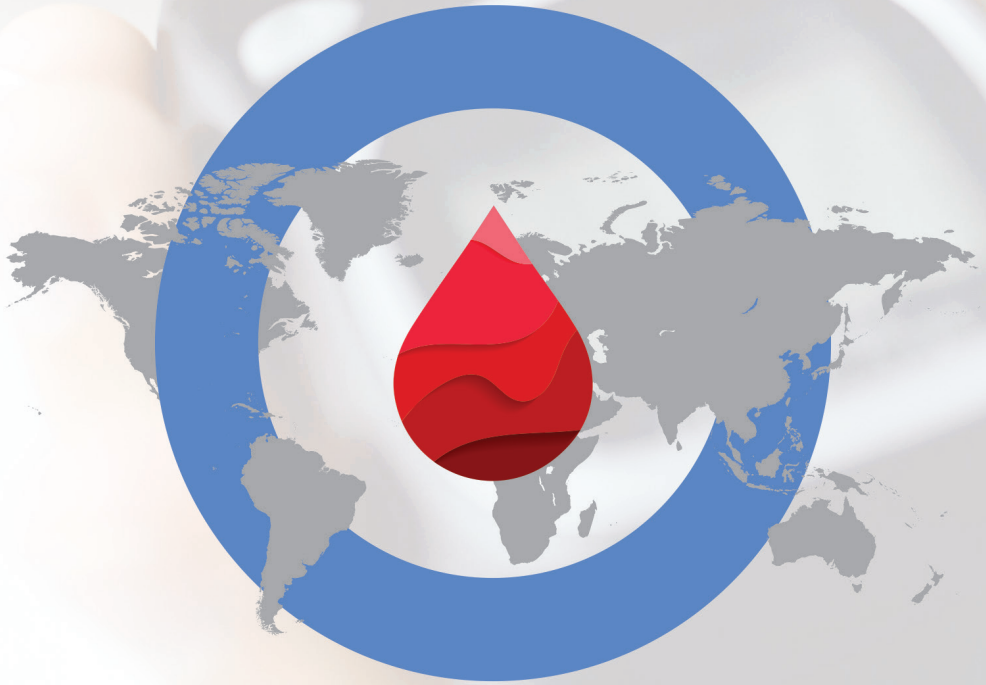
MODULE 2

IFDCD

INTERNATIONAL FEDERATION OF DIABETES AND CARDIOMETABOLIC DISORDERS

CLINICAL EXCELLENCE PROGRAM FOR

Diabetes PRACTITIONERS *in* MYANMAR



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SPEAKER

Dr. Banshi Saboo
MD, PhD, FACE
Chief Diabetologist & Chairman of Diacare - Diabetes Care & Hormone Clinic at Ahmedabad
International Diabetes Federation (IDF) Chair elect for South East Asian (2023-2024)
Immediate Past President of RSSDI (Research Society for Study of Diabetes in India) 2019-2020

PROGRAM OBJECTIVES

This clinical excellence program is an attempt to apprise participants on the concepts related to development of diabetes and its complications, together with updated recommendations on its diagnosis and management.

