Overview of hyperglycemia management

Hiba Abbasi, MD,Endocrinologist

Department of Internal Medicine

School of Medicine

University of Jordan

Edited by: Ruaa Hdeib

TREATMENT GOALS

1- **Diabetes Education** : instruction on nutrition, physical activity, optimizing metabolic control, and preventing complications.

2- Evaluation for micro- and macrovascular complication

3- **Attempts to achieve near normoglycemia**

4- Minimization of cardiovascular and other long-term risk factors

5- Avoidance of drugs that can exacerbate abnormalities of insulin or lipid metabolism.

Diabetes Education

Intensive lifestyle modification

In patients with established type 2 diabetes, intensive behavioral modification interventions focusing on weight reduction and increasing activity levels are successful in reducing weight, improving glycemic management and, at the same time, reducing the need for glucose-lowering and other medications.

behavioral therapy:
↳ nutrition
↳ physical activity

1- Medical nutrition therapy

Aiming for weight reduction or at least weight maintenance.

2- Weight reduction major problem in T2DM is insulin resistance due to obesity

- By diet control, pharmacological or surgical therapy.

- Improved glycemic state is induced by weight loss through partial correction of the two major metabolic abnormalities in type 2 diabetes: insulin resistance and impaired insulin secretion.

- Weight loss and weight loss maintenance supports all effective type 2 diabetes therapy and reduces the risk of weight gain associated with sulfonylureas and insulin.

3- Exercise

- Regular exercise is beneficial for diabetics independent of weight loss.

- It leads to improved glycemic management due to : increased responsiveness to insulin and so delay the progression of impaired glucose tolerance to overt diabetes.

- These beneficial effects are directly due to exercise.

- Unfortunately, in one study, only 50% of patients with type 2 diabetes were able to maintain a regular exercise regimen.

PHARMACOLOGIC THERAPY

when to start ??? since time of diagnosis

- A reasonable goal of therapy might be an A1C of ≤7% (7 – 7.5%) for most patients. special populations : elderly , comorbodities , limited life expectency ≤ 8%

- Target A1C goals in patients with type 2 DM should be tailored to the individual, balancing the potential for improvement in microvascular complications with the risk of hypoglycemia,

So there is NO ((ONE SIZE FITS ALL))

- Glycemic targets are generally set somewhat higher for older adult patients and those with comorbidities or a limited life expectancy who may have little likelihood of benefit from intensive therapy.

- For most patients with A1C at or above target level (>7.5 to 8%), pharmacologic therapy should be initiated at the time of diagnosis (along with lifestyle modification).

- A 3-6 month trial of lifestyle modification prior to initiation of pharmacologic therapy is reasonable for :

1- patients with A1C at or above the target (7.5 – 8%) who have clear and modifiable contributors to hyperglycemia and who are motivated to change them.

2- highly motivated patients with A1C near target (<7.5%).

Choice of initial therapy??

Considerations:

1. Patient presentation: presence or absence of symptoms of hyperglycemia
2. Comorbidities
3. Baseline A1C level
4. Individualized treatment goals and preferences
5. The glucose-lowering efficacy of individual drugs, and their adverse effect profile, tolerability, and cost.

Patient presentation:

Asymptomatic, not catabolic:

- The majority of patients with newly diagnosed type 2 diabetes are asymptomatic, without symptoms of catabolism (without polyuria, polydipsia, or unintentional weight loss). not catabolic → no weight loss

- Hyperglycemia may be noted on routine lab test or detected by screening.

- **Metformin**: In the absence of specific contraindications, it can be used as initial therapy for those patients.

Dosing: We begin with 500 mg once daily with the evening meal and, if tolerated, add a second 500 mg dose with breakfast. The dose can be increased slowly (one tablet every one to two weeks) as necessary to reach a total dose of 2000 mg per day. gradual → to decrease the side effects

Glycemic efficacy refers to the capacity of regulated glycemic levels to produce an effect in people with diabetes and heart disease.

Advantages of Metformin :

1- It is the preferred initial therapy because of **glycemic efficacy (1-2%)**

2- Absence of weight gain neutral effect (may ↓ weight)

3- Absence of hypoglycemia (very rare side effect)

4- General tolerability, and favorable cost.

5- It appears to decrease cardiovascular events and does not have adverse cardiovascular effects.

Main side effects we care about in any DM medication is?

hypoglycemia , weight gain

Adverse effects :

1- Gastrointestinal:

- are the most common side effects including a metallic taste in the mouth, mild anorexia, nausea, abdominal discomfort, and soft bowel movements or diarrhea.

Gradually to avoid this

- usually mild, transient, and reversible after dose reduction or discontinuation of the drug. They are minimized by taking the medication with food.

2- Vitamin B12 deficiency

- Due to reduced intestinal absorption of vitamin B12 by metformin.

- In some patients, vitamin B12 deficiency may present as peripheral neuropathy.

3- lactic acidosis : very low incidence but high mortality rate!!

↳ Most serious, very rare

Symptomatic (catabolic) or severe hyperglycemia: polyuria, polydypsia

The frequency of symptomatic or severe diabetes has been decreasing in parallel with improved efforts to diagnose diabetes earlier through screening.

-**Ketonuria and/or weight loss present**

- Insulin, rather than oral hypoglycemic agents, is often indicated for initial treatment of symptomatic (polyuria or weight loss) or severe hyperglycemia (fasting plasma glucose >250 mg/dl ,RBG >300 mg/dl or A1C >10%)
- Insulin should also be initiated whenever there is a possibility of undiagnosed type 1 diabetes, which should be suspected among those who are lean or present with marked catabolic symptoms, especially in the presence of a personal or family history of other autoimmune disease and/or the absence of a family history of type 2 diabetes.

