News and Views

Should Combination Therapy be the First-line of Treatment in Type 2 Diabetes?

Combined therapy with sodium-glucose cotransporter-2 inhibitors (SGLT2i) or glucagon-like peptide-1 receptor agonists (GLP-1RA), compared to either drug alone, is associated with reduced risk of all-cause mortality and cardiovascular disease (CVD), according to a new study published in the journal *Diabetes, Obesity and Metabolism*.[1]

This study retrospectively analyzed data of people with type 2 diabetes receiving insulin to examine the risk of all-cause mortality, hospitalization and cardiovascular outcomes at 5 years following monotherapy with either SGLT2i or GLP-1RA alone or their combination (SGLT2i + GLP-1RA). Out of the 2.2 million patients included, 143,600 received SGLT2i, 186,841 received GLP-1RA, while 108,504 were treated with the combination. The controls received neither SGLT2i nor GLP-1RA.

The risk of all-cause mortality was found to be decreased in all three intervention groups over a period of 5 years with hazard ratios (HR) of SGLT2i 0.49, GLP-1RA 0.47 and combination 0.25.

Similarly, the risks of hospitalization (HR 0.73, 0.69, 0.60) and myocardial infarction (HR 0.75, 0.70, 0.63) were also reduced in SGLT2i arm, GLP-1RA arm and the combination arm, respectively.

At 5 years, treatment with SGLT2i (vs. controls) reduced the risk of all-cause mortality with HR of 0.49. SGLT2i also reduce the risk of hospitalization (HR 0.73), myocardial infarction (HR 0.75), unstable angina (HR 0.79), heart failure (HR 0.73), atrial fibrillation (HR 0.74), stroke (HR 0.75), peripheral vascular disease or PVD (HR 0.79), lower limb amputation (HR 0.69) and chronic kidney disease or CKD (HR 0.79).

Similar trend was noted with GLP-1RA monotherapy (vs. controls) at 5 years with reduction in the risk of all-cause mortality (HR 0.47), hospitalization (HR 0.69), acute myocardial infarction (HR 0.70), unstable angina (HR 0.73), ischemic heart disease or IHD (HR 0.85), heart failure (HR 0.73), atrial fibrillation (HR 0.77), stroke (HR 0.77), PVD (HR 0.89), lower limb amputation (HR 0.66) and CKD (HR 0.90).

Treatment with combination therapy (SGLT2i + GLP-1RA) also reduced the risk of all-cause mortality (HR 0.25), of hospitalization (HR 0.60), acute myocardial infarction (HR 0.63), unstable angina (HR 0.75), IHD (HR 0.84), heart failure (HR 0.60), atrial fibrillation (HR 0.65), stroke (HR 0.69), PVD (HR 0.84), lower limb amputation (HR 0.59) and CKD (HR 0.72) vs. controls.

This study demonstrates that the risk of all-cause mortality and CVD in patients with type 2 diabetes was reduced in all the three intervention arms when compared to the control group. However, the greatest reduction in risk for all-cause mortality was seen with combination therapy. Similarly, the probability of hospital admission was lowest with combination therapy, which also conferred greater cardiovascular protection. Optimal timely glycemic control prevents or delays the onset of diabetes-related macro- and microvascular complications. The antidiabetic drugs should address the "ominous octet" of factors implicated in pathophysiology of type 2 diabetes. They should also be cardioprotective and renoprotective and not just lower blood glucose. SGLT2i and GLP-1RAs are relatively newer antidiabetic drugs, which have also shown extra-glycemic benefits with improvements in cardiovascular and renal outcomes, besides effective glucose-lowering effects in patients with type 2 diabetes, with cardiovascular risk factors or underlying heart disease. Hence, they are game changers in diabetes care. Their combination might potentially provide superior control of blood glucose with low hypoglycemic risk along with cumulative cardiovascular and renal protection.

Reference

1. Riley DR, et al. All-cause mortality and cardiovascular outcomes with sodium-glucose co-transporter 2 inhibitors, glucagon-like peptide-1 receptor agonists and with combination therapy in people with type 2 diabetes. Diabetes Obes Metab. 2023;25(10):2897-909.