MANAGEMENT OF NEWLY DIAGNOSED T2DM (WITH MODERATE TO HIGH HBA1C) IN 2023

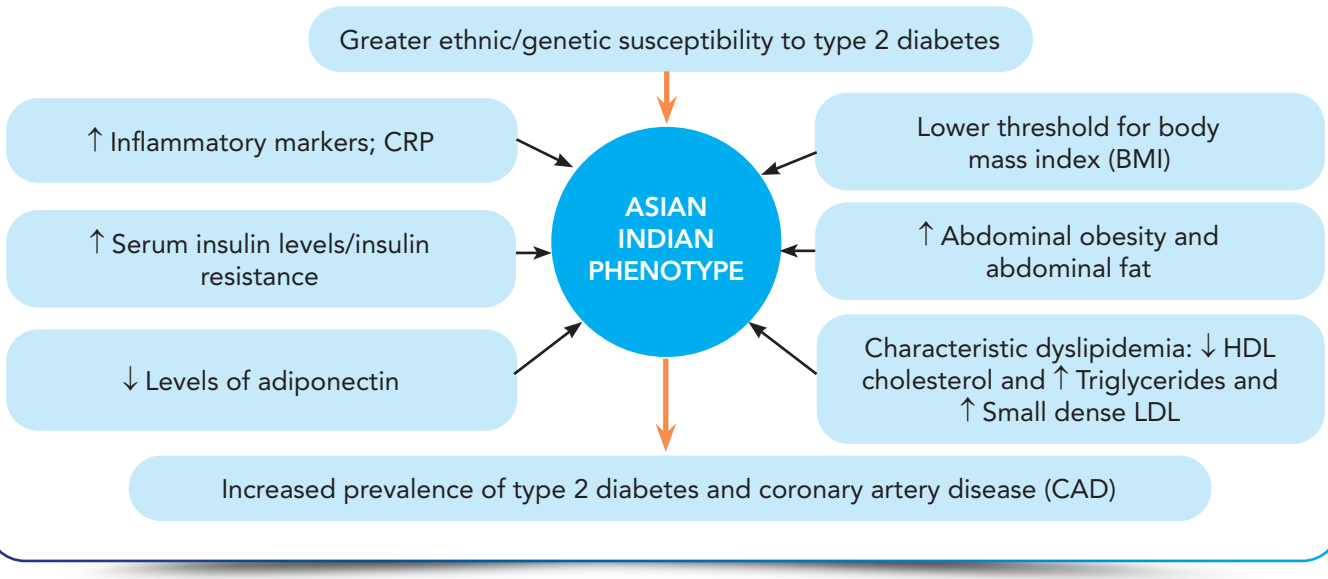
Dr. Banshi Saboo

In the second video lecture of the series forming part of the Clinical Excellence Program for Diabetes Practitioners, Dr. Banshi Saboo, Chief Diabetologist & Chairman of Diacare - Diabetes Care & Hormone Clinic at Ahmedabad, navigated the participants through contemporary concepts related to management of newly diagnosed type 2 diabetes mellitus, especially with relevance to the sub-continent, and focusing on sulfonylureas.

Dr. Banshi Saboo
MBBS, MD, Ph.D,
Fellow of American College
of Endocrinology (FACE)

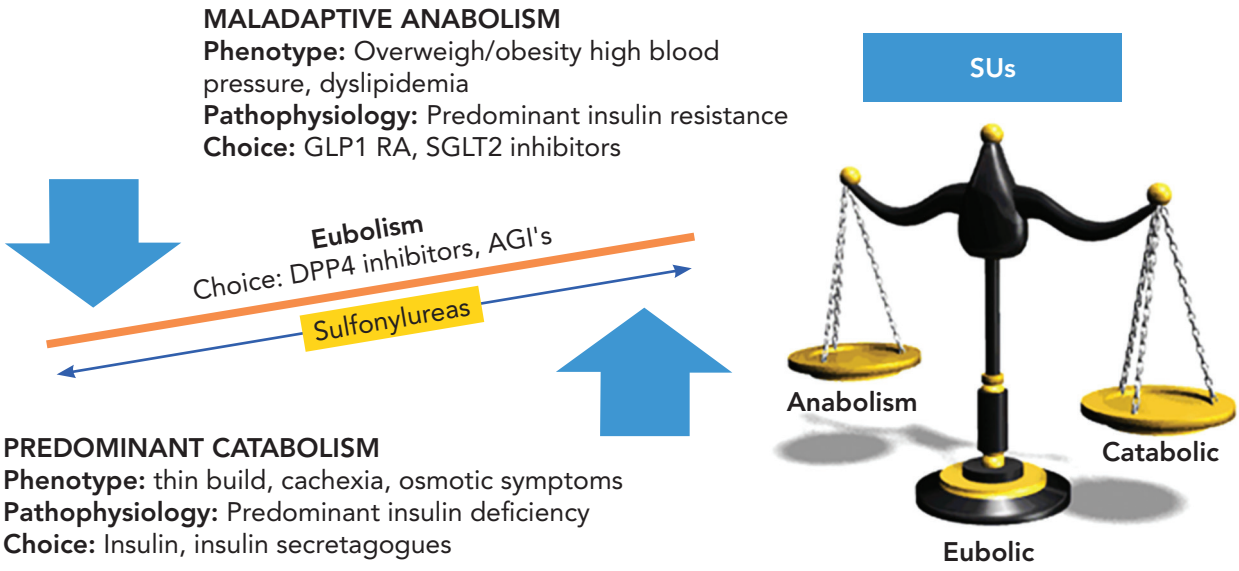
Dr Banshi started his presentation by highlighting the burden of diabetes in South Asia, and the fact that many South Asian countries feature in the list of top 10 countries for number of adults with diabetes. This could be attributable in part to the Asian Indian phenotype seen in this part of the world (Figure 1). South Asians generally have increased abdominal obesity and a lower threshold for body mass index (BMI), accompanied by greater ethnic/genetic susceptibility to type 2 diabetes.