- **Ketonuria and weight loss are absent**
- For patients presenting with severe hyperglycemia but without ketonuria or spontaneous weight loss (i.e type 1 diabetes is not likely) insulin or GLP-1 receptor agonists may be used (with or without metformin, depending on contraindications or intolerance).
- For patients who refuse injections, initial therapy with high-dose sulfonylurea is an alternative option.
- Metformin monotherapy is not helpful in improving symptoms in this setting ,however, it can be started at the same time as the sulfonylurea, slowly titrating the dose upward.

Comorbidities:

Established cardiovascular or kidney disease

- Patients with cardiorenal comorbidities should be treated with glucose-lowering medications that have evidence of cardiorenal benefit such as GLP-1 receptor agonists and SGLT2 inhibitors.

- The cardiorenal benefits of GLP-1 receptor agonists and SGLT2 inhibitors have not been demonstrated in drug-naïve patients without established CVD (or at low cardiovascular risk) or without severely increased albuminuria.

Without established cardiovascular or kidney disease

For patients without established CVD or kidney disease who cannot take metformin and :

A1C >9-10% we suggest insulin or a GLP-1 receptor agonist for initial therapy.

* Insulin may cause weight gain and hypoglycemia.

If weight loss is a priority, a GLP-1 receptor agonist is a reasonable alternative to insulin.

it's used for weight reduction without DM

For patients without established CVD or kidney disease who cannot take metformin and :

Injectable or non-injectable

A1C ≤ 9% : options includes insulin, GLP-1 receptor agonists, sulfonylureas, SGLT2 inhibitors, DPP-4 inhibitors, repaglinide, or pioglitazone.

↳ hypoglycemia يعني ممكن يصل كادي إذا أخذت منه وما اكلت

↳ insulin sensetizer

weight reduction — GLP-1 receptor agonist (↳ relation with thyroid Carcinoma & MEN)

+

weight neutral — DPP-4 inhibitors

} incretin based therapy

glucose stimulated insulin secretion

↳ advantage: does not cause hypoglycemia

↳ That's why Oral insulin is better than IV insulin

Incretins · GLP-1 → glucose like pepride -1

GIP → glucose- dependent insulinotropic pepride

extremly short T1/2 (90 seconds) due to DPP-4

Considerations in drug selection:

i. If weight loss is a priority, GLP-1 receptor agonists or SGLT2 inhibitors may be a helpful choice. DPP-4 inhibitors, which are weight neutral, also may be reasonable options.

ii. If cost is a concern, a short- or intermediate-acting sulfonylurea, remains a reasonable alternative. The choice of sulfonylurea balances glucose-lowering efficacy, universal availability, and low cost with risk of hypoglycemia and weight gain.

iii. Pioglitazone is another relatively low-cost oral agent, may also be considered in patients with specific contraindications to metformin and sulfonylureas. BUT….. The Side effects and risk of weight gain, heart failure, fractures, and the potential increased risk of bladder cancer may sometimes approach or exceed its benefits.

iv. If avoidance of hypoglycemia is a priority (ie, because of potentially dangerous work or an elderly patient with inability to self-manage himself at all times) ,GLP-1 receptor agonists, SGLT2 inhibitors, DPP-4 inhibitors are options as they are associated with a low hypoglycemia risk.

Insulin therapy:

Although historically insulin has been used for type 2 diabetes only when inadequate glycemic management persists despite oral agents and lifestyle intervention, there are increasing data to support using insulin earlier and more aggressively in type 2 diabetes.

Benefit ??!!

By inducing near normoglycemia with intensive insulin therapy, both endogenous insulin secretion and insulin sensitivity improve; this results in better glycemic management, which can then be maintained with diet, exercise, and oral hypoglycemics for many months thereafter with less future risk of microvascular complications.

Cardiovascular outcomes

- Virtually all trials evaluating the safety and efficacy of all anti diabetes drugs have recruited patients who were already had preexisting CVD or were at very high risk for CVD. So the long-term benefits and risks of using one agent over another in the **absence** of diagnosed CVD are unknown.

- Cardiovascular benefit has been demonstrated for many of these medications, but benefit has not been investigated in drug-naïve patients without established CVD or at low cardiovascular risk.

Microvascular outcomes

- In trials designed to evaluate renal outcomes in patients with DKD and severely increased albuminuria , SGLT2 inhibitors reduced the risk of kidney disease progression and death from renal disease.

- In trials of patients with type 2 diabetes with and without chronic kidney disease, GLP-1 receptor agonists slowed the rate of decline in eGFR and prevented worsening of albuminuria.

twice / year

MONITORING

- We obtain A1C at least twice yearly in patients meeting glycemic goals and more frequently (quarterly) in patients whose therapy has changed or who are not meeting goals.

- Self-monitoring of blood glucose (SMBG) is not necessary for most patients with type 2 diabetes who are on a stable regimen of diet or oral agents and who are not experiencing hypoglycemia.

- SMBG may be useful for some type 2 diabetes patients who use the results to modify eating patterns, exercise, or insulin doses on a regular basis.

PERSISTENT HYPERGLYCEMIA

- For patients who are not meeting glycemic targets despite diet, exercise, and metformin, combination therapy is necessary to achieve optimal results.

- The balance among efficacy in lowering A1C, side effects, and costs must be carefully weighed in considering which drugs or combinations to choose.

- Avoiding insulin, the most potent of all hypoglycemic medications, at the expense of poorer glucose management and greater side effects and cost, is not likely to benefit the patient in the long term.

Thank you