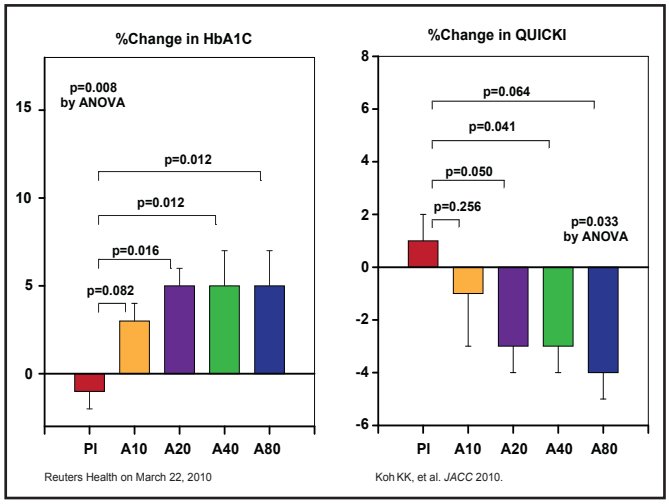
decreased plasma adiponectin levels by 10% (p=0.012) and insulin sensitivity by 6% (p=0.007) compared with baseline [Koh KK. *Atherosclerosis* 2009].

Treatment with atorvastatin also appears to adversely effect glucose metabolism. In a study of 213 patients with hypercholesterolemia, treatment with atorvastatin 10 to 80 mg/day significantly reduced LDL and apolipoprotein B levels compared with placebo after 2 months (p<0.001) [Koh KK et al. *J Am Coll Cardiol* 2010]. All doses of atorvastatin also significantly increased glycated hemoglobin levels (p=0.008) and significantly decreased insulin sensitivity (p=0.033) compared with placebo (Figure 1). These findings support the hypothesis that lipophilic statins, including atorvastatin, simvastatin, and rosuvastatin, might increase the onset of new diabetes in patients with hypercholesterolemia. Prof. Koh suggests a weak hydrophilic, but strong HMGCoA enzyme inhibiting statin, following rosuvastatin because rosuvastatin is not lipophilic.

Figure 1. Atorvastatin (10, 20, 40, or 80 mg/day) Significantly Increases HbA1C Levels and Insulin Resistance In Hypercholesterolemic Patients.



A10=atorvastatin 10 mg/day; A20=atorvastatin 20 mg/day; A40=atorvastatin 40 mg/day; A80=atorvastatin 80 mg/day; ANOVA=analysis of variance; Pl=placebo; QUICKI=Quantitative Insulin-Sensitivity Check Index.

Fibrate-Based Combination Therapy

Elevated triglyceride levels are another important target for combination therapy. According to a meta-analysis of 262,525 participants in 29 studies, there is a significant correlation between triglyceride values and CHD risk. Indeed, patients in the top tertile of triglyceride values have a 72% higher risk of CHD than those in the bottom tertile (OR, 1.72; 95% CI, 1.56 to 1.90) [Sarwar N et al. *Circulation* 2007].

Fibrates are emerging as an important therapeutic option for patients with elevated triglyceride levels. In addition to lowering triglyceride levels, fibrate therapy improves endothelium-dependent vasodilation, exerts anti-inflammatory effects, stabilizes atherosclerotic plaques, and inhibits platelet thrombus formation. In a meta-analysis of 18 trials, fibrates significantly reduced the risk of major cardiovascular events in patients with combined dyslipidemia (RR, 0.90; p=0.048), primarily by preventing coronary events (RR, 0.87; p<0.0001) [Jun M et al. *Lancet* 2010].

Fibrates also enhance the cardioprotective effects of other drug classes. In a randomized, double-blind, placebo-controlled study of 44 patients with hypertension and hypertriglyceridemia, combination therapy with fenofibrate and candesartan provided greater improvement in endothelial function and greater reduction in hsCRP level compared with fibrate or ARB monotherapy. All treatment options, including combination therapy, fenofibrate monotherapy, and candesartan monotherapy, also significantly increased adiponectin levels and insulin sensitivity compared with baseline [Koh KK et al. *Diabetes Care* 2006].