Figure 1: South Asian (Indian) phenotype in diabetes



Oral antidiabetic therapy is the cornerstone of diabetes management, and today's clinicians are presented with an extensive range of oral antidiabetic drugs for type 2 diabetes. Amongst this wide spectrum of antidiabetic medications, Sulfonylureas seems to be uniquely placed, which can be used in most patients with type 2 diabetes (Figure 2).

Figure 2: The metabolic fulcrum-based approach is a novel concept



Categorizes patients with T2DM based on their characteristics.

Sulfonylurea may be placed in the center of the fulcrum and can be used along with other OHAs to the left or right

SULFONYLUREAS IN T2DM MANAGEMENT

The journey of Sulfonylureas began in 1940s (Figure 3), and since then these drugs continue to be supported by robust-long-standing evidence. They control glycemic levels, reduce micro- and macrovascular complications, are safe, highly accessible, affordable, and have high patient acceptability, making them especially important in the global context of limited resources. Good glycemic control and safety profiles associated with the use of modern SUs, support their position as a key treatment option in patients with type 2 diabetes. Furthermore, emerging evidence – based on multiple trials – suggest that cardiovascular safety should no longer be a concern when choosing sulfonylureas, especially glimepiride, for people with type 2 diabetes (Figure 4). In addition to their well-known glucose-lowering effects, SUs have also been found to possess pleiotropic benefits (Figure 5). The modern SUs thus have several beneficial characteristics (Figure 6), and could play a effective role in managing type 2 diabetes in lower-Middle income countries where 80% people with diabetes mellitus live (Figure 7).

Figure 3: The journey of evergreen SUs since 1946s.....

