DIABETES MELLITUS

WHEN TO SUSPECT/RECOGNISE

Case definition:

Suspect /probable case of Diabetes mellitus (for level 1 & 2 facility) -The diagnosis of diabetes depends upon the presentation . The different types of diabetes presents as

Type 1 diabetes: This type of diabetes is associated with the destruction of insulin producing beta cells in the pancreas. This diabetes will require insulin for survival; this diabetes usually affects children and young adults. The presentation is acute and is often mistaken for an acute infective illness in children. This should be suspected when a child or young adult presents with fever, pain abdomen, polyuria and weight loss usually following a short febrile illness.

Type 2 diabetes: This is the common form of diabetes which is seen in adults. The symptomatic patients will present with polyuria ,polydipsia and weight loss . There may be an increase in infections such as skin infection, pruritus vulvae in women. Alternatively the asymptomatic patients are diagnosed to have diabetes when they present with high plasma glucose when the blood test is done for some other illness or screening.

Other less common types of diabetes are due to pancreatic disorders and fibrocalculous type of diabetes seen more commonly in southern states

Gestational diabetes : Diabetes detected with hyperglycemia during pregnancy.

Confirmed case of Diabetes mellitus (for level 2,3&4 facility)- A suspect case with any of the following criterion . The diagnosis of diabetes can be established by using any of the following criteria.

a) Fasting plasma glucose ≥7.0mmol/l (126mg/dl) after an overnight fast. This should be confirmed by repeat test.

b) Random plasma glucose (RPG) > 200 mg/dl and symptoms of diabetes (polyuria, polydipsia, ketoacidosis, or unexplained weight loss.)

c) Two hour plasma glucose ≥11.1mmol/l (200mg/dl) following a 75 gram glucose or 1.75 gm/kg weight in children.

EPIDEMIOLOGY OF THE CONDITION IN OUR COUNTRY

India has the largest number of diabetes patients in the world. India also has the dubious distinction of being termed the “diabetes capital of the world. The data published by the International Diabetes federation in the year 2006 the number of people with type 2 diabetes in India is around 40.9 million and this is expected to rise to 69.9 million by 2025. The more disturbing trend is the shift in age of onset of diabetes to a younger age.

Diabetes is defined as a metabolic disorder characterized by presence of hyperglycemia due to defective insulin secretion, insulin action or both. The chronic hyperglycemia is associated with significant long term sequels, particularly damage or dysfunction of various organs especially the kidneys, eyes, nerves, heart and blood vessels.

The present classification of diabetes is based on the etiology of diabetes. The classification of diabetes is

1. Type 1 diabetes mellitus (beta-cell destruction, usually leading to absolute insulin deficiency)
2. Type 2 diabetes mellitus (may range from predominantly insulin resistance with relative insulin deficiency to predominantly secretory defect with insulin resistance)
3. Gestational diabetes mellitus (onset or recognition of glucose intolerance in pregnancy)
4. Other specific types
    - Genetic defects of beta-cell function (maturity onset diabetes of young).
    - Genetic defects in insulin action.
    - Type A insulin resistance, Leprechaunism,RabsonMendenhall syndrome.

- Diseases of the endocrine pancreas
- Pancreatitis, Trauma, pancreatectomy, Cystic fibrosis, Hemochromatosis, Fibrocalculous pancreatopathy
- Endocrinopathies
- Acromegaly, Cushing's syndrome, Pheochromocytoma and Hyperthyroidism
- Drug or chemical induced, for e.g. Pentamidine, Nicotinic acid , Glucocorticoids, Diazoxide, Beta-adrenergic agonists and Thiazide diuretics.

DIAGNOSTIC CRITERIA, INVESTIGATIONS TREATMENT & REFERRAL CRITERIA

LEVEL 1: AT SOLO PHYSICIANS CLINIC

Clinical doagnosis : Essentially as described for a suspect case .Type 1 diabetes is suspected when a child or young adult presents with fever, pain abdomen polyuria and weight loss usually following a short febrile illness . Type 2 diabetes is usually in an adult who presents with polyuria,polydipsia and weight loss . There may be an increase in infections such as skin infection and pruritus vulvae in women. Diabetes may also be diagnosed during screening for some other disorder.

