Reducing cellular stress may prevent diabetes complications

Poorly controlled diabetes is often associated with various complications including blindness, kidney failure and pain secondary to damaged nerves. However, the most common complications are those related to large blood vessel disease such as heart attacks and strokes that account for 80% of mortality. The good news is that these complications have decreased over the last 20 years. Many factors account for this favorable change. One such factor is the availability of drugs that reduce the risk of heart attacks and strokes.

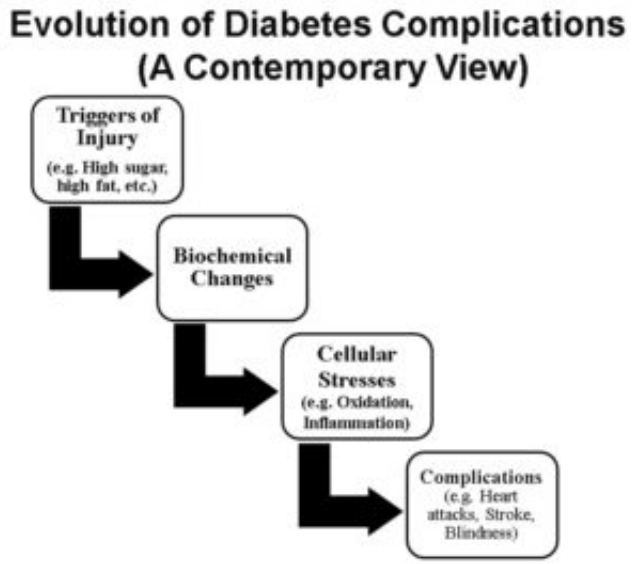

Fig. 1.

These drugs are aspirin, statins that lower blood cholesterol level and two classes of drugs that treat hypertension notable the beta adrenergic receptor blockers and angiotensin converting enzyme inhibitors or angiotensin receptor blockers. All these drugs have a common denominator namely they are capable of reducing cellular stresses such as oxidative stress, inflammatory stress and stress in the endoplasmic reticulum (ER), the site of protein packaging in the cell. Unfortunately, antioxidant vitamins do not reduce the complications of diabetes and in some cases may increase health-related risks. Experiments have shown that antioxidants as they reduce oxidative stress they aggravate ER stress. Thus drugs that are likely to decrease diabetes complications should be able to reduce all forms of cellular stress. These observations taken together suggest that diabetes complications may arise because of a cascade of events that start with some biochemical changes that cause cellular stress that ultimately lead to clinically demonstrable complications (Fig. 1).

It is noteworthy that the specific drugs that target the biochemical abnormalities that occur because

of high blood sugar levels have not been able to decrease diabetes complications. In addition, although controlling blood sugar levels has been proven to reduce the risk of blindness, kidney failure and painful nerve damage, clinical trials have not been able to show conclusively that controlling blood sugar levels would also decrease the risk of heart attacks or strokes. Therefore it is important to develop new strategies and new drugs that can decrease the risk of cardiovascular complications of diabetes. Understanding how stress emerges in various compartments of the cell and how these various stresses interact with each other would help in identifying drugs that can reduce cellular stress globally and possibly decrease the risk of serious complications of diabetes.

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Publication

Therapeutic Targeting of Cellular Stress to Prevent Cardiovascular Disease: A Review of the Evidence.
Mooradian AD
Am J Cardiovasc Drugs. 2016 Oct 24