

Diabetes Mellitus

Prohibited Substance: Insulin

1. Introduction

Diabetes is a global epidemic with 529 million people affected worldwide equivalent to the total population of the USA, Canada and Mexico. In recognition of this, the United Nations passed a resolution in 2006 declaring diabetes to be a major, global health threat; the first time this has ever happened for a non-infectious disease. At present, 1 in 12 of the world population has diabetes and this is estimated to rise to 10% of the world's population by 2040.

Diabetes is a chronic endocrine disorder characterized by high blood glucose levels resulting from an inability to produce or utilize the pancreatic hormone, insulin.

Diabetes is usually categorized in four subgroups:

1. Type 1 diabetes
2. Type 2 diabetes
3. Special forms (e.g., monogenic diabetes, pancreatogenic diabetes, diabetes associated with other endocrine diseases, etc.)
4. Gestational diabetes

The hallmark of type 1 diabetes (T1DM) is pancreatic beta cell destruction, usually leading to absolute insulin deficiency. Type 2 diabetes (T2DM) is characterized by insulin resistance and ongoing decline in beta cell function. However, there may be some overlap between the two categories.

Every doctor worldwide has been educated in the diagnosis and management of diabetes and the most current information is available from the International Diabetes Federation, the American Diabetes Association, the European Association for the Study of Diabetes, and NICE (see references).

2. Diagnosis and best practice treatment

The diagnosis of diabetes is made if the patient satisfies any one of the following criteria and, in all cases of T1DM, treatment will involve regular injections of insulin. Although the differentiation of T1DM and T2DM is usually made clinically, measurement of diabetes related autoantibodies and c-peptide levels could be helpful.

Criteria for the diagnosis of diabetes

FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥ 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C $\geq 6.5\%$ (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

* In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

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T1DM is more likely to be diagnosed in childhood but can develop at any age. The onset of T2DM is generally in later life but there has been a recent upsurge in children and adolescents. The management of T2DM has undergone a major overhaul the last decade. GLP-1 (glucagon-like peptide) receptor agonists or dual GLP1-/GIP RAs (glucose-dependent insulintropic polypeptide receptor agonist) are now the drugs of choice (and not insulin) when oral hypoglycemic agents do not lower glucose appropriately. Use of insulin at a much earlier stage has also been implemented in some cases where oral medication, diet, and exercise do not result in acceptable blood sugar control.

Optimal diabetes management should maintain the HbA1c (glycosylated haemoglobin) below 7.0%. If the HbA1c rises above this level, despite diet and oral/injectable antihyperglycemic medications, or if they are not achieving glycemic goals, treatment with GLP-1 receptor agonists, dual GLP1-/GIP RAs or insulin is indicated and should not be delayed. Insulin may be used in conjunction with other antihyperglycemics.

It should be noted that the HbA1c is a measure of glycemia control over the previous 2-3 months and will not change rapidly when insulin is introduced. In addition, switching to insulin will normally result in some weight gain, which may be of significance in athletes involved in weight sensitive sports. In this situation, patients may continue to take Metformin after starting insulin because this medication

attenuates the weight gain associated with a switch to insulin. It is not uncommon to continue metformin, sodium–glucose cotransporter 2 (SGLT2) inhibitors, and/or glucagon-like peptide 1 receptor agonists (GLP-1 analogues), especially if using basal insulin alone.

Although insulin is not usually considered as the first therapy of choice in T2DM, it may be utilized in the initial treatment for newly diagnosed T2DM if the patient is symptomatic and/or has an HbA1c over 10% and/or the fasting blood glucose is consistently over 250mg/dl (13.9 mmol/L).

Despite vast expenditure on healthcare worldwide, management of T2DM remains woefully inadequate, with patients spending an average of 5 years well outside the recommended glycemia range before treatment is initiated.

3. Prohibited substances

Insulin is prohibited under S4 of the [WADA Prohibited List](#)—Hormone and Metabolic Modulators. All individuals with diabetes on insulin require a TUE.

4. Other non-prohibited alternative treatments

There are currently few alternatives to insulin. However, recent developments in immunotherapy (teplizumab is approved) and stem-cell therapy (not yet approved) can replace insulin in some patients with T1DM, at least temporarily.

5. Consequences to health if treatment is withheld

Failure to utilize insulin in the treatment of patients with T1DM could result in the death of the patient.

As described above, in certain situations where T2DM is poorly controlled, insulin may be part of the recommended treatment regimen.

6. Treatment monitoring

Once the initial diagnosis of T1DM or T2DM is made, patients will be regularly monitored by a doctor or diabetes educator to ensure that the dosage of insulin is adequate for glycemic control.

7. TUE duration

The initial TUE request must include details of the onset, investigation, and diagnosis of the condition, with supporting documentation from a specialist in the management of diabetes, or a unit specializing

in the management of diabetes. It is recommended that for T1DM, an initial TUE for insulin is granted for 12 months. After 12 months, the TUE should be reviewed with documentation obtained from the general practitioner and/or the specialist, and a further TUE may be granted for 10 years.⁹⁻¹¹

Remission of T2DM and discontinuation of insulin therapy are common outcomes following significant weight reduction achieved through lifestyle modification, bariatric surgery, or pharmacologic intervention. It is recommended that for T2DM, an initial TUE is granted for 12 months. After 12 months, the TUE should be reviewed with documentation obtained from the general practitioner and/or the specialist, and a further TUE may be granted for up to 4 years.

8. Any appropriate cautionary matters

None.

References

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