

CLINICAL MANAGEMENT OF  
TYPE 2 DIABETES MELLITUS

# TYPE 2 DIABETES

GUIDELINES

2006



## FORWARD MINISTRY OF PUBLIC HEALTH

Diabetes is an increasing problem and is a major contributor to the growing burden of chronic disease in our country. It is associated with significant morbidity and decreased life expectancy due to its complications which include heart disease, stroke, amputation, blindness and kidney failure. Diabetes reduces quality of life, especially in people with complications. It is also associated with increased psychosocial problems including depression and anxiety.

There is good evidence that diabetes complications can be prevented or delayed through efforts to improve diabetes care and correct blood glucose, blood pressure and lipid abnormalities, as well as by avoiding smoking and excessive food intake, increasing physical activity and controlling body weight. The cost-effectiveness of interventions to improve diabetes care has been well established by many studies.

Unfortunately, the practice of diabetes care is still far from uniform. This guideline is an essential component of achieving diabetes care for all people with the condition. The guideline recommendations define standards for care, and use evidence-based interventions to achieve those standards, in order to guide healthcare professionals and people affected by diabetes.

As a minister of public health and as a physician, I recommend to my colleagues to make the best use of these recommendations for the benefit of the patients.

Finally, I would like to express all my gratitude towards the Lebanese Society of Endocrinology Diabetes and Lipids and the Non-Communicable Disease Program a joint program between the World Health Organization and the Ministry of Public Health who worked out this document, the Ministry of Public Health for their support to make this initiative feasible.

Dr. Mohamad Jawad Khalifeh  
Minister of Public Health.





## INTRODUCTION TO GUIDELINES

Diabetes is developing into an epidemic worldwide. It is the main cause of small and large blood vessel disease as well as cardiovascular mortality and morbidity. Effective treatment of diabetes and the metabolic syndrome decreases the risk of complications and diabetes-related mortality. Several leading national and international organizations, including the American Diabetes Association, International Diabetes Federation and the World Health Organization (WHO) have developed and endorsed standards for diagnosis and treatment of people with diabetes.

The purpose of this publication is to bring this information to you in a concise and detailed fashion. It was developed by a group of diabetes specialists, who represent various countries from Eastern and Central Europe and Mediterranean regions and endorsed by the Lebanese Society of Endocrinology, Diabetes and Lipids / World Health Organization Beirut Office / Lebanese Ministry of Public Health. The guidelines were developed on a basis of predetermined subjects and taking into consideration the most important goals that we want to achieve in the treatment of diabetic patients.

Each page of the guidelines has an appendix, which further explains the main recommendations provided in each chapter. Our hope is that these guidelines will promote better treatment for the diabetic patients in Lebanon and various countries in the region.

Sincerely,



Professor **Sami Azar**, MD, FACP

President of the Lebanese Society of Endocrinology, Diabetes and Lipids



## **These guidelines were revised by**

- The Lebanese Society of Endocrinology, Diabetes and Lipids
- World Health Organization Beirut Office
- Non Communicable Disease Programme
- Lebanese Ministry of Public Health

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## Abbreviations

<b>A1C</b>	–	Hemoglobin A1c
<b>ACE</b>	–	Angiotensin - converting enzyme
<b>ADA</b>	–	American Diabetes Association
<b>AMI</b>	–	Acute myocardial infarction
<b>ARB</b>	–	Angiotensin receptor blockers
<b>BMI</b>	–	Body mass index
<b>BP</b>	–	Blood pressure
<b>BPH</b>	–	Benign prostatic hyperplasia
<b>BW</b>	–	Body weight
<b>CHD</b>	–	Coronary heart disease
<b>CPK</b>	–	Creatinine phosphokinase
<b>DM</b>	–	Diabetes mellitus
<b>ECG</b>	–	Electrocardiogram
<b>FPG</b>	–	Fasting plasma glucose
<b>GI</b>	–	Gastrointestinal
<b>HDL</b>	–	High-density lipoproteins
<b>IFG</b>	–	Impaired fasting glucose
<b>IGT</b>	–	Impaired glucose tolerance
<b>LADA</b>	–	Latent autoimmune diabetes in adults
<b>LDL</b>	–	Low-density lipoproteins
<b>LSO</b>	–	Lifestyle optimization
<b>MDI</b>	–	Multiple daily injections
<b>OCT</b>	–	Oral combined therapy
<b>OGTT</b>	–	Oral glucose tolerance test
<b>OMT</b>	–	Oral monotherapy
<b>OT</b>	–	Oral therapy
<b>PPPG</b>	–	Postprandial plasma glucose
<b>RF</b>	–	Risk factors
<b>TG</b>	–	Triglycerides
<b>TZD</b>	–	Thiazolidinediones



