

# ADA-EASD

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## Abstract

The ADA and EASD have recently published a consensus algorithm to guide management of hyperglycemia in adults with type 2 diabetes. This article reviews the guidelines, and restates the recommendations in simple words, while emphasizing the salient points.

## INTRODUCTION

Newer understanding of the pathophysiology of diabetes, and development of novel classes of glucose lowering drugs have led to the need for an updated, modern algorithm to help healthcare providers manage diabetes appropriately.

The ADA and EASD have published a consensus algorithm in December 2008 which use information from clinical trials and clinical judgment (collective knowledge and experience) to suggest an algorithm to “guide therapy and result in improved glycemic control”

## GOALS OF THERAPY

Consensus has been reached regarding glycemic goals: an HbA1c  $\geq 7\%$  is a call to action to initiate or change therapy with the goal of achieving HbA1c  $< 7\%$ . This may not be appropriate or practical for all patients however, and one should consider potential benefits and risks, including life expectancy, risk of hypoglycemia and presence of cardiovascular disease, while deciding targets for individual patients. The guidelines also emphasize the need to treat hypertension and dyslipidemia as per existing guidelines.

## CHOICE OF THERAPY

Glycemic therapy should be selected keeping in mind effectiveness, extraglycemic effects, safety, tolerability, ease of use, and expense of various drugs.

Choosing a particular medication for an individual patient will depend on the ambient glucose level, duration of diabetes, and nature of previous therapy.

## DIFFERENT CLASSES OF DRUGS

The ADA- EASD guidelines list the advantages, disadvantages and important points of metformin,

sulfonylureas, glinides,  $\alpha$ -glucosidase inhibitors, thiazolidinediones, insulin, insulin analogues, GLP-1 agonists, amylin agonists and DPP-4 inhibitors.

Lifestyle interventions, weight loss and physical activity have multiple beneficial effects and do not cost much, but are usually insufficient alone.

The authors remind us to use sulfonylureas only till half maximal doses, and “unanimously advise against using rosiglitazone” while advising “caution in using either thiazolidinedione”

Metformin is recommended as it is economical, weight stable, and does not cause hypoglycemia. It can cause gastrointestinal side effects, reduce vitamin B<sub>12</sub> absorption, metformin associated lactic acidosis, and is contraindicated in renal dysfunction.

Repaglinide is effective in reducing HbA1c, and causes less hypoglycemia.

The  $\alpha$ -glucosidase inhibitors are shown to lower postprandial glucose, without hypoglycemia, while reducing cardiovascular risk, but are associated with a high discontinuation rate because of gastrointestinal symptoms.

DPP-4 inhibitors are weight neutral, well tolerated and do not cause hypoglycemia.

Exenatide has similar advantages, causes weight loss and can be given with sulfonylureas/ metformin &/or thiazolidinediones.

Pramlintide is an amylin agonist, with a profile similar to exenatide, which is approved for use with insulin, only in USA.

**INSULIN**

Insulin is the oldest antidiabetic drug, the most effective medication, can decrease any level of HbA1c, has the most clinical experience attached to it, and has beneficial effects on lipid profile.

The guidelines reiterate that  $\geq 1\text{U/kg/day}$  insulin may be necessary for control. Intermediate or long acting insulin should be used for initial therapy, but prandial therapy may be needed. Premixed insulin is not recommended during dose adjustment, but can be used otherwise, for convenience. Early insulin is also recommended in newly diagnosed patients.

Insulin analogues find mention, along with the note that they reduce the risk of hypoglycemia.

Initiation and adjustment of insulin therapy is discussed in detail. There is no need to hospitalize a patient, except in specific circumstances. We are reminded that the patient is the key player in diabetes management and should be trained and empowered, under the guidance of healthcare providers, to achieve goals and prevent/ treat hypoglycemia.

**SMBG AND HYPOGLYCEMIA**

The guidelines offer guidance on treating hypoglycemia, but are not clear on the need for, or number of required self-monitored blood glucose (SMBG) measurements, saying that this depends on the type of medication prescribed.

Targets for capillary glucose are mentioned as: fasting or preprandial plasma glucose: 3.9-7.2 mmol/l (70-130 mg %); postprandial plasma glucose, done at 90-120 minutes:  $<10$  mmol/l (180 mg %).

The goal of achieving and maintaining an HbA1c  $\leq 7\%$ , at as rapid a pace as titration of medications allows, is emphasized.

**TWO TIER ALGORITHM**

The algorithm divides all therapies into two tiers: tier 1, which has well-validated, effective and cost effective treatments, and tier 2, which lists less well validated drugs.

**TIER 1**

Tier 1, step 1 is lifestyle intervention and metformin, with detailed advice on titration of metformin (begin from 500mg od or bd/850mg od, and increase every 5-7 days, as required, to a maximum of 2-5 g/day over 1-2 months)

If step 1 fails to achieve or sustain glycemic goals, one should add insulin or sulfonylurea (step 2), within 2-3 months of therapy initiation, or at any time when target is not achieved, or if metformin is contraindicated or not tolerated.

Insulin is preferred in patients with HbA1c  $> 8.5\%$ , or in those with symptoms secondary to hyperglycemia.

Step 3 is to start, or intensify insulin therapy, as the case may be, using short or rapid- acting insulin, while stopping or tapering off secretagogues. The guidelines clearly discourage triple oral hypoglycemic combinations.

**TIER 2**

The consensus also provides a second tier algorithm, focusing on the advantages of pioglitazone and exenatide in avoiding hypoglycemia, and the weight loss associated with exenatide.

In tier 2, step 2 is to add metformin and pioglitazone, or metformin and GLP-1 agonist to lifestyle measures. Step3 will be to give a triple drug oral combinations (metformin+pioglitazone + sulfonylurea) or metformin + basal insulin in addition to lifestyle therapy.

**CONCLUSION**

A thorough understanding of the ADA-EASD guidelines will help health care providers choose the appropriate therapy for their adult patients with type 2 diabetes, and ensure better glycemic control and overall health.

**References**

1. Nathan DM, Buse JB, Davidoon MB, et al. medical management of hyperglycemia in type 2 diabetes; A consensus algorithm for the initiation and adjustment of therapy. Diabetes care 2008; 31 (12):1-11.

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