News and Views

Landmark SELECT Trial Shows Exciting Results: Will Semaglutide be the Game Changer in Obesity Management?

Use of semaglutide 2.4 mg reduced the risk of major adverse cardiovascular (CV) events in patients with overweight or obesity and known cardiovascular disease (CVD) but no diabetes by 20%, according to headline results from the landmark Semaglutide Effects on Heart Disease and Stroke in Patients with Overweight or Obesity (SELECT) CV outcomes trial (CVOT), released early this week. The trial involved participants across a wide range of clinically relevant risk categories.

According to the top-line results, a 20% reduction in the incidence of composite of major adverse cardiovascular event (MACE) was noted in patients treated with semaglutide compared with placebo, which was statistically significant. All the three components of MACE contributed to the decline with MACE seen with semaglutide. Moreover, it was also safe and well-tolerated.

Once weekly subcutaneous semaglutide 2.4 mg was the first glucagon-like peptide 1 (GLP-1) receptor agonist to be Food and Drug Administration (FDA) approved in June 2021 for management of weight in adult patients with a body mass index (BMI) of ≥27 kg/m^2 who have at least one weight-related ailment or in patients with a body mass index (BMI) of ≥30 kg/m^2. It is intended to be used as an adjunct to increased physical activity and a low-calorie diet.

About the SELECT trial

The SELECT study, initiated in 2017 was a multicenter, multicountry trial conducted in 41 countries and enrolled 17,604 adults aged ≥45 years (average age 61.6 years) with BMI of 33.34 kg/m^2. The trial compared the CV outcomes of treatment with subcutaneous once-weekly semaglutide 2.4 mg (vs. placebo) for prevention of MACEs over a period of up to 5 years in persons with overweight or obesity and past history of CV event, but without diabetes.

The study population was subgrouped into three pre-determined categories according to baseline glycated hemoglobin (HbA1c) (<5.7%, ≥5.7% to <6.0% and ≥6.0 to <6.5%), tertiles of waist-to-height ratio and type of pre-existing CV event namely myocardial infarction (MI), stroke or peripheral artery disease (PAD). The primary endpoint of the trial was the impact of semaglutide on the new-onset MACE comprising of nonfatal MI, nonfatal stroke and CV death. The effect on mortality, CV risk factors, glucose metabolism, body weight and renal function were selected as secondary outcomes. SELECT is the only CVOT till date, which examines the superiority of an antiobesity drug on 3-point MACE.

However, at this point of time, we do not have enough details to further characterize the results in terms of the magnitude of the reduction. The detailed results are likely to be presented at a conference later this year and make a strong case for regulatory approval of addition of a new indication in the label of semaglutide.

References

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Beneficial Effects of Vegetarian Diet on Cardiometabolic Risk in Heart Disease Patients

The role of vegetarian diet in prevention of cardio-metabolic diseases is well-established. The American Heart Association (AHA) emphasizes on eating a diet rich in fruits and vegetables and whole grains. It also recommends proteins from plants as healthy sources of protein, in addition to fish/seafood and low-fat dairy products.[1]

The American Diabetes Association (ADA) also advocates consumption of a fiber-rich diet containing plenty of vegetables, pulses, fruits and whole intact grains.[2]

But does a vegetarian diet exhibit similar beneficial effects in persons with heart disease or those at high risk of heart disease? To find an answer to this, a meta-analysis examined the effect of vegetarian diet on low-density lipoprotein cholesterol (LDL-C), hemoglobin A1c (HbA1c), systolic blood pressure (SBP) and body weight in people with or at high risk of CVDs.[3] After a comprehensive search of Embase, MEDLINE, CINAHL and CENTRAL databases, from their commencement

to July 2021, 20 randomized controlled trials were found to be eligible for the meta-analysis. These trials were conducted in New Zealand, USA and countries in Asia and Europe and involved a total of 1,878 participants comprising people with CVDs, diabetes and those with a minimum of two CVD risk factors.

Results published in *JAMA Network Open* showed that eating a vegetarian diet for 6 months (average) led to significant reduction in LDL-C and HbA1c beyond that achieved with standard therapy. Analysis of data from 19 studies showed reduction in LDL-C levels by 6.6 mg/dL in participants who consumed a vegetarian diet. "The most consistent reduction was observed among people at high risk of CVDs (–9.1 mg/dL)". The HbA1c was also found to decrease by 0.24% when data from 10 studies that had examined HbA1c were analyzed. Analysis of 16 trials observed a decrease of 3.4 kg in body weight in subjects in the vegetarian diet group. However, no statistically significant impact of the vegetarian diet on SBP in pooled analysis of 14 studies, which showed a decrease of –0.1 mmHg. "The GRADE assessment showed a moderate level of evidence for LDL-C and HbA1c reduction", write the authors.

According to the authors, theirs is the first study to analyze data from randomized controlled trials to investigate the association of vegetarian diets with outcomes in people with heart disease. In this study, eating a vegetarian diet was associated with significant improvement in LDL-C, HbA1c and body weight, which are traditional major risk factors for CVD. The beneficial effects relating to glycemic control were most pronounced in patients with type 2 diabetes. The weight changes were also favorable in those with type 2 diabetes and those at high risk of CVD. These results show that consuming a vegetarian diet can enhance the effect of pharmacotherapy in management of cardiometabolic diseases. "Additional high-quality trials are warranted to further elucidate the effects of healthy plant-based diets in people with CVDs" concluded the authors.

