Diabetes India 2022: 12th World Congress of DiabetesIndia

HFPEF: ROLE OF THE DIABETOLOGIST IN TACKLING A MULTIDISCIPLINARY PROBLEM

Dr Eberhard Standl, Germany

- The pathophysiology of type 2 diabetes and cardiorenal-metabolic syndrome have the same cluster complications such as insulin resistance, dysmetabolism, low-grade inflammation, oxidative stress, etc. these factors are driving the progression of type 2 diabetes and in turn affect the kidney and heart.
- Hence, the role of a diabetologist in this multi-disciplinary paradigm starts with an assuring diagnosis of heart failure.
- Assuring that the patient complies with the recommended cardiologic therapy (β-blockers, diuretics, statins and antithrombotics).
- Based on the patient history, diabetologists should address an appropriate cardio-metabolic approach including appropriate glucose-lowering therapy, a suitable exercise regimen, etc.
- Lastly, he/she should co-operate with cardiologists/nephrologists to reduce the risk of cardiovascular (CV) and renal outcomes.

GLUCOSE VARIABILITY AND ITS IMPLICATIONS

Dr Tsvetalina Tankova, Bulgaria

- Unpredictable fluctuations in blood glucose levels make it difficult to optimize insulin doses and reach desired glycemic targets.
- Glucose variability is a strong predictor of hypoglycemia leading to poor glucose control; increased risk of diabetes burden and poor compliance.
- Glycemic variability seems to have more deleterious effects than sustained hyperglycemia on endothelial function and oxidative stress and thus in the development of diabetic complications.
- Glycated hemoglobin (HbA1c) is the gold standard for the assessment of glycemic control, yet it has a lot of limitations.
- Glucose variability evaluated from continuous glucose monitoring (CGM) data should be considered in the overall clinical representation of glycemic control. Time in range has been shown to be associated with complications in both type 1 and type 2 diabetes.

CARDIOVASCULAR RISK FACTOR MANAGEMENT AND PROGNOSIS IN PATIENTS WITH DYSGLYCEMIA

Dr Jaakko Toumilehto, Finland

The 2019 ESC Guidelines on diabetes, prediabetes and cardiovascular diseases (CVDs) has given specific recommendations on CV risk categories in patients with diabetes mellitus (DM), for the use of laboratory, ECG and imaging testing for CV risk assessment in asymptomatic patients with DM, for lifestyle modifications in DM and pre-DM, for glycemic control in an individual with DM, for the management of blood pressure (BP) in patients with DM and pre-DM, for the management of dyslipidemia with lipid-lowering drugs, antiplatelet therapy in primary prevention in DM.

A few important recommendations are:

- Moderate to vigorous physical activity, notably a combination of aerobic and resistance exercise, for ≥150 min/week is recommended for the prevention and control of DM unless contraindicated, such as when there are severe comorbidities or a limited life expectancy.
- A Mediterranean diet, rich in polyunsaturated and monounsaturated fats, should be considered to reduce CV events. Vitamin or micronutrient supplementation to reduce the risk of DM or CVD in DM is not recommended.
- Tight glycemic control is recommended targeting near-normal HbA1c (<7.0% or <53 mmol/mol) to decrease microvascular complications.
- Antihypertensive drug treatment is recommended for people with DM when office BP is >140/90 mmHg.
- Lifestyle changes including weight loss if overweight, physical activity, alcohol restriction, sodium restriction and increased consumption of fruits, vegetables and low-fat dairy are recommended in patients with DM and pre-DM.
- To manage BP in patients with DM and pre-DM, it is recommended that treatment is initiated with

a combination of a renin-angiotensin-aldosterone system (RAAS) blocker with a calcium channel blocker or thiazide/thiazide-like diuretics.