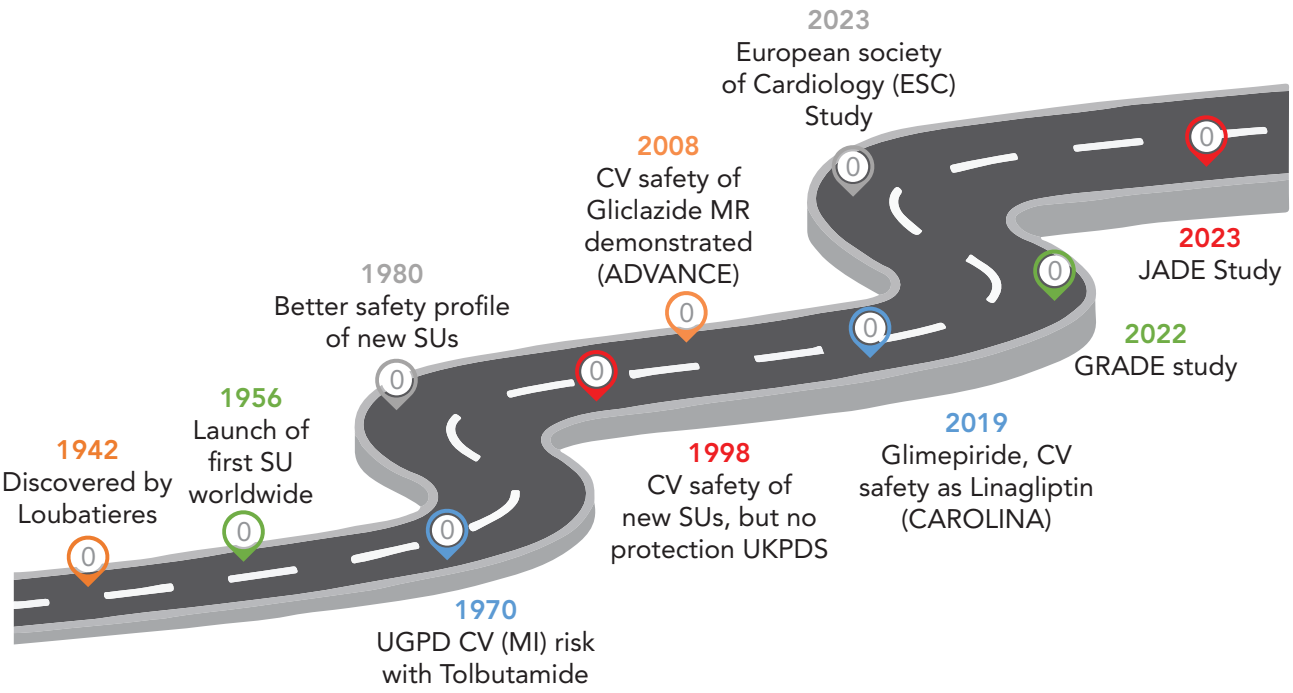


Figure 4: The wall of Evidences: Safety of Modern Sus

Cardiovascular safety **should no longer be a concern when choosing sulfonylureas, especially glimepiride,** for people with T2DM

