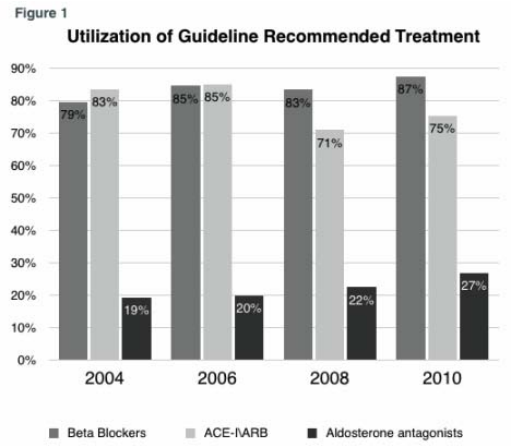
S14

Use and Safety of Aldosterone Blockers in Patients with Left Ventricular Dysfunction in ACSIS Survey

Klempfner, Robert[1]; Goldenberg, Ilan[1]; Fefer, Paul[2]; Matetzky, Shlomi[3]
[1]Leviev Heart Center, Sheba Medical Center, Cardiac Rehabilitation Institute, Ramat Gan, Israel; [2]Leviev Heart Center, Sheba Medical Center, Invasive Cardiology Department, Ramat Gan, Israel; [3]Leviev Heart Center, Sheba Medical Center, Intensive Care Unit, Ramat Gan, Israel

Background: The landmark EPHESUS trial, showed that treatment with the selective aldosterone blocker eplerenone is associated with a significant reduction in morbidity and mortality among patients with acute myocardial infarction (AMI) complicated by left ventricular dysfunction and heart failure. We sought to assess the implementation of this indication in a real world setting among patients enrolled in the ACSIS surveys.
Methods: The study population comprised 955 patients from ACSIS 2004-2010 who met the guideline criteria for treatment with aldosterone blockers including Killip class II or III on admission, serum creatinine≤ 2.4 mg\dL, and left ventricular ejection fraction (LVEF)≤ 40%.
Results: Among 7,696 patients enrolled in the ACSIS surveys from 2004, 955 (12%) were identified as eligible for treatment with an aldosterone blocker, meeting the above mentioned criteria. In this population treatment with an aldosterone blocker showed a modest increase from 19% to 27% over the six year period, whereas utilization of other recommended medications in this population was >2-fold higher (Figure 1). The underutilization of aldosterone blockers was consistent among all participant centers. Multivariate logistic regression analysis showed that independent predictors of aldosterone blocker under-utilization included LVEF 30-40% vs. <30% (adjustedOR = 1.89 [95%CI 1.30-2.78]); Killip class II vs. III on admission (adjusted OR = 2.46 [95%CI 1.71-3.53]); and prior CVA (adjusted 2.78 [95%CI 1.35-5.88]), whereas serum creatinine was not significantly different between eligible patients who did or did not receive an aldosterone blocker. Aldosterone-blocker administration was not associated with an increased rate of in-hospital complications or re-hospitalization following discharge.
Conclusions: Less than one third of AMI patients who are eligible for treatment with an aldsoterone blocker according to current guidelines receive this mode of medical therapy.

Figure 1



Vitamin D Inhibits the Rise in Inflammatory Cytokine and Adhesion Molecule Levels Post MI Patients

Arnson, Yoav[1]; Amital, Howard[2]; Mosseri, Morris[1]; Itzhaky, Dganit[3]
[1]Meir Medical Center, Cardiology, Kfar Saba, Israel; [2]Tel Hashomer, Internal Medicine, Tel Aviv, Israel; [3]Meir Medical Center, Biochemistry and Immunology Labs, Kfar Saba, Israel