## Diabetes Mellitus

The prevalence of diabetes mellitus is expected to double over the next 20 years, based on aging of the population and the rate of urbanization; this increase will be seen worldwide, in developed as well as in developing countries, and will create an additional financial and social burden on the public health sector. Estimates suggest a 13% prevalence of the disease in Lebanon, and as high as 30% in certain Gulf countries.

Most affected patients (90%) have type 2 diabetes, a chronic progressive disease characterized by insulin resistance due to abdominal obesity and relative insulin deficiency due to progressive deterioration of pancreatic beta-cell function. Many years of pre-diabetes or impaired glucose tolerance precede the onset of the disease, and intensive lifestyle modification or pharmacotherapy may prevent the progression to type 2 diabetes. The diagnosis of type 2 diabetes is typically made a few years late, which highlights the importance of early screening. Type 1 diabetes (10%) is seen in younger patients, and is due to autoimmune destruction of pancreatic beta-cells in genetically predisposed individuals.

The dreaded microvascular complications of type 1 and 2 diabetes such as retinopathy or nephropathy can be prevented by intensive therapy. Macrovascular complications are seen more often in older type 2 diabetic patients, and efforts to treat all risk factors should be undertaken to reduce the associated increase in morbidity-mortality, 75% of deaths being due to cardiovascular disease.

Public health campaigns should aim at preventing type 2 diabetes in high-risk individuals through education and increased awareness. In addition, early and periodic screening will lead to earlier diagnosis and therapy, which will prevent or delay the vascular complications of the disease. Only such an aggressive approach will help in slowing down the rampant epidemic of diabetes mellitus.



## APPENDIX

- ▶ Consider the following **risk factors** (RF) when performing annual screening for diabetes:
- $\geq 40$  years of age
  - habitual physical inactivity
  - family history of diabetes at age of 30 years in first degree relatives
  - delivery of a baby weighing  $> 4$  kg
  - previous gestational diabetes
  - previously identified IFG or IGT
  - overweight (BMI  $\geq 27$  kg/m<sup>2</sup>)
  - waist circumference (cm): 102 in men/88 in women
  - hypertension
  - history of vascular disease
  - HDL-cholesterol  $\leq 1.03$  mmol/l ( $\leq 40$  mg/dl) and/or triglycerides  $\geq 2.26$  mmol/l ( $\geq 200$  mg/dl)
  - polycystic ovary syndrome

# 1

## SCREENING

- ▶ for **screening**: perform fasting plasma glucose (FPG) test

1 or more  
**RFs**



Perform FPG yearly  
(if IFG/IGT are present more frequent tests may be planned)

in  
those  
with

IFG, IGT,  
gestational diabetes,  
delivery of baby  
with BW > 4 kg,  
or > 2 RFs



Perform 75-g  
OGTT every  
2 years



## APPENDIX

- \* In the absence of unequivocal hyperglycemia with acute metabolic decompensation, these criteria should be confirmed by repeated testing on a different day (minimum two separate measurements on two separate occasions).
- \*\* No caloric intake for at least 8 hours.
- \*\*\* Symptoms of marked hyperglycemia: polyuria, polydipsia, weight loss (sometimes with polyphagia), blurred vision.

Different criteria are used to diagnose diabetes in pregnant women.

