P-212

LONG-TERM EFFECTS OF MEDICAL THERAPY ON AUTONOMIC CONTROL OF HEART RATE IN PATIENTS WITH CONGESTIVE HEART FAILURE WITH OR WITHOUT HYPERTENSION

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Since reduced heart rate variability (HRV) is known to be a predictor of prognosis of congestive heart failure, we examined long-term effects of conventional medical therapy on HRV in 314 patients with congestive heart failure (62±1 years, NYHA classification 1 to 4), consisting with dilated cardiomyopathy, coronary artery disease, or hypertensive heart disease. Patients were randomly assigned to beta-blocker, angiotensin converting enzyme (ACE) inhibitor, dihydropyridine derivatives, diltiazem, nitrate, or these combinations with or without digitalis and furosemide therapy. 48 patients were treated only by life style modification (LIFE). 24-hour ECG recordings were repeated before and after the therapy (mean duration: 76 weeks), and HF (0.15-0.4 Hz), TF(0.004-1 Hz) and LF (0.04-0.15 Hz) /HF ratio of HRV were calculated by maximum entropy method. Both HF and TF were significantly ($p<0.01$) deceased in LIFE while those in beta-blocker were significantly ($p<0.01$) increased. None of the interval changes in the rest of therapy groups was significant. Although none of the baseline values between groups before therapy was significant, both HF and TF were significantly ($p<0.01$) lower after therapy in dihydropyridine and nitrate groups than those in beta-blocker group. However, when dihydropyridine and nitrate were used as a combination drug with ACE inhibitor or beta-blocker, these differences vanished. In conclusion, long-term beta-blocker therapy only improves autonomic control of heart rate in patients with heart failure. Furthermore, dihydropyridine or nitrate may be useful only when these drugs were used as combination drug with ACE inhibitor or beta-blocker.

Key Words: ACE inhibitor, beta-blocker, heart rate variability

P-213

COMPARISON OF HEMODYNAMIC EFFECTS OF NEBIVOLOL AND BISOPROLOL IN ESSENTIAL HYPERTENSION

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Nebivolol, the most selective clinically available antagonist of $beta_1$-adrenergic receptors, has an additional vasodilator action in human forearm resistance vasculature in normal and hypertensive patients, and in patients with coronary artery disease. This has been attributed to activation of the L-arginine/nitric oxide pathway. The present investigation compared hemodynamic effects of nebivolol with those of another selective $beta_1$-adrenergic receptor antagonist, bisoprolol. The study was approved by the local research ethics committee. 15 patients (11 men, 4 women age 29-69 years) with uncomplicated mild essential hypertension diagnosed by World Health Organisation criteria, consented to take part. The design was a double blind randomised crossover. Following a two week washout, subjects were randomised to receive nebivolol (5 mg po daily) or bisoprolol (10 mg po daily) for 2 weeks, followed by a 2 week washout and 2 weeks on the other treatment. Measurements were made at the end of each baseline and each active treatment period. Heart rate fell during active treatment (from 65±2 to 53±3 min^1 during bisoprolol, $P<0.01$ and from 64±3 to 59±3 min^1 during nebivolol). Blood pressure (by sphygmomanometry) fell (bisoprolol: 143±3/90±2 to 127±3/80±2; nebivolol: 144±4/92±2 to 131±3/83±3; each $P<0.01$) during active treatments to a similar extent. In contrast, systemic vascular resistance index (measured by bioimpedance) fell during nebivolol (from 2855±201 to 2646±186 dyn $min^{-5}m^{2}$, $P<0.01$) but did not change significantly during bisoprolol treatment (baseline 2848±177, on treatment 2788±159 dyn $min^{-5}m^{2}$,). We conclude that nebivolol has a systemic vasodilator action in essential hypertension distinct from its $beta_1$-adrenoceptor antagonist action.

Consultant - MENAUNI INTERNATIONAL

Key Words: vasodilator property, beta-receptors, nebivolol

P-214

NEBIVOLOL, A BETA-1-SELECTIVE AND VASODILATATING BETA-BLOCKER, REDUCES PLASMA VISCOSITY

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The aim of this pilot study was to investigate if under treatment with a beta blocker, Nebivolol, hypertensive patients showed an improvenment in viscosity parameters. Nebivolol is a beta-blocker with vasodilatating properties through an increased nitric oxide (NO) release in the endothelium. NO is known to have a positive effect on the rheological properties of the plasma.