Investigation: The diagnosis would be clinical. However laboratory and other investigation will have to be done outside

- The diagnosis will be made by the measurement of the plasma glucose. Diagnostic criteria are highlighted for the 'confirmed case'.
- The urine should be examined for glucose, protein, ketone bodies and microscopic examiantion done for presence of pus cells.
- The patient should be referred to Level 3 for the following investigations to asses target organ involvement, degree of glycemic control and comorbidities. These investigations are should be done twice a year:
- Glycosylated hemaglobin (HbA1C) for assesing the degree of control and monitoring treatment.
- Fasting lipid profile (Total cholesterol, triglycerides. Low density lipoprotein and high density lipoprotein)
- Serum electrolytes
- Blood urea and serum creatitinine
- Microalbumin and creatinine clearance
- Electrocardiography
- X Ray chest postero anterior view
- Fundus examination

Treatment

The treatment of diabetes is a combination of nutritional therapy, exercise and pharmacotherapy. At all levels of care, all the components of treatment have to be emphasized.

Nutritional Composition of the Diet: The nutrition should contain carbohydrate, fats and protein intake in the right amount. The caloric intake should be an average 30 Kcal /kg body weight .

- Carbohydrate intake: It is recommended that the carbohydrate intake is 55 to 60% of the total caloric intake.
- Fat intake: Normal intake of fat should be limited to a maximum of 30% of the total caloric intake. In patients with type 2 diabetes, weight is usually a factor in developing a treatment program. In overweight persons or those with dyslipidemia, fat intake should be reduced to as low as 15% of the caloric intake.
- Protein intake: Intake of protein should be 10 to 20% of the total daily caloric intake.

Physical Activity: Physical activity as a therapeutic modality in patients with diabetes mellitus is advised to a patient of both Type 1 and Type 2 diabetes. Exercise can also create a general sense of well-being.

Pharmacotherapy: The pharmacotherapy treatment of diabetes depends upon the type of diabetes. The treatment of type 1 diabetes and gestational diabetes is insulin. Type 1 diabetes requires life long insulin replacement. The following are the insulin preparations that can be started at level 3 & 4 and continued/ monitored at level 1 & 2:

- Rapid acting insulin: The rapid acting insulin preparations are regular insulin, insulin lispro and insulin aspart. Regular insulin can be administered by subcutaneous and intravenous route in diabetes related emergencies.
- Intermediate acting insulin. The intermediate acting insulin are NPH (isophane) and lente insulin. These get absorbed slowly and the total duration of action is 12 to 16 hours.
- Long acting insulin: The long acting insulins are basal insulins . The two insulins available are insulin glargine and insulin detremir. There total duration of action is for 24 hours
- Premixed insulin therapy: Rapid acting insulin such as plain insulin is mixed with NPH insulin in a concentration of (30/70) or (50/50) . These can be used in patients who are unable to mix insulin.
- Insulin delivery: The insulin is delivered in the subcutaneous space by using insulin syringes or insulin pens. The sites for injection are the anterior abdominal wall, thighs ,buttocks and arms are the preferred sites for subcutaneous injection

The initial insulin dosage is 0.5-1 unit /kg in patients of Type 1 diabetes. The treatment is started with the lower dose and titrated to a higher dose. The insulin is first started as three injections of regular insulin, later making up two - third of the insulin dose and the remaining one - third insulin is given at bedtime as a long acting or intermediate acting insulin .

Oral drug Therapy: The number of drugs available for treatment of Type 2 diabetes are many & the choice of oral drug therapy is extremely complex. The physician must use clinical judgment about the best combination of drugs for the patient with diabetes. This discretion is particularly important in the long-term treatment of a chronic disease that is unrelenting and progressive and in which the response to therapy changes over time.