# 2. DIAGNOSIS

➔ Criteria\* for the diagnosis of:

Venous plasma  
glucose concentration

## DIABETES MELLITUS (DM)

- fasting\*\*  $\geq 7.0$  mmol/l ( $\geq 126$  mg/dl)
- 2-h post glucose load  $\geq 11.1$  mmol/l ( $\geq 200$  mg/dl)
- symptoms\*\*\* of diabetes and casual plasma glucose  $\geq 11.1$  mmol/l ( $\geq 200$  mg/dl)

## IMPAIRED GLUCOSE TOLERANCE (IGT)

- fasting\*\*  $< 7.0$  mmol/l ( $< 126$  mg/dl)
- and
- 2-h post glucose load  $7.8$ - $11.1$  mmol/l ( $140$ - $200$  mg/dl)

## IMPAIRED FASTING GLUCOSE (IFG)

- Fasting\*\*  $< 5.6$  -  $6.9$  mmol/l ( $100$ - $125$  mg/dl)



## APPENDIX

- ▶ Less tight glycemic control may be appropriate for persons with history of repeated episodes of severe hypoglycemia (but only temporary), in elderly or in persons with limited life expectancy
  
- ▶ Foot - related risk conditions include:
  - peripheral neuropathy with loss of protective sensation
  - peripheral vascular disease
  - bone deformity
  - history of ulcers/amputations
  - evidence of increased pressure/altered biomechanics
  
- ▶ Further cardiac testing should be performed, if the following are present:
  - typical/atypical cardiac symptoms
  - resting ECG suggestive of CHD
  - cerebral/peripheral vascular disease
  - more than 2 risk factors (in addition to diabetes) from the following group:
    - $\geq 45$  years of age
    - physical inactivity
    - family history of premature CHD
    - smoking
    - micro/macroalbuminuria
    - hypertension
    - dyslipidemia

# 3. GLYCEMIC CONTROL AND CHRONIC COMPLICATIONS

## i. OBJECTIVES:

- FPG:**  
Optimal: < 4.4 - 6.7 mmol/l (80 - 120 mg/dl)  
*Reasonable:* < 7.8 mmol/l (<140 mg/dl)
- PPPG:**  
Optimal: < 6.7 - 8.9 mmol/l (120 - 160 mg/dl)  
*Reasonable:* < 10.0 mmol/l (<180 mg/dl)
- A1C:**  
Optimal: < 6.5%  
*Reasonable:* 6.5% < A1C < 7.5%
- Absence of microalbuminuria or other diabetic complications

## ii. FREQUENCY OF TESTING:

- A1C:
  - at least 2 times/year - if stable
  - quarterly - if treatment changes or objectives not achieved
- Dilated eye exam: at diagnosis and yearly thereafter (if normal eye background and no other risk factors: once every 2 years; abnormal findings require more frequent follow-ups)
- Foot exam: at diagnosis and then yearly (more often in patients with high-risk conditions)
- Microalbuminuria measurement: at diagnosis and yearly thereafter
- Resting ECG: further cardiac evaluation if 2 or more risk factors are present