- Statins are recommended as the first-choice lipid-lowering treatment in patients with DM and high low-density lipoprotein cholesterol (LDL-C) levels: administration of statins is defined based on the CV risk profile of the patient and the recommended LDL-C or non-HDL-C (high-density lipoprotein cholesterol) target levels.
- Lifestyle interventions (with a focus on weight reduction and decreased consumption of fast absorbed carbohydrates and alcohol) and fibrates should be considered in patients with low HDL-C and high triglyceride levels.
- In patients with DM at high/very high-risk, aspirin (75-100 mg/day) may be considered for primary prevention in the absence of clear contraindications.

POSITION OF AN SGLT2 INHIBITORS + DPP-4 INHIBITORS COMBINATION PILL IN THE MANAGEMENT OF A PERSON WITH T2DM

Dr JJ Mukherjee, Kolkata, West Bengal

- Sulfonylureas (SUs), metformin is often the last choice in T2DM treatment due to the declining trend of glycemic control time with monotherapy. Hence, a need to shift toward combination therapy, a step also supported by 2019 ADA-EASD (American Diabetes Association-European Association for the Study of Diabetes) updated guidelines.
- Diabetes should be treated based on the pathophysiological functions, such as neurotransmitter dysfunction, increased glucagon secretion and increased lipolysis.
- If Hb1Ac is more than 17 mmol/mol above the individualized Hb1Ac, considering early combination therapy is viable.
- Metformin + Dipeptidyl peptidase-4 (DPP-4) inhibitors combination produces early efficacy and reduces the risk of hypoglycemia. However, metformin + sodium-glucose co-transporter-2 (SGLT2) inhibitors + DPP-4 inhibitors + glucagon-like peptide-1 receptor agonist (GLP-1RA) provides a combination of early efficacy, and reduced risk of hypoglycemia, weight gain BP, CV events and renal failure.
- SGLT2 inhibitors and DPP-4 inhibitors have a complimentary efficacy and can reduce Hb1Ac levels to <7% in 24 weeks by regulating the pathophysiology of the disease progression.

HALTING THE PROGRESSION OF PREDIABETES TO DIABETES: MYTH OR REALITY?

Dr Adrian Vella, Rochester, MN

- Islet cell function and insulin signaling are the primary regulators of glucose metabolism in humans.
- Abnormal glucagon suppression is an early change in the pathogenesis of type 2 diabetes.
- To date, no therapy clearly changes the natural history of prediabetes progression.
- As such if treatment is to be undertaken there needs to be a careful appraisal of the risk vs. benefits.

EARLY COMBINATION THERAPY FOR THE TREATMENT OF T2DM

Dr Ralph A DeFronzo, San Antonio, TX

The ominous octet of hyperglycemia: decreased insulin secretion, decreased incretin effect, increased lipolysis, increased glucose reabsorption, decreased glucose uptake, neurotransmitter dysfunction, increased hepatic glucose production and increased glucagon secretion.

The treatment of T2DM

- Will require multiple drugs in combination to correct multiple pathophysiologic defects.
- Should be based upon known pathogenic abnormalities, and NOT simply on the reduction in HbA1c.
- Must be started early in the natural history of T2DM, if progressive β-cell failure is to be provided.

When effect of SU and metformin therapy when compared with conventional therapy led to a 37% reduction in microvascular complications. Pathophysiology based (DEFRONZO) algorithm is lifestyle + triple combination: pioglitazone + metformin/SGLT2 inhibitors + GLP-1RA to result in HbA1c <6.5%.

GLYCEMIC MANAGEMENT IN PATIENTS WITH CKD

Dr Guillermo Umpierrez, USA

- Overall, 80% of chronic kidney disease (CKD) cases are undiagnosed in diabetes patients with 6-time more probability of death by CVD than advance to end-stage renal disease (ESRD) and dialysis.
- The clinical diagnosis of diabetic kidney disease in a patient with diabetes is based on the reduced kidney function or presence of albuminuria with diabetic retinopathy and/or type 1 diabetes for more than 10 years.

