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CV OUTCOME OF CANAGLIFLOZIN

Dr Anirban Majumdar, Kolkata

- The CANVAS Program integrated data from two trials with a total of 10,142 participants with type 2 diabetes and high cardiovascular (CV) risk. The primary outcome was a composite of death from CV causes, nonfatal myocardial infarction (MI) or nonfatal stroke.
- The rate of the primary outcome was found to be lower with canagliflozin than with placebo (26.9 vs. 31.5 participants per 1,000 patient-years; hazard ratio [HR], 0.86; 95% confidence interval [CI], 0.75-0.97). Additionally, there was a lower risk of hospitalization for heart failure with canagliflozin.
- Thus, canagliflozin, compared to placebo, was associated with a lower frequency of adverse CV events.
- The US FDA has approved canagliflozin to reduce the risk of heart attack, stroke or CV death in adults with type 2 diabetes and established cardiovascular disease (CVD). Canagliflozin is now the only oral diabetes treatment approved to reduce the risk of these CV events.
- The lack of heterogeneity in results across countries, despite geographic variations in the use of specific sodium-glucose co-transporter 2 inhibitors (SGLT-2i), suggests a class effect of SGLT-2i. Initiation of canagliflozin in type 2 diabetes mellitus (T2DM) and with established CVD is associated with a lower risk of mortality, hospitalization for heart failure and major adverse cardiovascular events (MACE). Clinical trial results on canagliflozin are reproducible in broad general patient population.

DIABETES AND INFLAMMATION

Dr Mangesh Tiwaskar, Mumbai

The association between hyperglycemia and inflammation is well-established now. Antidiabetes

drugs may alleviate inflammation by reducing hyperglycemia, but their role in inflammation is ambiguous. Recent data suggest that immunomodulatory treatments may have beneficial effects on glycemia, β -cell function and insulin resistance. Thiazolidinediones (TZDs) have the best proven anti-inflammatory mechanism of action. Hydroxychloroquine is studied extensively for its anti-inflammatory benefits in diabetes. Other anti-inflammatory agents have only limited data to support. Anti-TNF- α , anti-IL-1 β , salsalate, diacerein, etc., are also being researched for their beneficial effects. Further studies are required to clarify the role of anti-inflammatory therapy in the management of type 2 diabetes. Better understanding of inflammatory basis for diabetes may provide novel modalities for diabetes prevention and treatment.

ARTIFICIAL SWEETENERS: SWEET OR SOUR

Dr Madhukar Mittal, Lucknow

Sugar is said to be the "New Cigarette!"

India's domestic sugar requirement is estimated to touch record 30 million tons by the year 2020. Sugar contributes to anxiety, depression, hyperactivity; increases risk of blood clots, strokes, fatty deposits in the liver; causes diabetes, weight gain, kidney damage, headache and migraines and tooth decay. Artificial sweeteners are a major part of our diet. They have been extensively studied for their safety and only then approved for long-term consumption. They help in compliance of consumers who are advised not to take sugar in their diets and thus assist in management of diabetes and obesity. The US FDA has approved seven NNS (saccharine, aspartame, sucralose, neotame, acesulfame-K, stevia, monk fruit extract) for use in humans and has classified two of them under generally recognized as safe (GRAS) category. Artificial sweeteners are closely regulated and have passed the necessary checks to be used in foods. Most of them are not metabolized in the body and so are generally considered safe for consumption. When consumed by diabetics in daily acceptable limits, they can help in

limiting carbohydrate and energy intake as a tool to manage blood glucose and weight.

IMPACT OF VITAMIN D DEFICIENCY ACROSS LIFE STAGES: STRATEGIES TO OVERCOME THIS PUBLIC HEALTH PROBLEM

Maj Gen RK Marwaha (Rtd), Delhi

- Poor bone health is responsible for causation of 8.9 million fractures annually worldwide. Lifetime risk for hip, vertebral and wrist fracture is 30-40%. High morbidity and mortality are associated with osteoporotic fractures.
- Vitamin D maintains blood calcium level in normal range which is vital for normal functioning of nervous system, bone growth and achieving peak bone density.
- Adverse effects of vitamin D deficiency - *Children and adolescents*: Poor growth velocity; rickets; short stature; low bone mass; genu varum; genu valgum. *Adults and old age*: Muscle pain and fatigue; osteomalacia; osteoporosis; hip, spine, forearm and other fractures; possibly an increased prevalence of autoimmune disorders, CVDs, skin disorders, cancers and infections. *Deficiency/insufficiency in pregnancy and lactation*: Adverse maternal outcomes such as osteomalacia, pre-eclampsia and preterm deliveries; lower birth weight; lower crown heel length, head circumference and mid arm circumference; low bone mass; poor/delayed growth; rickets *in utero/at birth*; tetany; neonatal hypocalcemic seizures; abnormal enamel formation and dental caries.
- Dietary calcium intake is low in children and adults in India. Indian diets are predominantly vegetarian, based on cereals and legumes, and are deficient in milk and milk products. Low calcium content is further compromised by high levels of phytates in the vegetarian diets.
- A dose of 6,00,000 IU of vitamin D is effective in treatment of nutritional rickets. A one time intramuscular injection of vitamin D is equally efficacious in treatment of nutritional rickets as staggered administration of the same dose orally over a period of 10 weeks.
- Combination therapy with both vitamin D and calcium yields better healing of rickets than either modality alone. In the absence of vitamin D fortification of foods, diet alone appears to have an insignificant role.

- Physical activity and adequate sun exposure are vital for attaining peak bone mass in Indian context. Supplementing milk fortified with vitamin D to children is an effective and safe method of addressing the major public health issue of vitamin D deficiency in children.