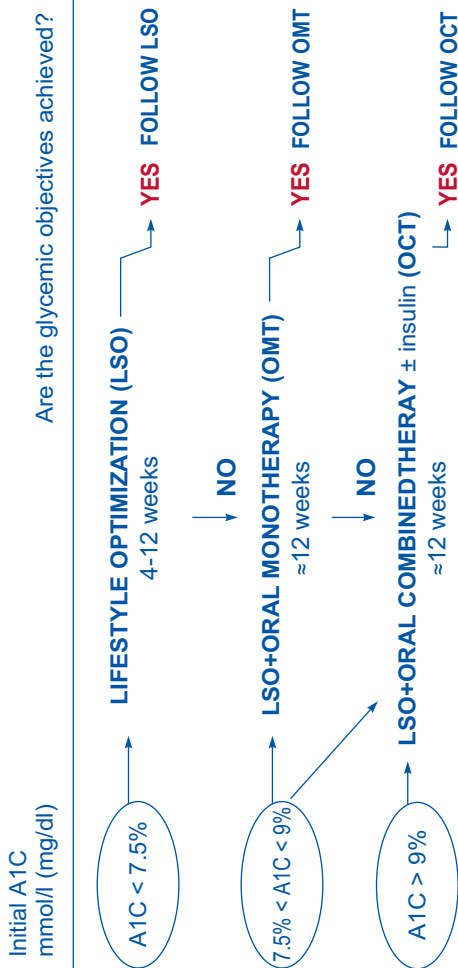


# APPENDIX

- ▶ Early start of insulin treatment should be considered in all non-responders or patients with very high glycemia, followed by scaling down to oral monotherapy or oral combination once glucotoxic effect of hyperglycemia ceases.
- ▶ When OMT is initiated:
  - if BMI:
    - < **25 kg/m<sup>2</sup>** - start with an insulin secretagogue (2nd / 3rd generation)
    - > **25 kg/m<sup>2</sup>** - start with biguanides (metformin)
  - and titrate to maximal/ tolerated dose
  - in case insulin secretagogue or biguanides are not well tolerated or are contraindicated, other oral agents can be used
- ▶ If treatment goals are not achieved on maximal dose, then OCT should be started. Some rational combinations:
  - sulphonylureas + biguanides / thiazolidindiones
  - biguanides / thiazolidindiones + prandial glucose regulators
  - sulphonylureas / biguanides +  $\alpha$  glucosidas inhibitors
  - the additional oral agents should be titrated to the maximal / tolerated doses
- ▶ If treatment goals are not met on oral agents / oral agents are contraindicated start insulin therapy. Many insulin regimens might be efficacious in individuals with Type 2 diabetes;
- ▶ Insulin + oral agents
  - metformin + insulin at bedtime or twice daily (bi-phasic premixed insulin or basal insulins [NPH or glargine])
    - » starting dose: 0.1 U/kg
  - sulphonylurea + insulin at bedtime or twice daily (bi-phasic premixed insulin or basal insulins [NPH or glargine]); consider decreasing previous dose of sulphonylurea
  - TZD + insulin at bedtime or twice daily (bi-phasic premixed insulin or basal insulins [NPH or glargine])
- ▶ Insulin without oral agents
  - start with conventional insulin regimen (twice daily insulin regimen, covering fasting and prandial needs)
    - » starting dose: 0.2-0.3 U/kg
    - » the insulin doses and the number of injections should be adjusted (eg, upgrade to MDI by adding short acting insulin) to achieve target glucose levels

Addition of metformin is indicated in all patients who require insulin in their treatment and who tolerate the drug well, due to its weight gain preventive effect and positive impact on metabolic control.

### iii. ALGORITHM OF MANAGEMENT



Adapted from N. Hâncu, A. Cerghizan:  
Cardiovascular risk in type 2 diabetes,  
Springer Verlag 2002: 240-277



## APPENDIX

- ▶ **Dietary** recommendations should be provided by a dietitian, physician or educator-nurse.

In patients who are overweight and glyemic control is not achieved with the current treatment, low carbohydrate diet is suggested (apart from patients with overt nephropathy and with caution in patients with mild nephropathy)

- ▶ **Alcohol:**

- abstinence from alcohol is advised during pregnancy, in pancreatitis, severe hypertriglyceridemia, advanced nephropathy, liver disease, psychiatric problems / history of alcohol abuse
- if a person chooses to drink alcohol, daily intake should not exceed 1 to 2 alcohol containing drinks
- alcohol should be consumed with meals, to avoid risk of hypoglycemia

#### **iv. LIFESTYLE OPTIMIZATION**

- **Diet:**

individual dietary recommendation should be provided to each patient. As a general rule, complex carbohydrate and fiber should be increased and saturated fat should be replaced with unsaturated fat.

**for overweight patients:**

moderate caloric restriction  
(500 or 1000 kcal less than previous intake)

**for patients with hypertension:**

salt intake should be restricted to less than 3g/day

for patients with dyslipidemia:

< 300 mg cholesterol/day;  
< 10% of energy intake from saturated fat

- **Alcohol intake:**

moderate intake could be allowed; alcohol may increase risk of hypoglycemia which should be taken into account when an individual advice is given