Ten hypertensive patients (2 males)were included and laboratory parameters measured before and in mean 97 days after initiating treatment with Nebivolol. Other medication remained unchanged. Plasma viscosity (PV) was in mean 1,4284 (range 1,1802-1,5645, normal 1,23), the platelet aggregation factor (PAF)was in mean 1,382 (range 1,09-1,79, normal 1,00-1,06) before treatment with nebivolol. After treatment mean PV was significantly reduced to 1,3208 ($p<0,05$), PAF to a mean 1,113 ($p<0,05$).

Hypertensive patients have an elevated plasma viscosity, which in turn increases peripheral vascular resistance, especially if endothelial dysfunction already exits.

Nebivolol seems to have, besides its antihypertensive also a positive effect on plasma viscosity. This may be due to its increased nitric oxide release.

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Key Words: rheological properties, Nebivolol, nitric oxide release

P-215

PERINDOPRIL AND INDAPAMIDE INCREASES ARTERIAL COMPLIANCE IN POSTMENOPAUSAL WOMEN

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Objective: Proximal arterial compliance may be a new therapeutic target in arterial hypertension. disease. The aim of the current study was to annualize the effect of ACE-inhibitor perindopril and diuretic indapamide on pulse wave velocity at 50 postmenopausal hypertensive women without hormone replacement therapy..

Methods: The whole body arterial compliance (WBAC) and pulse wave velocity (PWV) was measured in postmenopausal hypertensive women (mean age 52 ± 1.5 yr) at baseline and after 4 weeks treatment with perindopril (2-4 mg/day,25 patients) or indapamide (2.5 mg/day, 25 patients). Also ambulatory blood pressure and lipids were studied at these time points.

Results: Postmenopausal hypertensive women had significantly higher WBAC and PWV than women at control group (30 women with arterial

hypertension, age 24-36 years). After 4 weeks treatment with perindopril or indapamide WBAC and PWV was significantly reduced to the level measured in the control group.

	Baseline	Perindopril 4 wks
WBAC (A.C.U.)	0.52	0.32*
Mean arterial pressure (mmHg)	94	82*
.Control Group	Baseline	Indapamide 4 wks
WBAC (A.C.U.)	0.56	0.34*
Mean arterial pressure (mmHg)	96	84*

**P < 0.05 compared to baseline and treatment level; A.C.U. arbitrary compliance units.*

Conclusions: These data suggest that perindopril and indapamide may sucsesfully correct arterial compliance in postmenopausal hypertensive women.

Key Words: postmenopausal hypertensive women, arterial compliance, hypotensive drus

P-216

POSTMARKETING SURVEILLANCE STUDY TO EVALUATE THE EFFECTIVENESS AND SAFETY OF DOXAZOSIN GASTRO-INTESTINAL THERAPEUTIC SYSTEM (GITS) IN HYPERTENSIVE PATIENTS PREVIOUSLY TREATED WITH DOXAZOSIN TABLETS

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The purpose of this study was to evaluate the effectiveness and safety of the new GITS formulation of doxazosin in hypertensive patients previously treated with Doxazosin standard.

It was designed an open, multicenter, prospective, postmarketing surveillance study in hypertensive patients in primary care settings. 4512 hypertensive patients (SPB≥140 and/or DBP≥90 mmHg) were enrolled after obtaining their informed consent. 4512 were considered valuable for the safety analysis and 4227 for the effectiveness analysis. After a follow-up period of 3-9 months on Doxazosin standard (Phase 1) patients were switched to doxazosin GITS and followed during 3 additional months (Phase 2). The outcome measures included blood pressure and incidence of adverse events (AE).

Results: Mean age of the patients (59.6% male) was 62.4 ± 10.6 years. A statistical significant decrease in SBP and DBP mean values was observed from 160.9 mmHg at the beginning of this study, to 135.3 mmHg at the end, and from 93.3 mmHg to 79.3 mmHg respectively ($p<0.001$).The percentage of patients presenting optimal control (SBP<140 and DBP<90mmHg) grew significantly from 0% at the beginning to 63.4% at the end of the study ($p<0.01$).