Introduction: Atherosclerosis is a chronic inflammatory condition of the atrial wall. Accumulating evidence suggests the involvement of the innate and adaptive immune systems in atherosclerosis. Vitamin D has immune modulating properties. Low vitamin D levels are associated with higher prevalence of cardiovascular risk factors and a higher risk of myocardial infarction. In this paper we explore the effects of short vitamin D supplementation, after an acute coronary syndrome, on inflammatory cytokine levels.
Methods: Patients were recruited after presenting with an ACS. All patients received optimal medical therapy and underwent a coronary angiography. Half of the patients were treated with a daily supplement of vitamin D, 4000IU for 5 days. Circulating levels of vitamin D, VCAM-1, ICAM-1, E-selectin, VEGF, CRP, IL-6, IL-8 and TNF were tested upon arrival and after 5 days.
Results: Fifty patients were recruited. Average patient age was 60; thirty-nine patients were male. Average vitamin D levels were 18.5ng/mL. In the control group there was an increase in inflammatory cytokine levels after five days. Treatment group cytokine levels showed a decreased elevation or a reduction compared to the control. There were significant differences in VCAM-1 levels (decrease of 15.36 ng/mL vs. 103.03 increase, P=0.001) and iL-6 (-0.11 vs. 3.33 pg/mL, P=0.0005). There were trends towards significance in levels of ICAM-1 (-1.26 vs. 19.97 ng/mL, P=0.17), CRP (1.28 vs. 3.25, P=0.09), Selectin (-4.14 vs. -0.15 ng/mL, P=0.16), VEGF (137.4 vs. 263.1 pg/mL, P=0.16), IL-8 (-6.36 Vs. 7.95 pg/nL, P=0.1). There was no significant difference in TNF levels.
Conclusion: A short treatment with vitamin D effectively diminishes the increase in circulating inflammatory cytokines and interleukins after an. These findings shed a light on the anti-inflammatory effects of vitamin D on the vascular system, and may explain some of the cardio-protective properties attributed to vitamin D.

The Absorption of Magnesium Oxide Compared to Citrate in Healthy Subjects

Shechter, Michael[1]; Saad, Tomer[1]; Shechter, Alon[1]; Koren-Morag, Nira[1]; Silver, Burton[2]; Matetzky, Shlomi[1]

[1]Chaim Sheba Medical Center, The Sackler Faculty of Medicine, Tel Aviv University, Tel Hashomer, Israel; [2]IntraCellular Diagnostics, Inc., Magnesium Research, Medford, USA

Background: Magnesium content in food is steadily decreasing in the Western world. Hypomagnesemia is associated with increased incidence of diabetes mellitus, metabolic syndrome, all-cause and coronary artery disease mortality. Two common oral magnesium supplements are magnesium oxide and citrate; however, data regarding the differences in their absorption in humans are sparse.

Methods: In a randomized, prospective, double-blind, crossover study, 41 (20 women) healthy volunteers [mean age 53±8 (range 31-75) years] received either magnesium oxide monohydrate tablets (520 mg/day of elemental magnesium) or magnesium citrate tablets (295.8 mg/day of elemental magnesium) for 1 month (phase 1), followed by a 4-week wash-out period, and then crossover treatment for 1 month (phase 2). Intracellular magnesium concentrations ($[Mg^{2+}]i$) were assessed from sublingual cells through x-ray dispersion (normal values 37.9±4.0 mEq/L), serum magnesium levels, platelet aggregation, and quality-of-life questionnaires were assessed before and after each phase.

Results: Oral magnesium oxide, rather than magnesium citrate, significantly increased $[Mg^{2+}]i$ (34.4±3 vs 36.3±2 mEq/L, $p<0.001$ and 34.7±2 vs 35.4±2 mEq/L, $p=0.097$; respectively), reduced total cholesterol (201±37 vs 186±27 mg/dL, $p=0.016$ and 187±28 vs 187±25 mg/dL, $p=0.978$; respectively) and low-density lipoprotein (LDL) cholesterol (128±22 vs 120±25 mg/dL, $p=0.042$ and 120±23 vs 121±22 mg/dL, $p=0.622$; respectively). However, both treatments significantly reduced epinephrine-induced platelet aggregation (78.9±16% vs 71.7±23%, $p=0.013$ and 81.3±15% vs 73.3±23%, $p=0.036$; respectively).

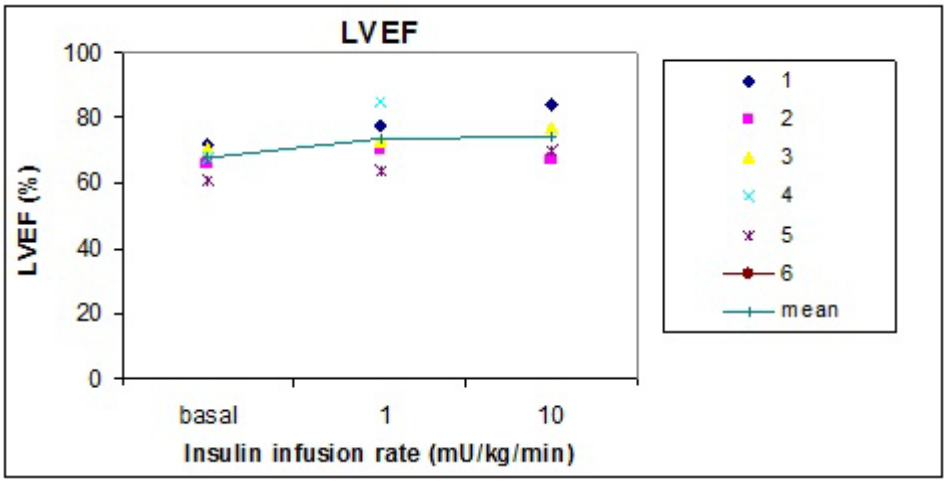
Conclusions: Oral magnesium oxide treatment significantly improved $[Mg^{2+}]i$, total and LDL cholesterol compared with magnesium citrate, although both treatments similarly inhibited platelet aggregation in healthy subjects with no apparent heart disease.