- **Physical exercise:**

30-60 min daily walking/other moderate physical activities

- **Smoking:**

advise all patients to quit



### 3. Glycemic control and chronic complications

#### V. PHARMACOTHERAPY

#### Recommendations for the use of oral agents

	BIGUANIDES	SULFONYLUREA	$\alpha$ -GLUCOSIDASE INHIBITORS	THIAZOLIDINEDIONE	PRANDIAL GLUCOSE REGULATORS
ADVANTAGES	No body weight increase Hypolipemic effect	Fast drop in BG level	Effect on postprandial hyperglycemia (failure of metformin or other oral agents)	Reduced insulin resistance (hypolipemic effect)  Not contraindicated in kidney failure	Flexible meal timing Can be administered in kidney failure Effect on postprandial hyperglycemia
CONTRAINDICATIONS	Hypoxia Age > 80 years Heart or kidney failure	Severe hepatic or kidney impairment	Certain GI diseases including inflammatory bowel disease Renal failure Cirrhosis	Anemia  Heart failure  Active liver disease	Severe hepatic impairment
COMMON SIDE-EFFECTS	Gastrointestinal	Hypoglycemia Weight gain	Gastrointestinal	Weight gain Fluid retention Anemia Increased level of liver enzymes	Hypoglycemia Weight gain Arthralgia Sinusitis

\* Safety in pregnancy has not been established for any of the oral hypoglycemic agent classes

#### Indications for insulin therapy in type 2 DM

- Failure to achieve glycemic control, despite maximum doses of combined oral therapy
- Decompensation due to intercurrent events (e.g. infections, acute injury, acute MI, other stress)
- Perioperative management
- Pregnancy and lactation
- Kidney or liver failure
- Allergy or other serious reactions to oral drugs
- Marked hyperglycemia at the time of presentation
- Acute myocardial infarction
- Hyperosmolar Syndrome / DKK
- Suspected LADA



## APPENDIX

- \* For diagnostic purposes it is necessary to measure BP on 2-3 different occasions within a period of minimum seven days, at least 2 measurements at each visit
- ▶ 24-h BP monitoring is suggested in every patient, especially in those suspected of “*white coat hypertension*”, drug resistance, iatrogenic hypotension, episodic hypertension and autonomic dysfunction.

# 4

## MANAGEMENT OF COMORBIDITIES

### A. BLOOD PRESSURE CONTROL

#### i. DIAGNOSIS\*:

1. Systolic BP:  $\geq 140$  mmHg
2. Diastolic BP:  $\geq 90$  mmHg

#### ii. TREATMENT OBJECTIVES:

1. Systolic BP:
  - Optimal (Target): < 130 mmHg
  - Reasonable:* 130-139 mmHg
2. Diastolic BP:
  - Optimal (Target): < 80 mmHg
  - Reasonable:* 80-89 mmHg

The main objective of the treatment is to achieve the target BP, not the type of pharmacological agents that is prescribed

#### ii. FREQUENCY OF MEASUREMENT:

Each regular diabetes visit; if BP >140/90 mmHg, then BP should be measured once monthly by nurse or physician, or by self monitoring, if possible.

#### iii. ALGORITHM OF MANAGEMENT:

BP mmHg	Are the BP objectives achieved?
S: 130-139 and/or D: 80-89	<p>→ <b>LIFESTYLE OPTIMIZATION (LSO) maximum 3 months</b></p> <p>→ YES → LSO</p>
S: > 140 and/or D: > 90	<p>→ <b>LSO + PHARMACOTHERAPY</b></p> <p>↓ NO</p>



## APPENDIX

- ▶ if drugs from one class are not tolerated, they should be substituted with drugs from other classes
- ▶ For initial therapy ACE - inhibitors, angiotensin-II receptor antagonists, thiazide diuretics should be used;  
If target is not achieved, drugs from these classes/other should be added
- ▶ if ACE - inhibitors and/or angiotensin-II receptor antagonists are used, monitor renal function and serum K<sup>+</sup> levels in the early period after the start of treatment
- ▶ if initial BP is above 160/90:  
start combination therapy
- ▶ combination of 2-3 drugs might be needed in most patients in order to control BP
- ▶ salt intake should be reduced to less than 3 g/day in patients with uncontrolled hypertension despite the use of antihypertensives under drug therapy - and checked by 24 h urine collection (less than 100 mEq NaCl/day); furosemide may be given 2-3 times/day, in patients who do not restrict salt intake
- ▶ if BP is high in the morning, BP-lowering drug should be taken at bedtime