Sulphonylureas : The sulphonylureas stimulate insulin secretion by the beta cell of pancreas. They also decrease hepatic glucose production; may improve insulin sensitivity at the receptor. They include

- Glimepiride (Tablet size 1 mg,2 mg ,4 mg) daily dose 1-6 mg once a day
- Glipizide (5 mg, 10 mg) daily dose 2.5-20 mg in 2-doses
- Gliblenclamide (1.25 mg 2.5 mg 5 mg) daily dose2.5-20 in 1-2 daily dose
- Gliclazide (40, 80 mg) daily dose is 40-240 mg in two doses

Biguanides : Metformin is a biguanide that has insulin sensitizing properties. It may be used as mono therapy or in combination with other classes of agents or insulin. It has to be avoided in patients prone to metabolic acidosis or hypoxic states, including renal failure, renal dysfunction with serum creatinine >1.5 mg/dl, liver failure, congestive heart failure requiring pharmacologic intervention, diabetic ketoacidosis and major surgical procedure. Metformin is available in tablet size 500 mg and 850 mg or an extended release preparation of 500 mg /1gm .The total daily dose is 500 mg-2gm /day

α-Glucosidase Inhibitors : These agents act locally in small intestine by inhibiting α-glucosidase enzymes; this action slows digestion of ingested carbohydrates, delays glucose absorption, and reduces the increase in postprandial blood glucose. The potential adverse effects are flatulence, abdominal bloating. They are contraindicated in patients with gastrointestinal disorders like inflammatory bowel disease, chronic ulceration, malabsorption, or partial intestinal obstruction. The drugs available are

- Acarbose 25-50 mg with major meals
- Miglitol 25 mg with major meals

Thiazolidinediones: They enhance tissue sensitivity to insulin in muscle through activation of intracellular receptors. These drugs take several weeks for onset of action and several months for “peak” action. They require the presence of insulin for action. These drugs cause increase in weight and increase of subcutaneous fat. They are contraindicated in people with congestive heart failure and liver disease. They require monitoring of the liver enzymes every 6 months. These drugs can be used as monotherapy or in combination with sulfonylureas and metformin. The drugs available are.

- Rosiglitazone (2-8mg daily)
- Pioglitazone (15-30 mg daily)

Complication of Diabetes

The complications of diabetes are involvement of major vessels causing coronary artery disease, cerbrovascular disease and peripheral arterial disease . The involvement of small vessels causes retinopathy, diabetic nephropathy and diabetic neuropathy. The patients of diabetes are more prone to infection. On the first visit a detailed history should be taken and a detailed clinical examination and preliminary test should be done. The examination should be done for blood pressure, peripheral pulse, examination of the nervous system . The eye examination should include assessment of visual acuity, cataract and fundus examination. . The investigation listed above will give an assessment of the complication.

The sequence of Investigation/ Treatment is given as algorithm (Attached after 'suggested reading')

Referral criteria

- Diabetes with pregnancy
- Diabetes with complication such as diabetic foot, coronary artery disease, anemia and edema suggesting diabetic renal disease at initial evaluation
- If uncontrolled hyperglycemia on oral drugs
- At least once a year for a detail assessment of the target organ involvement and investigation.
- Patients with severe infection , marked weight loss and breathlessness

LEVEL 2 : 6-10 BEDDED PRIMARY HEALTH CENTER

Clinical diagnosis: same as level 1 for a fresh case reporting directly .

Investigation : same as level 1 for a fresh case reporting directly

Treatment :

- same as level 1
- as given in the algorithm

Acute complications at level 1 & 2

The acute complication are hypoglycemia and hyperglycemic ketoacidosis are common which have to be diagnosed and managed at all levels

Hypoglycemia in patients of Diabetes: Usually associated with oral anti diabetic drugs such as sulphonylureas and insulin. It can also be precipitated by drugs such as quinine , fever and fasting. The symptoms are palpitation, anxiety, hunger and sweating . The clinical examination will demonstrate tachycardia and hypertension. The earliest symptom will start when the blood glucose is less than 70 mg /dl . If the blood glucose drops to less than 40 mg /dl the patient may develop confusion, seizures and coma .