POST-TRANSPLANT DIABETES: CURRENT UNDERSTANDINGS

Dr Debmalya Sanyal, Kolkata

Transplant patients may have pre-existing diabetes, develop post-transplant diabetes or transient post-op hyperglycemia. Post-transplant diabetes mellitus (PTDM) is common. It is associated with decreased patient and graft survival and increased CVD and infection. Risk stratification and intervention are required to minimize risk. Insulin secretion and sensitivity are impaired and need multifaceted management. Immunosuppressive medications may impair kidney function and dose adjustments of diabetes medications are often needed for this. Individualize glycemic targets according to prevalent comorbidities. There may be increased CVD risk with poorly tolerated hypoglycemia. Dipeptidyl peptidase-4 inhibitors (DPP-4i) and metformin can be given.

PREMIX INSULINS: EVIDENCE AND CLINICAL RELEVANCE

Dr Subhash Kumar Wangnoo, New Delhi

Premix insulins provide the convenience of having two variable acting insulins in the same dose. It enables the healthcare provider to address to fasting and postprandial sugar levels in the same shot. It provides a reasonably decent glycemic control, cuts down the number of insulin shots at the same time, providing a similar level of glycemic control.

ULTRAFAST-ACTING INSULINS: FUTURE DIRECTIONS AND CLINICAL POSSIBILITIES

Dr Antonio Ceriello, Milan, Italy

Ultrafast-acting insulins are rationally designed as a closer approach to the physiological mealtime insulin action. Faster acting insulin aspart is an ultrafast-acting insulin with an earlier onset of appearance and greater early insulin action than conventional insulin aspart. Fast-acting insulin aspart has demonstrated improvements in postprandial glucose (PPG) increments with reductions in the risk of nocturnal hypoglycemia.

MEDICAL NUTRITION THERAPY FOR DIABETES

Dr Vineet K Surana, New Delhi

Medical nutrition therapy (MNT) is a therapeutic approach to treating medical conditions and their associated symptoms through the use of a specifically tailored diet devised and monitored by healthcare professionals. Evidence shows adding MNT to be significant in preventing prediabetes and managing diagnosed diabetes. MNT also prevents or slows down the complications of diabetes: Reduction of 1% A1c in patients with newly diagnosed type 1 diabetes mellitus (T1DM); Reduction of about 2% A1c in persons with newly diagnosed T2DM; Medical supervision is necessary for the monitoring: Weight/BMI; glycemic parameters; metabolic parameters. MNT for prevention and treatment of T2DM and CVD has a broad range of benefits including satiety and weight stabilization; reduced low-grade inflammation; improved insulin sensitivity; improved glucose control; improved lipid profile; reduced risk of T2DM complications.

IMMUNE CHECK POINT INHIBITORS: ENDOCRINE CONSEQUENCES

Dr Anil Bhansali, Chandigarh

Evolution of immune check point inhibitors (ICPi) is a breakthrough in the management of metastatic carcinomas. ICPi include CTLA-4 inhibitor ipilimumab; PD-1 inhibitors and PDL-1 inhibitors. Recognition of endocrine complications following ICPi therapy requires a high index of suspicion. Thyroid dysfunction and hypophysitis are common endocrine consequences. Development of endocrine complications predicts favorable outcome. Those with pre-existing hypothyroidism may require increase in dose after initiation of ICPi therapy. Discontinuation of ICPi is not warranted unless patient is severely thyrotoxic.

DIABETIC FOOT AND INTENSIVE GLYCEMIC CONTROL

Dr Altamash Shaikh, Mumbai

Patients with type 2 diabetes are at increased risk of macro- and microvascular disease. In type 2 diabetes, intensive glycemic control has been associated with a reduction in the risk for lower-extremity amputation (LEA). Improved glycemic control seems to be a strong predictor of decreased risk for subsequent LEA. The Society for Vascular Surgery guidelines suggest that intensive glycemic control (A1c <7) should be targeted.

TASC II guidelines suggest targeting an HbA1c goal of <7% (or as close to 6% as possible) in patients with concomitant diabetes and peripheral artery disease (PAD). Society for Vascular Surgery (SVS) suggests a goal of <6.5-7.

MANAGEMENT OF ADRENOCORTICAL CARCINOMA

Prof Gary D Hammer, USA

- Adrenal-focused imaging is recommended in all patients with suspected adrenocortical carcinoma (ACC).
- Histopathologic diagnosis and grading - Use of Weiss system is recommended. Ki67 immunohistochemistry is recommended for every adrenocortical tumor.
- In patients with advanced ACC at the time of diagnosis not qualifying for local treatment, either mitotane monotherapy or mitotane + EDP is recommended depending on prognostic parameters.
- Owing to the high rate of recurrence and metastatic disease, treatment often relies on systemic therapies.
- Cytotoxic therapy in unresectable ACC - EDP-M is recommended as first-line treatment for recurrence <6 months, rather than repeat locoregional measures. In patients who progress under mitotane, addition of EDP is recommended.
- It is recommended that adrenal surgery for suspected/confirmed ACC should be performed only by surgeon experienced in adrenal and oncological surgery.
- Complete en bloc resection is recommended.
- Open surgery is the standard surgical approach for confirmed or highly suspected ACC.
- It is suggested that routine locoregional lymphadenectomy should be performed.
- For adrenal tumors with uncertain malignant potential, adjuvant therapy is not recommended.
- There is a suggestion for adjuvant mitotane treatment without macroscopic residual tumor but with high risk of recurrence.
- Radiation can be considered in addition to mitotane therapy on an individualized basis therapy in patients with R1 or Rx resection or in stage III.
- Adjuvant chemotherapy can be considered in selected patients with very high risk for recurrence.

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