➔ **LIFESTYLE OPTIMIZATION:** see above

### ➔ **PHARMACOTHERAPY**

#### **Drugs of choice:**

- **ACE-inhibitors**  
or  
**Angiotensin-II receptor antagonists**  
are considered first line therapy
  - **Thiazide diuretics** (low dose should be added)
  - **Calcium channel blockers**  
(preferably long-acting dihydropyridines or non-dihydropyridines)
  - **$\beta$ -2 blockers** (especially in the presence of tachycardia or chronic coronary artery disease and in post AMI patients)
  - **$\alpha$ -1 blockers** (especially if dyslipidemia or BPH is present)
  - **Other classes** (direct vasodilators, anti-adrenergic drugs other than  $\beta$ -2 blockers, imidazoline receptor agonists)
- 
- Many patients require combined pharmacological therapy to achieve BP targets.
  - Initial drug therapy should include a drug class that reduces risk of CV events (ACE inhibitors, ARBs,  $\beta$ -blockers, diuretics or calcium channel blockers)



## APPENDIX

▶ **Non HDL-cholesterol**

=

Total Cholesterol - HDL Cholesterol

▶ **LDL-cholesterol**

=

Total Cholesterol - HDL Cholesterol - Triglycerides /5  
(if values are in mg/dl)

or

**LDL-cholesterol**

=

Total Cholesterol - HDL Cholesterol - Triglycerides /2.2  
(if values are in mmol/L)

## B. LIPID CONTROL

### i. OBJECTIVES:

1. LDL-cholesterol:

**Optimal** (Target): <2.6 mmol/l (<100 mg/dl)

In very high risk patients : <1.82 mmol/l (<70 mg/dl)

2. HDL-cholesterol:

**Optimal** (Target): men: > 1.1 mmol/l (>45 mg/dl)

women: > 1.4 mmol/l (> 55mg/dl)

3. Triglycerides:

**Optimal** (Target): <1.7 mmol/l (< 150 mg/dl)

4. Non HDL-cholesterol:

**Optimal** (Target): < 3.2 mmol/l (< 130 mg/dl)

### ii. FREQUENCY OF MEASUREMENT:

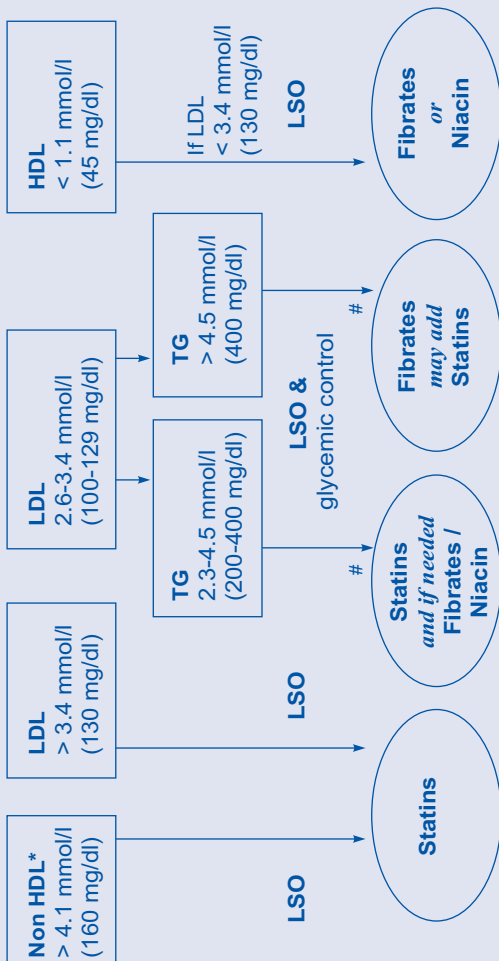
yearly if lipids are within target;  
every 3 months if above target.