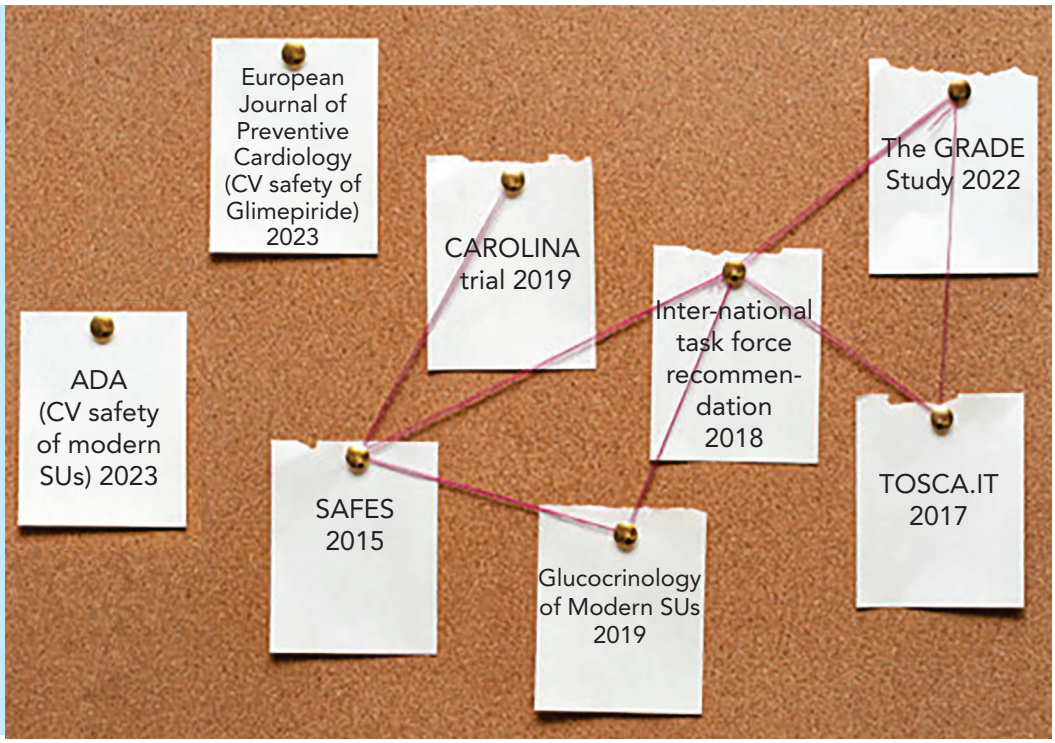


Figure 5: The newer shades of SUs: Pleiotropic Benefits

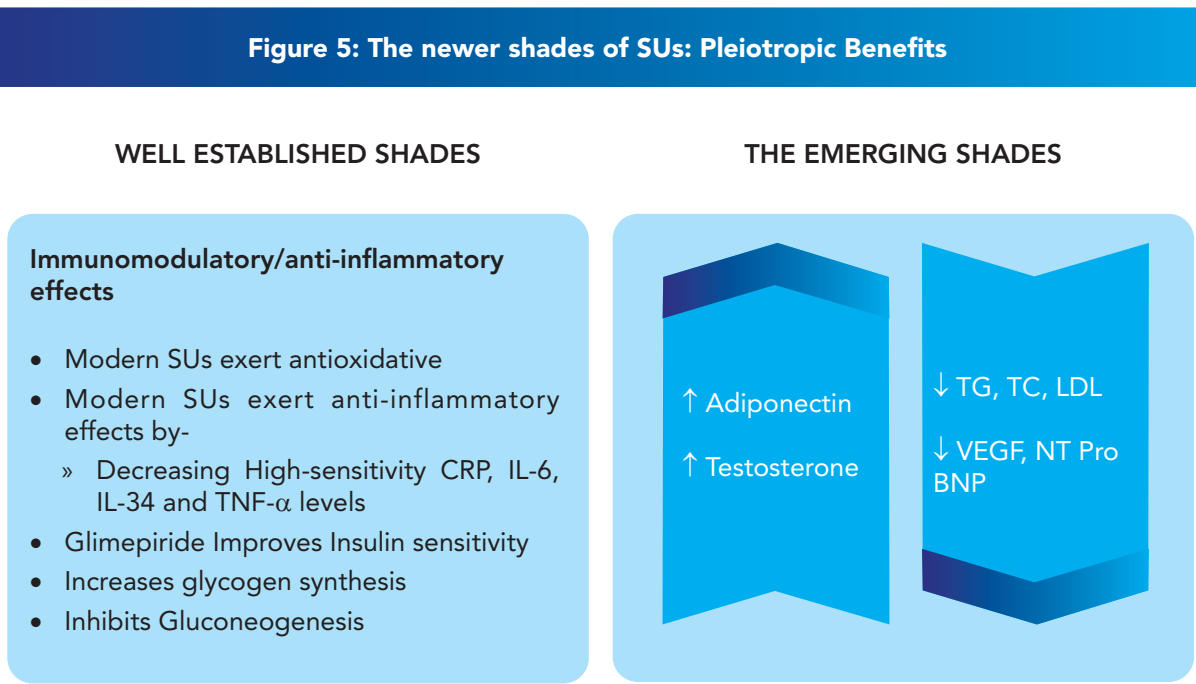


Figure 6: The "Seven shades" of modern SUs

Sweeping experience
Sufficiently available
Sublimely affordable
Supremely effective
Safety-proven CV safe
Splendidly acceptable
Surpassingly researched

Figure 7: We must NEVER Forget...

80% people with DM live in Lower-Middle income countries

We need medications those are

- Effective
- Affordable
- Available
- Acceptable
- Minimal AEs

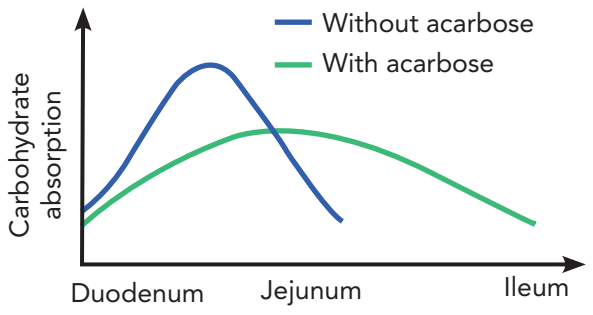
Modern SUs

ALPHA-GLUCOSIDASE INHIBITORS IN T2DM MANAGEMENT

Alpha-glucosidase inhibitors (AGIs) have a unique mode of action, and are primarily suitable to Indian diabetes patients considering the carbohydrate rich diet (Figure 8). AGI drugs reduce PPG and PPI responses among individuals with and without diabetes, with reductions in incremental PPG of ~45–50% and of ~20–75% in incremental PPI.

Figure 8: AGIs has Unique Mode of Action

Slow down carb absorption from small intestine



Local GLP-1 release

Alpha-glucosidase inhibition leads to

- Delay in intestinal carbohydrate absorption
- Lower postmeal hyperglycemia
- Less insulin needed, protection of β-cells
- Improves insulin sensitivity
- Carbohydrates in lower intestine facilitate GLP-1 release and GUT symbiosis

GLIPTINS IN T2DM MANAGEMENT

Incretin based therapies present an alternative therapeutic strategy for patients with type 2 diabetes and, in general, show significant improvements in glycemic control and are well tolerated, particularly with regard to weight change and hypoglycemia. In addition, this class may preserve or even reverse the decline in β-cell function that is observed in patients with diabetes. These characteristics suggest that gliptins should be considered useful agents in monotherapy and combination therapy for the treatment of type 2 diabetes (Figure 9).