In summary, there are multiple etiologies for atherosclerosis and cardiovascular disease. Thus, combination therapy with drugs that have distinct and separate mechanisms of action appear to provide greater protection against cardiovascular events than individual monotherapies. Clinicians should select specific combination regimens that have been shown to provide comprehensive protection against the adverse consequences of abdominal obesity and increased cardiometabolic risk, Prof. Koh said.

Abdominal Obesity and Diabetes Are on the Rise in Latin America

Obesity is replacing malnutrition as an urgent public health concern throughout Latin America, especially among lower-income populations. Walmir Coutinho, MD, Catholic University, Rio de Janeiro, Brazil, described the adverse consequences of obesity on the cardiometabolic risk profiles in this region.

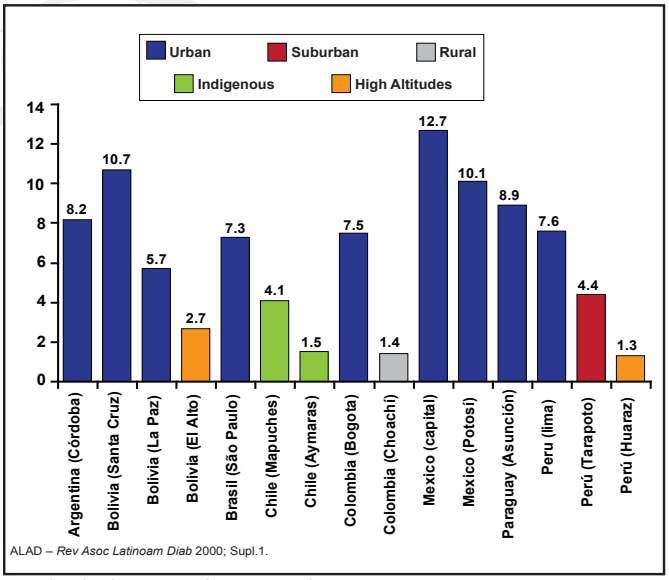
In Chile, obesity increases with age and is most common among those in the lowest socioeconomic class. The overall prevalence of obesity is 15.7% among men and 23% among women [Jadue L et al. *Rev Med Chil Nutr* 1999]. Rates of obesity are similar among men (16%) and women (23.5%) in Peru, where obesity is also inversely associated with socioeconomic status [Jacoby et al. *Prev Med* 2003].

Latin American populations may be particularly susceptible to central fat deposition. Mexican women are significantly more likely than North American women to have central adiposity, particularly when BMI is low. Among those

with a BMI of 18–25 kg/m^2, 76% of Mexican-American women and 42% of North American women have a waist circumference >80 cm (p<0.001) [ENSA 2000. Mexico]. In Peru, 59% of women and 13% of men with normal body weight have an abdominal circumference that exceeds recommended thresholds, defined as <80 cm for women and <94 cm for men [Jacoby et al. *Prev Med* 2003].

Diabetes is also on the rise in Latin America; yet, it remains poorly recognized. The estimated prevalence of diabetes in urban areas is 12.7% in Mexico, 10.7% in Bolivia, and 8.9% in Paraguay. In rural areas, such as Choachi, Columbia, approximately 1.4% of the population has diabetes (Figure 1) [ALAD. *Rev Assoc Latinoam Diab* 2000]. Overall, 30% to 50% of diabetes cases are undiagnosed. In rural areas, where up to 40% of the population resides, the rate of undiagnosed cases approaches 100%.

Figure 1. Prevalence of Type 2 Diabetes in Latin American Populations.



ALAD – *Rev Asoc Latinoam Diab* 2000; Supl.1.

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Cardiometabolic risk factors, such as psychological stress, may have a stronger detrimental impact on Latin American populations. In the INTERHEART Study, the presence of moderate/severe stress increased the risk of myocardial infarction (MI) by 54% across all regions (OR, 1.54; 95% CI, 1.39 to 1.71). Specifically, within South America, moderate/severe stress more than doubled the risk of MI (OR, 2.26; 95% CI, 1.70 to 3.00) [Yusuf S et al. *Lancet* 2004].

Population growth, aging, and urbanization are among the many factors that contribute to a rise in obesity and diabetes among Latin American populations. Managing the emerging obesity epidemic will require education, early diagnosis of diabetes and other risk factors, and aggressive intervention, including increased physical activity and healthier food options, Prof. Coutinho concluded.