Short Term Insulin Improves Cardiac Function in Diabetic Patients

Daoud Naccache, Deeb[1]*; Bar-Yoseph, Ronen*[2]
[1]*Rambam Health Campus, Institute of Endocrinology, Diabetes and Metabolis, Haifa, Israel;*
[2]*Rambam Health Campus, Paediatrics A, Haifa, Israel*

Aims: To study: a. the potential role of insulin in reversing diastolic abnormalities, b. its effective level and c. it's applicability in the routine clinical setting.
Methods: Seven male patients were compared to a group of healthy persons, aged 46.7 vs. 28.4 yrs, diabetes duration 12.9 vs. 0 yrs, BMI 28.3 vs. 24.8 kg/m2 and HbA1c 6.7 vs. 4.8%, respectively. Each diabetic subject was evaluated for hemodynamic parameters and for insulin-induced glucose disposal rates, during a 2-steps euglycemic hyperinsulinemic clamp technique. Echocardiographic systolic and diastolic left ventricular function parameters were taken at baseline, and at the end of each 2-hr clamp step.
Results: On the first insulin load, both systolic and diastolic blood pressure had significantly decreased, by 7 mm and 4 mmHg, respectively, and remained stable during the second insulin load. First insulin load significantly increased left ventricular systolic function, in terms of ejection fraction and fractional shortening by 9% and 12%, respectively. The second insulin load did not change further these two parameters. In contrast, left ventricular diastolic function measurements revealed no significant change after insulin administration. However, under 1st and 2nd insulin loads, Maximal mitral flow velocity had improved by 20% and 26% respectively.
Conclusion: Insulin acutely affected the diabetic heart at a therapeutic insulin blood level, within a time course of two-hour. Insulin mainly affected positively systolic left ventricular function, a leading parameter in the clinical settings of acute pulmonary edema and acute myocardial infarction.

Fig. 1 - Left ventricular ejection fraction vs. insulin loads. Baseline value was 68±2%. 1st insulin load increased LVEF to 74±3.5% ($p<0.05$). 2nd insulin load increased LVEF to 74.5±3.8% in (p= insignificant).



Superficial Subcutaneous Fat - A Putative Distinct Protective Fat Sub-Depot in Type 2 Diabetes

Golan, Rachel[1]; Shelf, Ilan[2]; Rudich, Assaf[3]; Gepner, Yftach[1]; Shemesh, Elad[2]; Chassidim, Yoash[4]; Harman-Boehm, Ilana[5]; Henkin, Yaakov[6]; Schwarzfuchs, Dan[7]; Shai, Iris[8]

[1]Ben Gurion University of the Negev, Epidemiology, Beer Sheva, Israel;
[2]Soroka University Medical Center, Radiology, Beer Sheva, Israel;
[3]Ben Gurion University of the Negev, Clinical Biochemistry and The S. Daniel Abraham Ce, Beer Sheva, Israel;
[4]Soroka University Medical Center, Physiology and Neuroradiology, Beer Sheva, Israel;
[5]Soroka University Medical Center, Internal Medicine and Diabetes, Beer Sheva, Israel;
[6]Soroka University Medical Center, Cardiology, Beer Sheva, Israel;
[7]Nuclear Research Center Negev, Dimona, Israel;
[8]Ben Gurion University of the Negev, The S. Daniel Abraham Center for Health and Nutrit, Beer Sheva, Israel