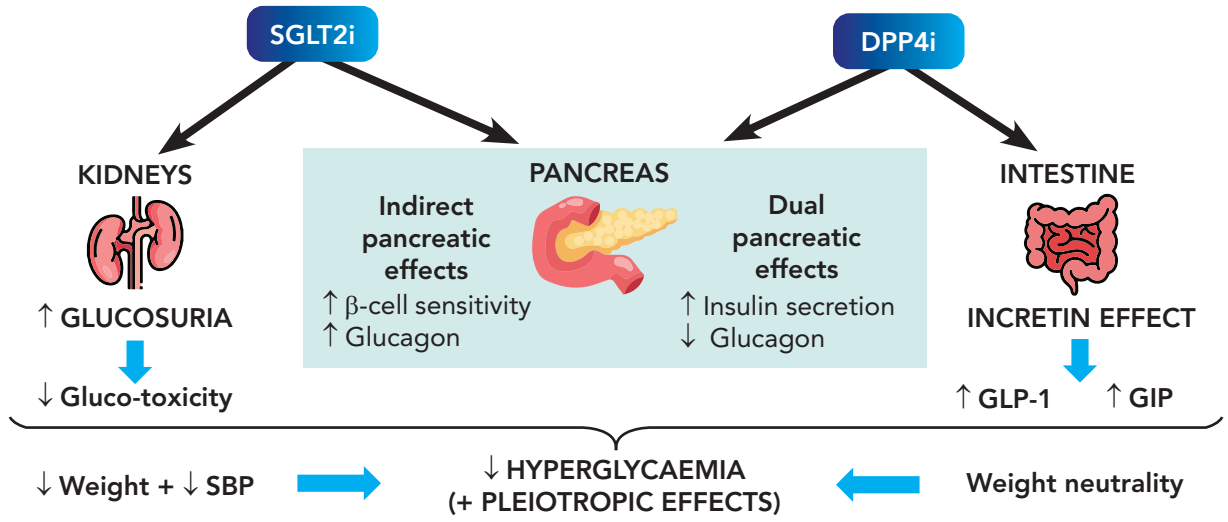
Figure 9: Comparison between Gliptins

	Sitagliptin	Vildagliptin	Saxagliptin	Linagliptin	Teneligliptin
HbA1c reduction	0.8%	0.7%	0.5%	0.6%	0.8%
Effect on body weight	Mild neutral	Mild neutral	Mild neutral	Mild neutral	Mild neutral
Effect on SBP	Reduction	Reduction	Reduction	Modest effect	Reduction
Effect on heart failure	Yes, as per TECOS trial	No dedicated CVOT trials	SAVOR TIMI 53	CAROLINA	Not well designed and with small no of patients
Dose adjustment in renal failure	No dose adjustment up to eGFR or ≥45 mL/min/1.73 m^2; 50 mg OD (30-45 mL/min); 25 mg OD (25 mL/min)	No dose adjustment up to eGFR or ≥45 mL/min/1.73 m^2	No dose adjustment up to eGFR or ≥45 mL/min/1.73 m^2 2.5 mg OD (<45 mL/min)	No dose adjustment in mild/moderate impairment)	No dose adjustment up to eGFR or ≥45 mL/min/1.73 m^2
Dose adjustment in hepatic failure	No dose adjustment in mid/moderate impairment	Contraindicated in any stage	No dose adjustment in mild/moderate impairment	No dose adjustment in mild/moderate impairment	No dose adjustment in mild/moderate impairment

NEW CLASS SGLT2I: PLACE IN THERAPY

SGLT-2 inhibitors can primarily be used as an add-on therapy for the treatment of type 2 diabetes in combination with metformin, insulin, sulfonylureas, thiazolidinediones, or DPP-4 inhibitors (Figure 10). Their mechanism of action is independent of pancreatic β-cell function or insulin sensitivity, so they may be used at any stage of type 2 diabetes. SGLT-2 inhibitors may also be considered for monotherapy in patients with an entry A1c <7.5% who are unable to tolerate metformin. Non-glycemic benefits of SGLT-2 inhibitors include modest weight loss and reductions in blood pressure, albumin/creatinine ratio, and uric acid.

