group (33.4±3.6 vs 36.6±7.9 mg/dl). Although no significant differences were registered on fasting serum insulin, we observed a significant decrease on 120 min. of insulin concentrations in M group (139.5±33.0 vs 71.2±14.5 μU/ml, p<0.05 ) but not in AM group (94.4±19.3 vs 88.5±11.5μU/ml, p<ns). The changes on art NE were directly associated to changes on 2h insulin (r=0.53, p<0.04) serum triglycerides (r=0.63, p<0.03) only in M group. The changes on serum leptin were also directly associated to 2h insulin (r=0.58, p<0.04) in M group.

The beneficial effect achieved by Moxonidine goes beyond blood pressure control as result of a better metabolic profile associated with lower sympathometric activity.

Key Words: Sympathetic Activity, Insulin Resistance, Moxonidine

P-53
ACE-INHIBITOR AND SPIRONOLACTONE INDUCED HYPERKALEMIA IN ELDERLY PATIENTS WITH SUBCLINICAL RENAL DISEASE
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The treatment of refractory congestive heart failure currently includes combination therapy with an angiotensin converting enzyme-inhibitor [ACE-I] and spironolactone [Sp]. This combination is not recommended in patients with serum creatinine [S.Cr]≥ 2.0 mg/dl because of the risk of hyperkalemia. Elderly patients with apparently normal S.Cr may already have advanced renal disease thus, at risk for hyperkalemia when exposed to ACE-I and Sp combination. The frequency of that risk is unknown. We prospectively monitored cases of hyperkalemia admitted to an inner city hospital over a 12 month period. After exclusion of patients on dialysis and those with pre-existing renal disease (S.Cr > 1.5 mg/dl), 18 of 220 cases of hyperkalemia (8%) occurred in patients with no obvious renal disease but were receiving ACE-I and Sp combination. The mean (±SD) age of the patients was 75 ±6 yr, their base line ejection fraction was 30± 5 %. The base line creatinine clearance [C.Cr] was 43.5± 10.6 ml/min. Despite the base line S.Cr of 1.1± 0.1 mg/dl. The admission serum potassium was significantly higher than the base line values 6.6 mmol/L vs 4.2 mmol/L. (p < 0.0001). The mean difference in S.Cr between base line and admission was 3.7 mg/dl ( p < 0.0001).

Thus elderly patients with apparently normal renal function may be at risk for hyperkalemia renal failure when exposed to the combination of ACE-I and Sp. Their C.Cr should be routinely estimated by formula 1 prior to initiation of therapy with these combination of drugs. 1[Cockcroft and Gault Nephron 1976; 16:31-41].

Key Words: Spironolactone and Ace-Inhibitor, Renal Failure, Hyperkalemia

P-54
Efficacy and safety of diltiazem hcl extended release (g99) dosed at nighttime (10pm) compared to placebo and to morning dosing (8am) in moderate to severe essential hypertension
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The efficacy and safety of chronotherapeutic diltiazem hcl er (G99) at doses of 120mg, 240mg, 360mg and 540mg administered once-daily at nighttime (10PM) were evaluated in a 7-week randomized, double-blind, parallel group, dose-response, multicentre trial by comparison to placebo and to G99 360mg administered once-daily in the morning (8AM) in adult patients (n=478) with moderate to severe essential hypertension. The primary efficacy parameters were change from baseline to endpoint in trough diastolic BP (DBP) recorded by ABPM between 6PM and 10PM for each nighttime dose of G99 and placebo, and change from baseline to endpoint in mean DBP recorded by ABPM between 6AM and 12NOON for G99 360mg PM and 360mg AM. Systolic BP (SBP) at these time points was a secondary variable. Safety was evaluated through adverse events (AEs), vital signs, physical examination, clinical laboratory tests and ECG. Nighttime doses of G99 showed dose-related reductions in trough DBP and SBP (6PM-10PM) and were statistically significantly different from placebo for G99 240mg (p<0.0001), 360mg PM (p=0.002), and 540mg (p<0.0001). Nighttime G99 360mg was associated with significantly greater reductions in mean DBP and SBP between 6AM and 12NOON compared to morning G99 360mg with least squares mean treatment difference of -3.3 mm Hg (p=0.0004) for DBP and -5.3 mm Hg (p<0.0004) for SBP. Incidence of AEs for all G99 treatment groups combined (44.5%) was less than the corresponding value obtained for the placebo group (49.3%). Discontinuation rates due to AEs were 3.2% for the G99 groups and 4.3% for the placebo group. In conclusion, nighttime dosing with G99 provides effective BP control throughout a 24-hour dosing interval while at the same time producing clinically meaningful further BP reductions between 6AM and 12NOON to that achieved by the identical dose administered in the morning. The highest dose (540mg) was particularly effective and very well tolerated.

Key Words: Diltiazem HCl Extended Release, Chronotherapy, Nighttime Dosing

P-55
Use of doxazosin gits by primary care physicians: an observational study in patients with hypertension
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Objective: A clinical practice study in Germany assessed the efficacy and tolerability of controlled release doxazosin gastrointestinal therapeutic system (GITS) for HTN.

Methods: This multicenter study evaluated the efficacy and tolerability of doxazosin GITS in hypertensive patients, either previously treated with doxazosin standard (STD) and switched to GITS (group 1) or hypertensive patients treated with GITS who did not receive prior treatment with an alpha, antagonist (group 2). Starting dose of GITS was 4 mg/d, titrated to 8 mg/d if BP did not reach goal. BP and pulse rates were measured at baseline and monthly x3. The efficacy and tolerability of previous therapy with STD was compared to GITS. Antihypertensive efficacy was evaluated by investigator and drug tolerability was evaluated by patient according to a subjective scale with very good, good, moderate, and inadequate categories. A successful BP response was defined as DBP ≤90 mmHg.

Results: 8320 patients were evaluated, 5428 in group 1 and 2892 in group 2. By study end, approximately 98% of patients in both groups were receiving the starting dose of GITS. 24.6% (group 1) and 22.2% (group 2) of patients received combination therapy. In group 1, mean SBP and DBP were reduced by 12 mmHg and 7 mmHg respectively 3 months after switching from STD to GITS. Responders increased from 59.6% to 92.1%. In group 2, mean SBP and DBP was reduced by 25.3 mmHg and 14.6 mmHg, respectively. Responders increased from 18.3% to 89.3%. Overall, GITS efficacy was rated “very good” or “good” by 95.0% of investigators. In group 1, STD was rated “very good” or “good” in 76.5% of patients compared with 99.2% for GITS. The tolerability of GITS was rated “very good” or “good” in 99.0% of patients overall. The incidence of adverse events in patients taking GITS was 0.18%.

Conclusions: DOX GITS as monotherapy or in combination therapy is an effective and well-tolerated antihypertensive treatment in general practice. The improved BP efficacy may be a function of ease of dosing and greater tolerability.

Key Words: Doxazosin GITS, Hypertension, Blood Pressure