPECTIVE STUDY OF HEMODYNAMICS AND ADVERSE EVENTS IN A COMMUNITY TEACHING HOSPITAL. S. Rasty, PharmD, S. H. Mohammed, MD, Advocate Christ Medical Center, Oak Lawn, IL.

Nesiritide (NTD) is a synthetic brain natriuretic peptide and is promoted as a new therapy for decompensated congestive heart failure (CHF).

Purpose: To assess the hemodynamics and adverse effects of NTD in CHF patients(pts) admitted to the hospital.

Methods: 26 pts were evaluated retrospectively.

Results: Our pts average (AVG) age was 78 (14) years, most had significant past history(HX) for CHF, CAD, DM, A.fib, HTN while 45% had HX of COPD. All pts reported dypnea and most presented with rales and edema in the ER and represented with class III and IV NYHA. The AVG heart rate and blood pressures were 74 (10), SBP 134(24) mmHg and DBP 71(18)mmHg at time of admission. AVG serum creatinine of 2.4 (1.2) mg/dl and BNP of 913 (418) pcg/ml was reported. NTD was given as a bolus dose of 2mcg/kg and fixed dose of 0.01 mcg/kg/min, the AVG length of infusion was 65(39) hours and diuretics were used in all cases. 5 cases received inotropes and vasopressors. We performed repeated mesaure ANOVAs on the blood pressure data during the NTD infusion. Over the entire time period there was no significant changes in either systolic ($p=.248$) or diastolic ($p=.358$) blood pressure within pts. Although linearly the systolic BP significantly differed from baseline to 24 hour BP ($p=.038$). 9 of our pts suffered from non-sustained ventricular tachycardias (NSVT) while on NTD.

Conclusions: In our population, no significant variation in BP was seen but high number of NSVTs were reported.