- However, in the absence of any sign or symptom of the primary cause of kidney damage, most patients usually progress to ESRD.
- Management approaches to diabetes and reducing the progression of CKD is multifactorial such as BP-lowering, treatment of dyslipidemia, RAAS and sympathetic nervous system blockade, glycemic control, SGLT2 inhibitors and other medications.

The EMPA-Reg, CANVAS and DECLARE trials showed that empagliflozin, canagliflozin and dapagliflozin were associated with slower progression of kidney disease and clinically proven fewer renal events in comparison to placebo in standard care.

DIABETES TREATMENT IN AN ELDERLY PATIENT

Dr Florian Toti, Albania

- Patients have different requirements depending on their diabetes status.
- Many choices exist to individualize treatment.
- Reinforce healthy lifestyle, treat blood sugar, lipids and BP.
- Avoid using medications to achieve HbA1c <7.5% in most adults ≥65 years old; moderate control is generally better.
- There is no evidence that using medications to achieve tight glycemic control in most older adults with type 2 diabetes is beneficial.
- Tight control has been consistently shown to produce higher rates of hyperglycemia in older adults.

IS THERE A CURRENT PLACE FOR SULFONYLUREAS IN DIABETES MANAGEMENT?

Dr Anuj Maheshwari, Lucknow, Uttar Pradesh

The availability of new drug classes has sparked a debate regarding the utility and viability of SUs as a therapeutic option with views on CV risks and hypoglycemia. However, this may hold true for older SUs due to their non-selective mechanisms of action.

Sulfonylurea has reigned over the other antidiabetic agents in diabetes management for over 40 years. The development of modern SUs that do not block ischemic preconditioning has rendered the University Group Diabetes Program (UGDP) controversy moot and preserved a place for SUs in the treatment of type 2 diabetes. Modern SUs are proven to be effective, safe and well-tolerated in various clinical situations.

Sulfonylurea, when compared to the other oral antidiabetic agents (OADs) has the highest efficacy in reducing HbA1c levels by up to 2%, moderate risk of hypoglycemia, neutral CV event and a cost-effect therapy. Sulfonylureas are also reported as the most cost-effective therapy compared to other OADs.

There have been several key studies advocating the superiority of SU, namely, the UKPDS trial which reported that intensive glucose therapy with the SU has reduced the risk of microvascular complications. In a 10-year follow-up study of the trial, it was determined that SU maintained a risk reduction in microvascular, macrovascular and myocardial infarctions up to 9%.

Similarly, the ADVANCE trial and ADVANCE-ON echoed the same results with the added benefit of renal outcomes. The trial showed that intensive glucose control strategically reduced HbA1c by 6.5% thereby reducing the risk of renal failure and nephropathy by 11% and 21%, respectively.

TOSCA.IT and CAROLINA trial established the status of SU as an OAD with a safe CV profile with similar risk reduction in 3P-Mace and 3P-Mace with hospitalization. Meanwhile, CAROLINA study reassured that the use of SU leads to weight gain in the initial therapy, yet it is stabilized over the long-term, especially with glimepiride.

Also, the use of SU with metformin was reported to have negated the weight gain and hypoglycemia. In cases of elderly patients, people in Ramadan or patients diagnosed with CKD, gliclazide was a choice for reducing the risk of secondary failure and Hb1Ac. Hence, it can be confirmed that SU is an effective second-line agent for glycemic control for type 2 diabetes.

The renaissance of SUs therapy might ensure that it remains the drug of choice for uncontrolled diabetes in the future with enough room for flexibility.

GETTING BASICS RIGHT IN IMPROVING OUTCOMES FOR PEOPLE WITH DIABETES

Dr Sunil Kota, Berhampur, Odisha

Vascular complications are common in patients with type 1 and 2 diabetes. Annual screening for retinopathy with retinal eye exams, for nephropathy with urine albumin-to-creatinine ratio and neuropathy with physical examination allows early identification and appropriate interventions; these may delay progression or intensity. Metabolic control of glucose levels. Blood pressure with a combination of lifestyle interventions and pharmacological therapy (including insulin) can

prevent the onset or delay the progression of each of these diabetes-related microvascular and neuropathic complications. We need to be alert for emerging risk factors.

