Medical News

Semeglutide and Linagliptin are Finally Here in Pakistan

Semaglutide is a GLP1-RA and once weekly injection for the treatment of T2 diabetes mellitus. It has shown robust glucose lowering effect plus good effect on major adverse cardiovascular effects (MACE). It offers titration from 0.25 mg OW to 1 mg OW in three steps. In higher doses (2.4 mg) it can also be used as anti-obesity drug, but that preparation is not yet available in Pakistan.

Linagliptin is one of the DPP4 inhibitors. In some studies, it has shown superior HbA1c lowering effect and is also safe from kidney point of view. Unlike other DPP4 inhibitors such as sitagliptin or vildagliptin, linagliptin does not require any dose adjustment in people with diabetes and moderately compromised kidney function tests. Linagliptin has also been marketed in Pakistan.

Does Vitamin D Benefit Only Those Who Are Deficient?

Source: Medscape

Liam Davenport

November 24, 2021

There is a significant inverse relationship between concentrations of circulating 25-hydroxy-vitamin D (25[OH]D) and all-cause mortality, but only in people with vitamin D deficiency, suggests a new large-scale analysis.

Data on more than 380,000 participants gathered from 35 studies showed that, overall, there is no significant relationship between 25(OH)D concentrations, a clinical indicator of vitamin D status, and the incidence of coronary heart disease (CHD), stroke, or all-cause death, in a Mendelian randomization analysis.

However, Stephen Burgess, PhD, and colleagues showed that, in vitamin D deficient individuals, each 10 nmol/L increase in 25(OH)D concentrations reduced the risk of all-cause mortality by 31%.

The research, published in The Lancet Diabetes & Endocrinology, also suggests there was a nonsignificant link between 25(OH)D concentrations and stroke and CHD, but again, only in vitamin D deficient individuals.

In an accompanying editorial, Guillaume Butler-Laporte, MD, and J. Brent Richards, MD, praise the researchers on their study methodology.

They add that the results "could have important public health and clinical consequences" and will "allow clinicians to better weigh the potential benefits of supplementation against its risk," such as financial cost, "for better patient care — particularly among those with frank vitamin D deficiency."

They continue: "Given that vitamin D deficiency is relatively common and vitamin D supplementation is safe, the rationale exists to test the effect of vitamin D supplementation in those with deficiency in large-scale randomized controlled trials."

However, Butler-Laporte and Richards, of the Lady Davis Institute, Jewish General Hospital, Montreal, Quebec, Canada, also note the study has several limitations, including the fact that the lifetime exposure to lower vitamin D levels captured by Mendelian randomization may result in larger effect sizes than in conventional trials.

Prior RCTs Underpowered to Detect Effects of Vitamin D Supplements

"There are several potential mechanisms by which vitamin D could be protective for cardiovascular mortality, including mechanisms linking low vitamin D status with hyperparathyroidism and low serum calcium and phosphate," write Burgess, of the MRC Biostatistics Unit, University of Cambridge, UK, and coauthors.

They also highlight that vitamin D is "further implicated in endothelial cell function" and affects the transcription of genes linked to cell division and apoptosis, providing "potential mechanisms implicating vitamin D for cancer."

The researchers note that, while epidemiologic studies have "consistently" found a link between 25(OH)D levels and increased risk of cardiovascular disease, all-cause mortality, and other chronic diseases, several large trials of vitamin D supplementation have reported "null results."

They argue, however, that many of these trials have recruited individuals "irrespective of baseline 25(OH)D concentration" and have been underpowered to detect the effects of supplementation.

To overcome these limitations, the team gathered data from the UK Biobank, the European Prospective Investigation Into Cancer and Nutrition Cardiovascular

Disease (EPIC-CVD) study, 31 studies from the Vitamin D Studies Collaboration (VitDSC), and two Copenhagen population-based studies.

They first performed an observational study that included 384,721 individuals from the UK Biobank and 26,336 from EPIC-CVD who had a valid 25(OH)D measurement and no previously known cardio-vascular disease at baseline.

Researchers also included 67,992 participants from the VitDSC studies who did not have previously known cardiovascular disease. They analyzed 25(OH)D concentrations, conventional cardiovascular risk factors, and major incident cardiovascular morbidity and mortality using individual participant data.

The results showed that, at low 25(OH)D concentrations, there was an inverse association between 25(OH)D and incident CHD, stroke, and all-cause mortality.

Next, the team conducted a Mendelian randomization analysis on 333,002 individuals from the UK Biobank and 26,336 from EPIC-CVD who were of European ancestry and had both a valid 25(OH)D measurement and genetic data that passed quality control steps.

Information on 31,362 participants in the Copenhagen population-based studies was also included, giving a total of 386,406 individuals, of whom 33,546 had CHD, 18,166 had a stroke, and 27,885 died.

The mean age of participants ranged from 54.8 to 57.5 years, and between 53.4% and 55.4% were female.