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Increased Sedentary Screen Time during Childhood Increases Risk of Future Metabolic Syndrome

Children who watch television (TV) frequently are likely to develop metabolic syndrome as adults, suggests a study published in the journal *Pediatrics*.[1]

Researchers from the Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago in New Zealand examined the impact of TV viewing time during childhood on health outcomes at 45 years of age. Subjects born in Dunedin, New Zealand in 1972 and 1973 were selected for the study. They were enquired about the time they spent watching TV at ages 5, 7, 9, 11, 13, 15 and 32 years. The blood pressure, blood sugar levels, body weight, waist circumference, blood cholesterol (HDL-C) and triglycerides were measured at 45 years of age. Presence of any 3 or more (high levels of A1c, BP, triglycerides, waist circumference and low HDL-C) of these were defined as metabolic syndrome, which was the primary endpoint of the study. Out of the 997 participants, data for TV viewing time and metabolic syndrome was available for 870.

Results showed an association between mean TV viewing time, from 5 to 15 years of age, with metabolic syndrome. After adjusting for confounding variables such as sex, socioeconomic status and BMI at 5 years of age, the odds ratio (OR) for this association was 1.30. This association was seen to persist even after adjusting for TV watching as adults with OR of 1.26. Children who watched TV for a longer duration of time were found to have higher BMI and lower cardiorespiratory fitness at 45 years of age.

This study highlights the adverse effects of childhood television watching on long-term metabolic health as children and adolescents who spent longer hours watching TV were at higher risk of developing obesity and metabolic syndrome by middle age. They were also more likely to have poor cardiorespiratory fitness. Hence, TV viewing including other screen time should be limited for children and adolescents for better future health.

The World Health Organization (WHO) does not recommend any sedentary screen time for children younger than 1 year of age. For children under 5 years of age, WHO restricts screen time to maximum of 1 hour.[2] The American Academy of Pediatrics (AAP) the age for no screen time to under 2 years of age. For children aged 2 to 12 years, AAP recommends 1 hour of screen time per day and for teenagers, 2 hours per day. The Indian Academy of Pediatrics (IAP) recommends that children below 2 years age should not be exposed to

any type of screen, whereas exposure should be limited to a maximum of 1 hour of supervised screen time per day for children 24 to 59 months age, and less than 2 hours per day for children 5 to 10 years age.[3]

References

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COVID's Effects: Researchers Identify Mitochondrial Dysfunction in Heart and Organs

A recent study published in the journal *Science Translational Medicine* showed a link between the coronavirus and mitochondrial genes, which are crucial in generating energy within human cells. The study highlighted that the coronavirus can adversely affect these genes, leading to dysfunction in various organs beyond just the lungs.

To determine the impact of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus on mitochondria, scientists analyzed tissues of different organs collected from individuals affected by the virus. The scientists observed that while mitochondrial gene expression recovered in the lungs, its functionality in other vital organs, such as the heart, kidneys, and liver, was compromised.

They also observed that the period of highest viral load in the lungs also did not coincide with the presence of the virus in the brain. However, even in the cerebellum, a part of the brain, the expression of mitochondrial genes appeared to be suppressed.

These findings indicated that the body's cells primarily respond through lung involvement upon initial infection. However, over time, mitochondrial function recovers only in the lungs, while other organs, particularly the heart, maintain impaired mitochondrial function.

Dr Douglas C Wallace, PhD, co-senior author of the study, emphasized the significance of these findings, suggesting a paradigm shift in the understanding of coronavirus disease (COVID-19). He added that instead of solely categorizing it as an upper respiratory disease, perceiving COVID-19 as a systemic disorder capable of affecting multiple organs is crucial.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1108590*)

AI-Powered Microscope Triumph: Effective Detection of Malaria in Travelers

A multinational group of researchers has conducted a rigorous evaluation of the precision of an automated microscope coupled with advanced AI software. This technology was employed to detect malaria parasites within blood samples from travelers, a method tested in an authentic clinical environment, presenting an innovative approach to disease identification.

Malaria afflicts over 200 million individuals annually, with over 5,00,000 of these cases resulting in fatalities. The WHO advocates for parasite-centered diagnosis as a prerequisite before commencing treatment for diseases attributed to Plasmodium parasites.

Published in the journal "*Frontiers in Malaria*", the recent study scrutinized more than 1,200 blood samples obtained from travelers who had returned to the United Kingdom from nations where malaria is prevalent.

The researchers meticulously gauged the precision of the AI-augmented microscope setup in an authentic clinical context, carefully emulating ideal conditions. The achieved level of performance in this clinical setup stands as a notable feat for AI algorithms aimed at addressing malaria. The research team meticulously assessed samples through conventional manual light microscopy and the innovative AI-microscope fusion.

Through manual examination, 113 samples were diagnosed as harboring malaria parasites. In comparison, the AI-integrated system accurately detected 99 of these cases as positive, culminating in an impressive 88% precision rate. The researchers highlighted multiple potential advantages stemming from automated malaria diagnosis.

(*Source: https://indiatribune.com/ai-based-automated-microscope-successfully-detects-malaria-in-travellers/*)

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