## APPENDIX

- ▶ the first priority is to lower LDL-cholesterol
- ▶ for hypertriglyceridemia the initial approach is to improve glycemic control along with behavioural changes (increased physical activity, restricted alcohol consumption); in case of severe hypertriglyceridemia ( $>1000$  mg/dl), severe dietary fat restriction is necessary
- ▶ increased physical exercise and smoking cessation can raise HDL-cholesterol levels
- ▶ if the target is not achieved with LSO, pharmacotherapy should be started
- ▶ if statins and/or fibrates are used - follow liver function test and CPK at 2 and 6 months after starting treatment; combined use of fibrates and statins is a relative contraindication in renal failure
- ▶ although niacin is effective in increasing HDL-cholesterol levels, it should be used with caution due to risk of increase in blood glucose
- ▶ the continuation of statins with fibrates should be used with caution due to increase risk of rhabdomyolysis; repeated measurements of CPK and of myoglobin are recommended

### iii. ALGORITHM OF MANAGEMENT



Adapted from ADA recommendations 2002 and Int. Expert Group on HDL: 2003

- Test lipids 2 times before starting drugs: control lipids at 6 weeks after starting drugs (and change the therapy accordingly) and at 3-6 months after the achievement of objectives
- Obtain liver function test before starting statins (in order to exclude liver disease)

\* For patients with high triglycerides > 300mg/dl



## APPENDIX

▶ **BMI** = Weight(kg)/Height(m<sup>2</sup>)

## C. WEIGHT CONTROL

### i. OBJECTIVES:

<u>Optimal:</u>	BMI	< 25 kg/m <sup>2</sup>
	Waist:	men: < 94 cm women: < 80 cm

#### Goals in obese individuals:

##### *Short-term goals:*

- moderate weight loss of 5-10% in
- 3-6 months, followed by
- new weight maintenance for 6-9 months

##### *Long-term goals:*

- successive cycles "weight loss-weight maintenance" until a reasonable weight is achieved
- long term maintenance of reasonable weight
- prevention of weight regain

### ii. FREQUENCY OF MEASUREMENT:

of weight and waist:  
each regular diabetes visit



- ▶ Drugs should never be used without LSO

- ▶ **Sibutramine**

- mechanism of action: blocks the reuptake of neurotransmitters: dopamine, norepinephrine, serotonin (centrally acting appetite suppressant)
- dosing: once daily (usually in the morning)- starting dose: 10 mg
- most common side effects: dry mouth, anorexia, constipation, insomnia, increased blood pressure, palpitations
- can be given continuously for 2 years

- ▶ **Orlistat**

- mechanism of action: prevents the absorption of dietary fat by lipase inhibition
- dosing: 120 mg three times daily (one hour after/during a meal containing fat) multivitamins containing fat-soluble vitamins should be taken during treatment with Orlistat
- most common side effects: gastrointestinal (abdominal discomfort/pain, flatulence, fatty/oily stools)

### iii. ALGORITHM OF MANAGEMENT

Are the objectives achieved?



- ➔ **LIFESTYLE OPTIMIZATION** (see above) and **behavioral changes:** always recommended low energy containing diet (i.e. below 1200 kcal)
- ➔ **PHARMACOTHERAPY:** Sibutramine  
Orlistat
- ➔ **GASTRIC REDUCTION SURGERY:** only for very high risk patients with BMI > 40 kg/m<sup>2</sup> (or > 35 kg/m<sup>2</sup> if comorbidities are present) and failure of pharmacological therapy
- ➔ **THERAPEUTIC EDUCATION** and **BEHAVIORAL THERAPY:** are compulsory to implement lifestyle changes and pharmacological therapy



# 5. MANAGEMENT OF SPECIAL SITUATIONS

## i. DIABETIC KETOACIDOSIS

- **Fluid and Electrolyte Replacement**
  - Based on the degree of dehydration and the patient's cardiovascular status.
  - Most adults require IV fluid administration with normal (0.9%) or half normal (0.45%) saline.
  - One liter of fluid should be given per hour for the first 2 hours; the rate can be decreased to 500 ml per hour when signs of intravascular volume depletion have subsided.
  - IV fluids are continued until intravascular volume has been fully restored.
  - When glucose reaches 250 mg/dl, shift to glucose containing solution.
- **Insulin Therapy**
  - A low dose of regular insulin can be administered via IV infusion at a rate of approximately 5 units per hour.
  - If a 10% decrease in glucose concentration is not observed after 2 hours, the infusion rate should be doubled to 10 units per hour.
  - When insulin infusion can be discontinued, intermediate or long acting insulin can be started.
- **Potassium Replacement**
  - Usually is necessary after fluid and insulin therapy have been started because all modes of therapy reduce (K)
  - The goal is to maintain the serum (K) within the normal range.
- **Phosphate Replacement**
  - Phosphate levels should be measured initially, may use potassium phosphate for replacement if PO<sub>4</sub> is in the low or low-normal range.