Up to 7% of Study Participants Were Vitamin D Deficient

The 25(OH)D analysis indicated that 3.9% of UK Biobank and 3.7% of Copenhagen study participants were deficient, compared with 6.9% in EPIC-CVD.

Across the full range of 25(OH)D concentrations, there was no significant association between genetically-predicted 25(OH)D levels and CHD, stroke, or all-cause mortality.

However, restricting the analysis to individuals deemed vitamin D deficient (25[OH]D concentration < 25 nmol/L) revealed there was "strong evidence" for an inverse association with all-cause mortality, at an odds ratio per 10 nmol/L increase in genetically predicted 25(OH)D concentration of 0.69 (P < .0001), the team notes.

There were also nonsignificant associations between being in the deficient stratum and CHD, at an odds ratio of 0.89 (P = .14), and stroke, at an odds ratio of 0.85 (P = .09).

Further analysis suggests the association between 25(OH)D concentrations and all-cause mortality has a "clear threshold shape," the researchers say, with evidence of an inverse association at concentrations below 40 nmol/L and null associations above that threshold.

They acknowledge, however, that their study has several potential limitations, including the assumption in their Mendelian randomization that the "only causal pathway from the genetic variants to the outcome is via 25 (OH)D concentrations."

Moreover, the genetic variants may affect 25(OH)D concentrations in a different way from "dietary supplementation or other clinical interventions."

They also concede that their study was limited to middle-aged participants of European ancestries, which means the findings "might not be applicable to other populations."

The study was funded by the British Heart Foundation, Medical Research Council, National Institute for Health Research, Health Data Research UK, Cancer Research UK, and International Agency for Research on Cancer. Burgess has reported no relevant financial relationships. Disclosures for the other authors are listed with the article.

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Sacubitril/Valsartan May Alter Trajectory of Preclinical HFpEF

Source: Medscape

Patrice Wendling

November 23, 2021

Sacubitril/valsartan (Entresto) appears to improve measures of cardiac structure and function compared with valsartan alone in asymptomatic preclinical heart failure with preserved ejection fraction, results of the PARABLE trial suggest.

The angiotensin receptor-neprilysin inhibitor (ARNI) was also associated with a trend toward fewer serious adverse cardiac events (10.7% vs 19.5%; P = .061) and a longer time to first major adverse cardiovascular (CV) event (adjusted hazard ratio, 0.38; P = .039).

"Modifying cardiovascular compliance may favorably alter the disease trajectory in preclinical heart failure with longer term clinical benefits," concluded co-principal investigator Kenneth McDonald, MD, St. Vincent's University Hospital, Dublin, Ireland, during the virtual American Heart Association Scientific Sessions 2021.

The 2021 Universal Definition and Classification of HF highlights the importance of identifying preclinical HF (stages A and B). Still, he noted, no specific intervention exists and it's becoming increasingly common.

"By the time we hit 60 years of age, more people in society have stage B heart failure than a normal heart."

Preclinical heart failure with preserved ejection fraction (HFpEF), the dominant form of preclinical HF, is largely driven by CV compliance abnormalities. Sacubitril/valsartan, through preservation of natriuretic peptide (NP), may improve CV compliance, especially if introduced early in the disease process, McDonald said.

Earlier this year, the ARNI was granted an expanded indication, making it the first drug in the United States indicated for chronic heart failure not specifically characterized by EF.

The phase 2 PARABLE trial randomly assigned 250 patients in a 1:1 ratio to receive sacubitril/valsartan 50 mg twice daily titrated to 200 mg twice daily, or valsartan 40 mg twice daily titrated to 160 mg twice daily.

The patients were older than 40 years of age (mean, 71.8 years; 61.6% male) with treated hypertension and/or diabetes and elevated NP levels (B-type NP, 20-280 pg/mL or N-terminal pro-B-type NP, 100-1000 pg/mL) and abnormal left atrial volume index (above 28 mL/m^2).

At baseline, the left atrial volume index (LAVI) was 33.2 mL/m^2 using Doppler echocardiography and 50 mL/m^2 using cardiac MRI. "The discrepancy you see with cardiac MRI is a notable feature in the literature, but maybe something that's not as widely appreciated as it should be," McDonald said.

The primary outcome of change in maximal LAVI over 18 months by cardiac MRI was 6.9mL/m^2 with sacubitril/ valsartan vs 0.7 mL/m2 with valsartan alone (adjusted P < .0001).

Sacubitril/valsartan was also associated with a significant change in left ventricular end-diastolic volume index (7.1 mL/m2 vs 1.4% mL/m^2; adjusted P < .01).

Notably, neither change was "picked up by the echocardiographic measurements made at the same time," McDonald observed.

Over a median 16.9 months of follow-up, sacubitril/valsartan reduced 24-hour pulse pressures by -4.2 mm Hg vs -1.2 mm Hg with valsartan alone (adjusted intergroup; P<.001) and N-terminal pro-BNP by 17.6% vs a 9.4% increase with valsartan alone (adjusted intergroup P < .001).