Figure 10: Synergistic Effect of SGLT2i & DPP4i



Care should be taken when using various OADs in patients with CKD (Figure 11).

Figure 11: Indication of various OADs in CKD

Agent	Stage 1 eGFR ≥90	Stage 2 eGFR 60-89	Stage 3A eGFR 45-59	Stage 3B eGFR 30-44	Stage 4 eGFR 15-29	Stage 5 eGFR <15
Metformin	No dose adjustment needed/can be continued			don't initiate (can continue)	Don't use	
Sitagliptin	100 mg/day			50 mg/day	25 mg/day	
Vildagliptin	As per CrCl and not eGFR: No dose adjustment is required in patients for CrCl ≥ 50). In CrCl <50 dose is 50 mg once daily					
Linagliptin	5 mg/day					
Teneligliptin	20 mg/day					
Dapagliflozin					Don't use	
Empagliflozin	5/10 mg				Don't use	
Canagliflozin	100/200 mg		100 mg		Don't use	
Glimepiride	1-8mg				Higher risk of hypoglycemia	
Glipizide	2.5-20mg					
Gliclazide	40-320mg					
Pioglitazone15/ 30mg	15/30mg (No dosage adjustment needed)				Higher risk of edema, HF	

Q1. WHAT WOULD BE THE PREFERRED SULFONYLUREA IN A PATIENT WITH HbA_{1c} OF 8 AND ABOVE, AND SHOULD WE USE MONOTHERAPY OR START USING COMBINATION THERAPY?

A. Usually, the newer generation sulfonylureas like gliclazide and glimepiride are used in patients with such glycemic levels; though together considering the patient phenotypic profile. Sulfonylureas can be used both as monotherapy and part of combination therapy with other antidiabetics depending on the patient profile, hyperglycemia and glycemic goals. Concurrently, it is important to counsel the patient on importance of lifestyle changes and regular glucose monitoring.

Q2. WHILE INITIATING THE FIXED DOSE COMBINATIONS (FDCs) OF ANTIDIABETIC DRUGS, IS THERE ANY CHALLENGE REGARDING DOSE TITRATION OF INDIVIDUAL COMPONENTS?

A. Titration & dose flexibility can often be an issue while using FDCs; however, it is important to note that FDCs can significantly reduce the pill burden for the patients, which in turn can positively affect the treatment compliance. Finally, treatment regimen needs to be individualized for each patient based on the disease and patient characteristics.

Q3. HOW RELEVANT IS IT TO CONSIDER THE ADA GUIDELINES IN THE CONTEXT OF SOUTH-ASIAN SUBCONTINENT?

A. While guidelines do provide standard recommendations on the disease, it is important to note that these are not absolute, and one should always consider the regional conditions & patient profiles while tailoring the treatment for each patient. Furthermore, regional guidelines are also available for the help of physicians.

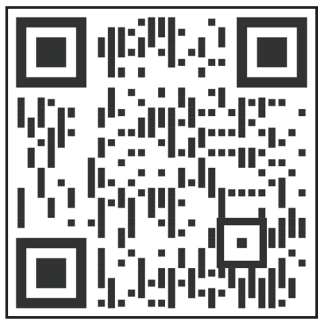
Q4. CAN SULFONYLUREAS BE ADDED TO A PATIENT ALREADY ON A COMBINATION OF A DDP4i & METFORMIN OR SGLT2i & METFORMIN?

A. Yes, sulfonylureas can be added in such cases to enhance the beta-cell function and glycemic control. This could also help in delaying the need for insulin in some patients. Furthermore, triple-drug combinations can also be considered in select patients already receiving dual therapy in order to reduce the pill burden while trying to achieve good glycemic control. Again, it is important to consider the patient profile before modifying and individualizing the treatment. Always add medicines with complimentary actions to gain positive associations.

Q5. REGARDING α-GLUCOSIDASE INHIBITORS, WHAT IS THEIR POSITION IN THE CURRENT CLINICAL PRACTICE OF DIABETES MANAGEMENT?

A. These drugs are often used as add-on agents particularly for their effect on post-prandial hyperglycemia. However, it is important to note that adverse gastrointestinal (GI) symptoms are also common with these agents, particularly considering the fact that most such patients would already be receiving multiple antidiabetic drugs.

Scan the QR code to access the video lecture



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