studies for this therapeutic effect of acetylcysteine.
Methods: The initial electronic search queried both the Medline database and the Cochrane Library for the perior of January 1996 ttrough May 2003. Furthermore a manual inspection of articles published in New England Journal of Medicine, Circulation, Journal of the American College of Cardiology was conducted for the years 1998-2002. Bibliographies of the identified articles were searched for additional pertinent articles as well as the bibliographies of three prominent cardiovascular textbooks. A meta-analysis of the data meeting specific criteria for inclusion was performed.
Results: Five studies with a total of 641 patients were identified that evaluated the effect of oral prophylactic administration of acetylcysteine on CIN in randomized controlled trials vs. placebo. The baseline serum creatinine concentrations varied from 1.4+/_ 0.4 mg/dlto 2.8+/_ 0.8 mg/dlin the five trials. Contrast dose ranged from< 80 ml to > 375 ml. Acetylcysteine dosage was 400 mg or 600 mg bid started the day prior to or on the day of the procedure and continued thereafter for two days. All patients received hydration with 0.45% normal saline or 0.9% normal saline pre and post procedure. Acetylcysteine administration reduced the incidence of CIN (defined as a 0.5 mg/dl or a 25% increase in creatinine concentration) from 11%-45% in the placebo group to 2%-8% in the acetylcysteine group. The combined risk ratio of the treated group was 0.19 with a combined 95% confidence interval of 0.093 to 0.379 and a p-value of <0.0001.
Conclusions: Based on this meta-analysis, prophylactic administration of oral acetylcysteine significantly reduces the risk of CIN in patients with mild to moderate renal insufficiency.

1141-192 Genetic Variation in Cyclooxygenase-1 Associates With the Antiplatelet Effect of Aspirin in Stable Coronary Artery Disease

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Impaired antithrombotic effect of aspirin may be a risk factor for coronary events in stable coronary artery disease (CAD). The pharmacogenetics of the COX-1, the target of the antithrombotic effect of aspirin, have not been studied previously. In the current series, we have analysed platelet responses in stable CAD patients on aspirin. The platelet responses were determined with optical aggregometry as well as PFA-100. The phenotypes were related to patient characteristics as well as COX-1 haplotype.
We took blood samples from 101 patients with stable CAD on aspirin (100mg/day). The antiplatelet effect of the treatment regimen was studied in whole blood with PFA-100 and in platelet-rich plasma with turbidometric aggregations using arachidonic acid (AA)-induced (1.5mmol/L) aggregation to identify the aspirin response. We used 170s. closure time (CT-CEPI) for PFA-100 and aggregation slope of 10%/min for AA as predetermined cut-off points for aspirin response.
7% (AA) and 22% (CT-CEPI) of patients were defined as poor aspirin responders. Individuals carrying the rare (20%) COX-1 haplotype had shorter mean CT-CEPI (222s., SD 81s.) compared to carriers of the common (80%) haplotype (261s., SD 67s.) (p=0.03). In addition, platelets of individuals from the rare haplotype group showed more preserved mean AA-induced maximal aggregation (31% +-6.5) compared to the common haplotype (21%+-1.3) (p=0.02).
We conclude that impaired response to aspirin measured with PFA-100 and aggregometry is common among individuals with angiographically proven severe CAD and is associated with common genetic variation of COX-1.

1141-193 Short Burst Oral Amiodarone Improves Cardioversion Success Rates for Patients in Persistent Atrial Fibrillation

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Background: Increasing efforts have been made to improve the success rates for external direct-current cardioversion (EDC) for patients in persistent atrial fibrillation, without exposing them to prolonged toxic side effects of antiarrhythmic treatment.
Methods: 35 patients with rate controlled persistent atrial fibrillation (>1month), listed for EDC, were randomized to 2 groups. Group A received 4 weeks of oral amiodarone: 200mg Tds for 1 week prior to DCCV, then 200mg Tds week 2, 200mg Bd week 3 and then 200mg daily for week 4. Group B did not receive amiodarone. The cardioversion protocol of up to 5 synchronized shocks, was the same for the 2 groups (anterior-anterior 200J, 360J, 360J then anterior-posterior 360J and 360J).
Results: All results are expressed as mean ± standard deviation. The 2 groups, A and B respectively, were demographically well matched: age (61.2 ± 12.3 vs. 61.6 ± 7.6 years, p=0.96), weight (85.4 ± 8.90 vs. 85.4 ± 12.5 kg, p=1.0), left ventricular ejection fraction (50.2 ± 13.5 % vs. 51 ± 13.0 %, p=0.9), left atrial size (4.4 ± 0.6 cm vs. 4.1 ± 0.8 cm, p=0.55), mean duration of AF (7.2 ± 4.2 months vs. 10.2 ± 6.0 months, p=0.16), and heart rate pre-cardioversion (90.8 ± 14.7/min vs. 88.1 ± 18.0/min, p=0.64). The initial cardioversion success rate was 17/17=100% for group A vs. 17/18=94% for group B, p=1.0). There was a non-significant trend to the use of fewer shocks (1.7 ± 0.9 vs. 2.2 ± 1.4, p=0.42) and less total shock energy (454 J ± 331.1 vs. 620J ± 497.8, p=0.42) in the amiodarone group. The number of patients remaining in sinus rhythm at 6 weeks and 6 months respectively was significantly higher in group A than group B (15/17=88% vs. 3/18= 16.7%, p=<0.0001 and 11/17=65% vs. 3/18= 17%, (p=0.0016) respectively. However, by a mean follow-up of 16.2 (± 4.1) months there was only a non-significant trend to a higher rate of sinus rhythm in the amiodarone group as compared with the control group (8/17, 47.1% vs. 3/18, 16.7%; p=0.075).
Conclusion: For patients in persistent AF, a short course of oral amiodarone appears to improve 6 week and 6 month sinus rhythm rates following external direct-current cardioversion. This interesting data needs to backed up by a larger randomized study.