In terms of cardiac function, there were minor but significant reductions in the E/e' ratio within the sacubitril/valsartan (-0.5; P < .0001) and valsartan (-0.3; P < .0001) groups, with no adjusted intergroup difference.

Left atrial ejection fraction did not show any change in either group, whereas left ventricular ejection fraction declined in both groups with no adjusted intergroup difference.

Left atrial stroke volume index did not differ within groups, although a modest but significant intergroup difference was observed, McDonald said.

"Further work is needed to confirm these observations of a phase 2, single-center study and examine these findings as a potential new [therapeutic] strategy in this at-risk cohort," he said.

Following the presentation, an audience member asked whether the results may endorse the use of sacubitril/valsartan as an antihypertensive — an indication already approved in some countries.

“That's a fascinating question," McDonald replied. "When you look at the mechanisms of action of this agent compared to other antihypertensive agents and, particularly its beneficial effect of vasoprotective peptides, there's good reason to suspect it may be of more benefit than standard therapies, especially in those people who've shown at risk for the development of cardiovascular events."

The study was supported by Novartis AG, the Heartbeat Trust, Health Research Board, Government of Ireland, and European Commission. McDonald reports serving as a consultant/speaker for Astra Zeneca, Bayer, Boehringer Ingelheim, Novartis, Vifor, and FIRE 1.

American Heart Association Scientific Sessions 2021. Abstract FS.03. Presented November 14, 2021.

Follow Patrice Wendling on Twitter: @pwendl. For more from theheart.org | Medscape Cardiology, join us on Twitter and Facebook.

Meeting for 2nd PSIM Research Award (PSIMRA)

PSIM has always been uplifting research and academics. After the success of 1st PSIMRA in 2nd international conference at Marriot hotel Islamabad, a meeting was held in collaboration of PSIM with PRF for 2nd PSIMRA. There is good news for the participants that it has been divided into two categories of pre-fellowship and post-fellowship up to the level of Assistant Professor. Prize money for 1st, 2nd and 3rd position is 150 thousand, 100 thousand and 50 thousand respectively. It has also been extended for the vitamin-D research projects. The prize money for 1st, 2nd and 3rd research proposal are 3, 2 and 1 hundred thousand respectively. A MOU will be soon signed between PSIM and PRF soon.

Psim Session in Familycon Conference 2021

PSIM had one full session in 31st annual Familycon conference 2021 held in Royal Swiss hotel Lahore from 18th to 21st November 2021. The session was chaired by Prof Javed Akram, President PSIM, Prof Sajid

Abaidullah Vice President PSIM Punjab, and Prof Tariq Waseem, Senior Vice President PSIM. State of the art lectures were delivered by PSIM office bearers. Prof Aftab Mohsin gave a talk on Acute fatty liver disease, Prof Aziz-ur-Rehman delivered talk on Cushing Syndrome and Dr Somia Iqtadar on Dengue fever.

1st Ever National Guidelines on Nausea and Vomiting

PSIM has always stressed to make local guidelines in order to have better understanding of our nations medical problems. As a part of this activity, PSIM was able to formulate first ever guidelines on nausea and vomiting in collaboration with Pakistan society of gynecology and Pakistan society of oncology in year 2021.

1ST ASCVD prevention Course By PSIM

PSIM in collaboration with World Heart Federation conducted a unique state of the art 0ne month course on prevention of atherosclerotic cardiovascular disease (ASCVD) in the month of October 2021 under the leadership of Prof Tariq Waseem, Senior Vice President PSIM. Among the other organizers were Prof Javed Akram, Prof Shahbaz Ahmed Kureshi, Prof Aziz Ur Rehman, Prof Sajid Abaidullah, Prof Aftab Mohsin, Prof Bilal Mohy Ud Din , Dr Somia Iqtadar , Dr Sami Ullah Mumtaz and Mr Kashif Riaz. It had 5 weekly modules on every Saturday. National and international speakers gave state of the art lectures. National and international experts in the field of medicine and cardiology were the panelists and over 700 doctors attended the course.

PSIM Participation in International Diabetes Conference

PSIM had a session on developing consensus in controversies in type 2 diabetes mellitus (DCCT2) in international diabetes conference held in regent plaza hotel Karachi from 13th to 14th November 2021, organized by diabetic association of Pakistan in collaboration with diabetes in Asia study group. Prof Bika Ram Deverjani, Prof Sabeen Naz, Prof Zaman Sheikh, Prof Aziz Ur Rehman ,Prof Aftab Mohsin, Prof Sajid Abaidullah, Prof Tariq Waseem and Dr Somia Iqtadar participated in the conference.


Diabetic Association Of Pakistan (DAP)
Diabetes in Asia Study Group (DASG)
INTERNATIONAL DIABETES CONFERENCE
On the occasion of
WORLD DIABETES DAY