# 5. MANAGEMENT OF SPECIAL SITUATIONS

- **Bicarbonate Therapy**

- Not necessary for most patients but may be considered under certain circumstances, such as for patients with life-threatening hyperkalemia, lactic acidosis, or severe acidosis (pH < 7.2) with shock that does not respond to fluid replacement.

## ii. **HYPERSMOLAR HYPERGLYCEMIC NONKETOTIC SYNDROME**

- The primary treatment goal is to restore circulating plasma volume and correct electrolyte deficits.
- The precipitating event should be identified and corrected.
- Other goals similar to those described for the treatment of DKA should be instituted, including providing adequate insulin to restore and maintain normal glucose metabolism.
- Cardiovascular status should be monitored closely and frequently during fluid replacement to avoid precipitating congestive heart failure.
- Insulin is administered in the same manner as for patients with DKA. At glucose concentrations of 250 mg/dl, the rate of insulin infusion should be decreased to 2-3 U/h and dextrose should be added to the IV fluid.
- Potassium replacement follows the same guidelines as for DKA, with consideration of the special conditions of patients with HHNS (underlying renal disease is associated with lower urinary potassium losses, pre-existing heart disease is associated with greater susceptibility to the effects of potassium).
- Bicarbonate therapy is contraindicated.
- Phosphate replacement follows the same guidelines as for DKA, with consideration of the effect of phosphate on underlying renal disease.



## APPENDIX

# 6. DIABETES AND RAMADAN FASTING

## **i. PATIENTS WHO SHOULD NOT FAST**

- Severe hypoglycemia within the last 3 months prior to Ramadan
- Patient with a history of recurrent hypoglycemia
- Patients with hypoglycemia unawareness
- Ketoacidosis within the last 3 months prior to Ramadan
- Uncontrolled Type 1 diabetes
- Hyperosmolar hyperglycemic coma within the previous 3 months
- Pregnancy
- Patients on chronic dialysis
- Patients living alone, treated with insulin or sulfonylureas
- Acute illness



# 6 DIABETES AND RAMADAN FASTING

## ii. SUGGESTED TREATMENT REGIMENS

Before Ramadan	During Ramadan
a. Patients on diet + exercise	Ensure adequate fluid intake
b. Patients on oral agents: <ul style="list-style-type: none"><li>• Metformin</li><li>• TZDs, pioglitazone or rosiglitazone once daily</li><li>• Sulfonylureas once a day, e.g. glimepiride, gliclazide MR</li><li>• Sulfonylureas twice a day, e.g. glibenclamide or gliclazide</li><li>• Insulin secretagogues e.g. metiglinides</li></ul>	<p>Metformin at Iftar and Suhur</p> <p>No change needed</p> <p>Dose should be given before the Iftar and Suhur</p> <p>Half the usual morning dose at Suhur and full dose at Iftar</p> <p>Before Iftar and Suhur</p>
c. Patients on Insulin: <ul style="list-style-type: none"><li>• 70/30 premixed insulin twice daily</li></ul>	<p>Ensure adequate fluid intake</p> <ul style="list-style-type: none"><li>- Use the usual morning dose at Iftar and half the usual evening dose at Suhur</li><li>- Use intermediate / long acting insulin + regular / rapid acting insulin before meal</li></ul>



## APPENDIX

- ▶ In case of aspirin-intolerance, other agents (like clopidogrel - 75 mg/day) may be considered as a substitute

**ASPIRIN THERAPY**

Use aspirin:

- for secondary prevention:

- history of myocardial infarction
- angina
- vascular bypass procedure
- stroke or transient ischemic attack
- peripheral vascular disease
- claudication

- consider as primary prevention:

– in diabetic subjects > 50 years

– in diabetic subjects with > 2 of the following:

- age > 30 years
- family history of coronary heart disease
- cigarette smoking
- hypertension
- dyslipidemia
- albuminuria

Dosage: use 75-100 mg/day - enteric coated aspirin

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*Lilly*