Objective: Unlike Visceral Adipose tissue (VAT), the association between Subcutaneous-Adipose Tissue (SAT) and obesity-related morbidity is controversial. We assessed in patients with type 2 diabetes if this variability can be explained by a putative favorable, distinct association between abdominal superficial-SAT (absolute amount or its proportion) with cardio-metabolic parameters.
Research Design and Methods: We performed abdominal Magnetic Resonance Imaging (MRI) among 73 patients with diabetes [mean age=58, 83% men] and cross-sectionally analyzed fat distribution at S1-L5, L5-L4 and L3-L2 levels. Patients completed food frequency questionnaires, and subgroups had 24-hour ambulatory-blood-pressure (ABP)-monitoring and 24-hour ambulatory-ECG.
Results: Women had higher %SSAT (37% vs. 23% in men; $p<0.001$), despite a similar mean waist circumference. Fasting plasma glucose ($p=0.046$) and HbA1c ($p=0.006$), were both lower with increased tertile of absolute SSAT. In regression models adjusted for age, waist circumference and classes of medical treatments used in this patient population, increased %SSAT was significantly associated with decreased HbA1c (beta=-0.317;$p=0.013$), decreased daytime ABP (beta=-0.426;$p=0.008$) and increased HDL-c (beta=0.257;$p=0.042$). In contrast, increased %DSAT was associated with increased HbA1c (beta=0.266;$p=0.040$) and with poorer heart rate variability parameters ($p=0.030$). Although total fat and energy intake were not correlated with fat tissue distribution, increased intake of trans fat tended to be associated with total SAT($r=0.228$;$p=0.05$) and DSAT ($r=0.20$;$p=0.093$), but not SSAT.
Conclusions: Abdominal SAT is composed of two sub depots that associate differently with cardio-metabolic parameters. Higher absolute and relative distribution of fat in abdominal SSAT may signify beneficial cardio-metabolic effects in patients with type 2 diabetes.

Fibrate/Statin Treatment Following an Acute Coronary Syndrome

Medvedofsky, Diego[1]; Goldenberg, Ilan[2]; Fisman, Enrique[3]; Bubyr, Liudmila[4]; Matetzky, Shlomi[1]; Tanne, David[4]; Klempfner, Robert[1]; Shemesh, Joseph[5]; Tenenbaum, Alexander[1]
[1]The Chaim Sheba Medical Center, Tel-Hashomer, Leviev Heart Institute, Ramat Gan, Israel; [2]Leviev Heart Institute and the Israeli Society for the Prevention of Heart Attacks, The Chaim Sheba Medical Center, Tel-Hashomer, Cardiac Rehabilitation Institute, University of Rochester Medical Center, New York, Heart Research Follow-up Program, Ramat Gan, Israel; [3]Cardiovascular Diabetology Research Foundation, Holon, Israel; [4]The Chaim Sheba Medical Center, Tel-Hashomer, Israeli Society for the Prevention of HeartAttacks, Ramat Gan, Israel; [5]The Chaim Sheba Medical Center, Tel-Hashomer, Cardiac Rehabilitation Institute, Ramat Gan, Israel

Background: The effect of combination of fibrate with statin on major adverse cardiovascular events (MACE) following acute coronary syndrome (ACS) hospitalization is unclear. The main aim of this study was to investigate the 30-day rate of MACE in patients participated in the nationwide ACS Israeli Surveys (ACSIS) treated on discharge with a fibrate (mainly bezafibrate) and statin combination vs. statin alone.
Methods: The study population comprised 8982 patients from the ACSIS 2000, 2002, 2004, 2006, 2008 and 2010 enrollment waves who were alive on discharge and received statin. Of these, 8545 (95%) received statin alone and 437 (5%) received fibrate/statin combination. MACE was defined as a composite measure of death, recurrent MI, recurrent ischemia, stent thrombosis, ischemic stroke and urgent revascularization.
Results: Patients from the combination group were younger (58.1±11.9 vs. 62.9±12.6 years). However, they had significantly more co-morbidities (hypertension, diabetes, current smokers) and unfavorable cardio-metabolic profile (with respect to glucose, total cholesterol, triglyceride and HDL-cholesterol). Development of MACE was recorded in 513 (6.0%) patients from the statin monotherapy group vs. 13 (3.2%) from the combination group, p = 0.01. 30-day re-hospitalization rate was significantly lower in the combination group: 68 (15.6 %) vs. 1691 (19.8 %) of patients, respectively; p = 0.03. Multivariable analysis identified the fibrate/statin combination as an independent predictor of reduced risk of MACE with odds ratio of 0.54, 95% confidence interval 0.32-0.94.
Conclusion: A significantly lower risk of 30-day MACE rate was observed in patients receiving combined fibrate/statin treatment following ACS compared with statin monotherapy.