A total of 343 AE (7.2%) were reported in 322 patients, regardless their relationship with the drug treatment, being serious 38 (0.9%). Most of the AE were mild or moderate. The most common AE in both phases (Standard/GITS) were:49(20%)/3(1.2%) dizziness, 21(8.6%)/6(2.4%) headache, 19(7.8%)/3(1.2%) hypotension, 3(1.2%)/4(1.6%) diarrhea, 5(2%)/0(0%) arrhythmia and asthenia 10(4.1%)/2(0.8%), respectively. The incidence observed while doxazosin GITS therapy was lower than while standard form. Only one serious AE was considered drug-related.

Conclusion: the study showed that switching doxazosin standard to doxazosin GITS is safe and seems to improve the drug toleration.

Grant/Research Support: Pfizer

Key Words: Safety, Effectivness, Doxazosin GITS

P-217

BLOOD PRESSURE CONTROL DOES NOT ENSURE THE CONTROL OF MICROALBUMINURIA IN PREVIOUSLY UNTREATED HYPERTENSION

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The aim of this study was to investigate the prevalence of microalbuminuria (MA) in 502 newly diagnosed and never treated essential hypertensives (EH) (mean age 58 + 12 y, 54.7% female) and the effect of treatment during a follow-up of 3 month with either ramipril R (5-10 mg od) or atenolol (A) (50-100 mg od) on those with MA (+). MA was measured in a central laboratory in 3 consecutive urine samples collected in the early morning, being considered positive when at least two determinations were above 15 mg/g creatinine.

The prevalence of MA (+) was 12,5% (63 out of the 502 EH). These patients exhibit higher SBP, triglycerides, serum uric acid and creatinine than those MA (-). Forty-five EH MA(+) entered in the double blind randomized comparative study. MA was measured in 24h urine samples collected at the beguinning and at the end of the follow-up. Treatment with R reduced significantly both BP (baseline: 152±14/90±7; 3 month: 142±16/85±9 mmHg,$p<0.005$) and MA (baseline: 88±64; 3 month: 60±71 mg/24h, $p<0.002$). EH treated with A had similar reduction of BP but the decrease of MA (baseline:55±29; 3 month:47±46 mg/24h) was not statistically significant.

The prevalence of MA among newly diagnosed, non-treated essential hypertensives was 12.5%. Treatment with ramipril or atenolol induced a significant reduction of BP but only ramipril achieved a significant reduction of MA.

Key Words: microalbuminuria, newly diagnosed patients, treatment of hypertension

P-218

EFFECTS OF ATENOLOL AND QUINAPRIL ON SERUM PARATHYROID HORMONE LEVELS IN RENAL TRANSPLANT RECIPIENTS

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Renal transplant recipients bear an elevated risk of cardiovascular morbidity due to a high prevalence of risk factors, such as hypertension or elevated serum parathyroid hormone (PTH) levels. PTH has to be considered a cardiovascular risk factor, since it has been recognized to be associated with left ventricular hypertrophy and with an increased carotid intima-media thickening in patients under hemodialysis treatment. The objective of this prospective rando-mized study was to compare the effects of the antihypertensive agents atenolol and quinapril on serum PTH levels in 25 hypertensive renal allograft recipients throughout a 5-years obser-vation period. 12 patients were randomly selected to be treated with quinapril, 13 received an antihypertensive treatment with atenolol. Both agents decreased blood pressure to a similar extent and kept allograft function stable. Starting from similar serum PTH levels at baseline, PTH levels increased less under atenolol treatement than under the use of quinapril (Δ61,8 ± 31,5 vs Δ158,2 ± 50,7 pg/ml), while serum total calcium and phosphorus levels remained within normal range throughout the 5-years observation. As a conclusion, in hypertensive renal transplant recipients, antihypertensive treatment with atenolol seems to have a metabolic advantage on the cardiovascular risk factor PTH compared to quinapril.

Key Words: renal transplant recipients, effects of atenolol and quinapril, parathyroid hormone