BETA-CELL PRESERVATION: MYTH OR FACT?

Dr Vijay Negalur, Thane, Maharashtra

Prolonged hyperglycemia leads to oxidative stress, endoplasmic reticulum (ER) stress, hypoxic stress and cytokine induction leading to β-cell compensation, stress and later failure and de-differentiation.

Beta-cell identity is fragile, but islet identity is stable: islet cells share chromatin structure and methylome. Other than hormone genes, they represent flexibility and plasticity states rather than stable subtypes.

FoxO1 plays an important role in the de-differentiation and re-differentiation of β cells. Reprogramming of other cell types to β cells is a possibility and can be a potential treatment option for diabetes in the future.

GLP-1, SGLT2 inhibitors, thiazolidinediones, metformin and intensive insulin therapy offer β-cell protection and preservation.

DIABETES PREVENTION: PRIMARY CARE. WISH OR REALITY?

Dr Francesc Xaviers Cos, Spain

- The FINDRISC questionnaire is a practical screening tool applicable to the European population, particularly in primary health care.
- Men and women with a FINDRISC score above 20 points had a prevalence of glucose alterations of approximately 80%. Fifty percent of men and women had type 2 diabetes that had not been diagnosed before.
- A structured diabetes prevention program based on an intensive intervention in the lifestyle of high-risk people is feasible, effective and cost-effective in primary care.
- Implementation and long-term lifestyle program benefits require further research and commitment from the public health department and primary care community.

OVERCOMING BARRIERS TO IMPROVE OUTCOMES IN UNINSURED PATIENTS WITH DIABETES

Dr Otis W Kirksey, USA

"*People don't care about how much you know until they know how much you care.*" –*Theodore Roosevelt*

- Neighbourhood Medical Centre (NMC) is a federally qualified Health Centre that provides services including primary care, chronic disease management, mental health, dental care, specialty care, case management, etc.
- About 18% of the NMC patients have been diagnosed with diabetes with 22% of the hypertension patient population; however, after diabetic education, most of the patients have switched to SGLT2 inhibitor docks.
- Social Determinants of Health (SDOH) has identified economic stability, education, social and community context, health and health care, neighborhood, and built environment as the barriers to healthy outcomes.
- NMC Diabetes Education and Management Service (DEMS) is a pharmacist-led multidisciplinary composed of certified diabetes and education specialist, medical assistants, nurses, physician, practitioners, mental health counselors and case management counselors. The overall goal of the DEMS management plan is to decrease the progression of and improve the quality of life and include patients with HbA1c levels of more than 9%, patients with a history of noncompliance and patients with multiple comorbidities.

SGLT2 INHIBITORS – ORGAN BENEFITS, WITH EMPHASIS ON CKD AND HEART FAILURE

Dr Jiten Vora, UK

- SGLT2 inhibitor therapy is recommended for all diabetes patients, irrespective of the subtypes and sometimes for patients without a diabetes diagnosis for organ protection.
- CKD progression is a major risk among diabetes patients, with more than 50% having lost kidney functions to an extent.
- SGLT2 inhibitors produces a protective effect at all stages of renal disease, from prevention of development and progression to nephropathy and ESRD, as well as renal death. From the perspective of CV failure, it improves CV outcomes (composite primary endpoint of CV death or HHF) in patients with or without pre-existing HFrEF, diabetes, CKD and different types of background HFrEF medical therapy.
- Several studies have also proven the positive effect of SGLT2 inhibitors in HFrEF, predominantly in cases of HHF such as CANVAS program, VERTIS program, DECLARE-TIMI 58, etc.