1141-194 Chronic Therapy With Phospodiesterase 5 Inhibitor Tadalafil Has a Sustained Effect on Endothelial Function

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Erectile dysfunction (Ed) is often associated with a cluster of risk factors for coronary artery disease and with a reduced endothelial function. Acute administration of phosphodiesterase-5 inhibitors (PDE5) improves endothelial function in patients with ED. Tadalafil is a newer PDE5 inhibitor with a long half life that allows chronic administration and chronic therapy with Tadalafil has been suggested to be beneficial in patients with ED.
We hypothesized that chronic therapy with T may improve endothelial function in patients with ED and increased cardiovascular risk. To this end we randomized 32 patients with ED to receive either T 20 mg on alternate days or matching placebo (P) for 1 month. Brachial artery flow-mediated dilation (FMD) was assessed at baseline, at 1 month and at 6 weeks. At 1 month FMD was significantly improved by T (from 4.2±3.2 to 9.3±3.7%, p=0.01 vs. baseline), but was not affected by PL (from 4.1±2.8 to 4.0±3.4%, p=0.09 vs. baseline). At 6 weeks the benefit in FMD was sustained in patients that received T (9.1±3.9% vs 4.2±3.2%, p=0.01 vs. baseline; 9.1±3.9% vs 9.3±3.7%, vs 1 month, p=NS) while no changes in FMD were observed in patients randomized to P.
In conclusion, chronic therapy with T improves endothelial function. The benefit of this therapy seems to be sustained after discontinuation of therapy. Larger studies are needed in order to assess the clinical implications of this scheme of therapy.

1141-195 Chromium Supplementation Shortens QTc Interval Duration in Patients With Type 2 Diabetes

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Background. QTc interval duration is predictive of mortality in diabetic patients. Since hromium supplementation has been shown to improve insulin sensitivity, lower plasma insulin levels, and improve glucose homeostasis, we sought to investigate the potential effects of chromium on QTc interval duration in patients with type 2 diabetes.
Methods. We performed a double-blind, randomized, placebo-controlled cross-over trial enrolling 60 patients with diet-treated type 2 diabetes, who were randomly assigned to either Group A or Group B. Group A (n=30) received 1 mg of chromium picolinate (CrPic) daily for 12 weeks, followed by placebo in the next 12 weeks; Group B (n=30) was treated with placebo for the first 12 weeks and CrPic in the next 12 weeks. At each visit, QT interval was measured on a standard surface ECG by averaging 3 consecutive beats in leads II, and V4, and corrected for heart rate with the Bazett formula. QTc interval shortening was defined as a difference between two consecutive QTc interval measurements of at least 10 ms.
Results. Baseline QTc interval was similar in both group (422±34 ms in Group A vs. 425±24 ms in Group B, p=0.77). Within first 12 weeks, QTc interval shortened in Group A, but not in Group B, which led to a significant difference in QTc interval duration between the groups (406±35 ms in Group A vs. 431±26 ms in Group B, p=0.01). In the following 12 weeks, QTc interval shortened in Group B but not in Group A, which resulted in a comparable QTc interval duration of both groups at the end of the study (414±28 ms in Group A vs. 409±22 ms in Group B, p=0.50). Overall, QTc interval shortening (>10 ms) with CrPic therapy was observed in 62% of patients. Except for body mass index (31.4±4.2 kg/m^2 in patients with QTc shortening vs. 28.7±4.2 kg/m^2 in patients without QTc shortening, p=0.03) none of the clinical and laboratory variables were predicitve of QTc shortening in our patient cohort.
Conclusions. Short-term chromium supplementation shortens QTc interval duration in patients with type 2 diabetes. These effects appear to be especially pronounced in diabetic patients with a higher body mass index.

1141-196 Effect of Atorvastatin and Sildenafil on Endothelial Function in Patients With Erectile Dysfunction and Increased Cardiovascular Risk

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Erectile Dysfunction is often associated with an increased cardiovascular risk and with a decrease in endothelial function. In patients with increased cardiovascular risk statin therapy reduce cardiovascular events and improves endothelial function. Oral therapy with phosphodiesterase-5 inhibitors improves erectile function through an amelioration of endothelial function.
Aim of the present study was to compare the effects of Sildenafil (S, 25 mg tds), Atorvastatin (A, 20 mg od) and their combination (CT) on endothelium-dependent flow mediated vasodilation (FMD), plasma nitrite, nitrate and endothelin-1 in 16 male with increased cardiovascular risk and erectile dysfunction in a double-blinded double-crossover study. Patients were randomized and treated for 1 weeks with either S, A or CT. Brachial artery diameter, FMD, endothelin-1 and plasma nitrite and nitrate levels were measured at baseline and after each treatment phase.
Brachial artery diameters remained unchanged after each treatment phase. All treatments significantly improved FMD compared to baseline.
In conclusion chronic therapy with S improves endothelial function by a similar extent of statin therapy. Combination of Sildenafil and Atorvastatin is more effective that either therapies alone in improving endothelial function and reducing plasma levels of endothelin-1 in male patients with increased cardiovascular risk.