Simple Blood Test for Bipolar Disorder: Study

Researchers at the University of Cambridge created a straightforward blood test to improve the precision of bipolar illness diagnoses, according to a study published in *JAMA Psychiatry*. This test was found to be very helpful when used in conjunction with a digital

mental health assessment. It can identify up to 30% of bipolar individuals with accuracy.

Bipolar disorder and major depressive disorder are diseases that have similar symptoms but require distinct pharmacological treatments; biomarker testing may help physicians differentiate between them.

This study's findings suggest that the blood test can complement existing psychiatric diagnostic methods while shedding light on the biological underpinnings of mental health disorders. Notably, around 1% of the population experiences bipolar disorder, yet nearly 40% of those affected receive a misdiagnosis of major depressive disorder. The researchers utilized samples and data from the Delta study conducted in the UK from 2018 to 2020. The data included information of individuals previously diagnosed with major depressive disorder within the last 5 years, and who were currently displaying depressive symptoms.

The study identified a distinct biomarker signal for bipolar disorder, even after adjusting for confounding factors like medication. The combination of patient-reported information and the biomarker test significantly enhanced diagnostic accuracy for individuals with bipolar disorder, particularly in cases where the diagnosis was less evident.

(Source: https://www.tribuneindia.com/news/health/simple-blood-test-can-help-diagnose-bipolar-disorder-accurately-study-557857)

Study: Extreme Heat Linked to More Cardiovascular Death

A study published in *Circulation* suggests that extreme heat will drive an increase in cardiovascular-related fatalities in the US between 2036 and 2065. The impact of underlying health issues and socioeconomic challenges will be disproportionately felt by vulnerable groups, particularly those 65 years of age and older and persons of color. The study projects an increase in summer days with temperatures reaching at least 90 degrees, as indicated by the heat index, which takes humidity into account. As a result, this tendency is anticipated to change. Although extreme heat currently contributes to less than 1% of cardiovascular deaths, the modeling analysis forecasts a change in this pattern. While most individuals can adapt to extreme heat through mechanisms like perspiration, those with underlying health issues, including diabetes and heart disease, face heightened risks of heart attacks, irregular heart rhythms or strokes.

The study's predictions were generated by evaluating county-level data from 48 states between May and September in the years 2008-2019, during which more than 12 million cardiovascular-related deaths occurred. Environmental modeling estimates indicated that the heat index exceeded 90 degrees approximately 54 times each summer. Researchers linked these extreme temperatures to an average of 1,651 annual cardiovascular deaths nationally. Further modeling analyses, incorporating environmental and population changes, anticipate that between 2036 and 2065, there will be about 71 to 80 days each summer with temperatures feeling 90 degrees or hotter. The general population is expected to experience a 2.6-fold increase in heat-related cardiovascular deaths, requiring minimal greenhouse gas emissions. If these emissions increase and are not controlled, then extreme heat would potentially triple the fatality.

(Source: https://www.daijiworld.com/news/newsDisplay?newsID=1135159)

Research Reveals Mobile Phone Use Linked to Lower Semen Quality

A University of Geneva study published in *Fertility & Sterility* revealed that frequent mobile phone usage can reduce sperm concentration and total count. However, it found no connection between mobile phone use and sperm motility and morphology.

The study analyzed data from 2,886 Swiss men aged 18 to 22 (recruited between 2005 and 2018) and found a significant decrease of 21% in sperm concentration for those who used their phones more than 20 times a day compared to those who used them less than once a week. Sperm quality is evaluated based on parameters including sperm concentration, total count, motility and morphology. Over the past half-century, numerous studies have reported a decline in semen quality, with sperm count dropping from an average of 99 million per milliliter to 47 million per milliliter. This decrease is believed to result from a combination of environmental factors like endocrine disruptors, pesticides and radiation, as well as lifestyle factors such as diet, alcohol consumption, stress and smoking. Notably, the study did not find a correlation between the position of the phone, such as being in a trouser pocket, and lower semen parameters.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1135820*)

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