Emergency treatment of hypoglycemia: At the earliest symptom the blood glucose can be recorded by a glucometer and oral sweets / sugar can be given in a conscious patient . In an unconscious patient administer 50/100 ml of 50% dextrose followed by a 10 % dextrose infusion to keep the blood glucose more than 100 mg% . In a patient who had hypoglycemia following oral drugs a frequent monitoring of blood glucose should be done.

Diabetic ketoacidosis : once diagnosed should be referred to level 3 after the initial treatment.This may occur due to the cessation of insulin , infection, surgery , stress and acute myocardial infarction . This is generally seen in patients of Type 1 diabetes but can also be seen in Type 2 diabetes patients. The symptoms are nausea, vomiting, pain abdomen, thirst, polyuria and altered sensorium. On clinical examination the findings are of tachycardia, Kaussmaul's breathing and patients may come in a comatose state. Investigation show hyperglycemia, ketone bodies in the urine, metabolic acidosis (pH 6.8-7.3), bicarbonates < 10 mmol/L, serum sodium raised/normal and there is a decrease in total body K+.

Emergency treatment of Diabetic ketoacidosis

- Regular insulin 10 units IV stat , followed by an iv infusion at the rate of 0.1unit/Kg /hour
- Intravenous fluid initially 2-3 L/normal saline over 1-3 hours followed by 0.45 % saline at 150-300 ml/hour.
- When plasma glucose comes under 250mg/dl, 5% dextrose should be started with 0.45% normal saline at 100-200 ml /hour.
- In severe acidosis with pH < 7, 50-100 ml NaHCO3 in 250 ml of 0.45 % saline over 2 hours till the bicarbonate is > 10 mmol/L.
- K+ replacement is started when the serum K+ is <4.5 meq/L, at the rate of 10 meq/ hour.
- Appropriate antibiotics to treat the infection.
- Start treatment of the precipitating cause.

Referral criteria

- Same as level 1
- No response to the emergency treatment

LEVEL 3: AT 30-100 BEDDED COMMUNITY HEALTH CARE CENTRE

Clinical Diagnosis : At this center there is availability of a physician, a surgeon, a specialist in obstetrics and gynecology and an anesthetists . There is a facility for treatment of indoor patients. The physician along with the surgeon and the obstetrician and a health care worker should form the diabetes care team . This team can carry out the following activities .

- A complete clinical examination and recording of the complications at the time of diagnosis of diabetes .
- Plan nutrition therapy and pharmacotherapy to be followed at the lower centers.
- Care of the complication such as diabetic foot, treatment of severe hyperglycemia, treatment of hyperglycemic emergencies such as diabetic ketoacidosis.
- Screening and treatment of the pregnant women with gestational diabetes.

Investigations:

The following investigation should be done to confirm diagnosis and assessment of severity of complication.

The patinet should be referred to Level 3. These investigations are :

- Glycosylated hemaglobin (HbA1C) for assesing the degree of control and monitoring treatment.
- Fasting lipid profile (Total cholesterol, triglycerides. Low density lipoprotein and high density lipoprotein)
- Serum electrolytes
- Blood urea and serum creatinine
- Microalbumin and creatinine clearance
- Electrocardiography
- X Ray chest postero anterior view
- Fundus examination

Treatment :

Same as level 1& 2

Treatment of emergency complications as mentioned earlier

Referral criteria

If no signs of improvement in 5 days or complications not controlled by specialist at the center, refer to the next level.

- The patient who has the following complication
- Coronary artery disease
- Diabetic retinopathy
- Peripheral artery disease requiring intervention
- Diabetic nephropathy requiring assessment by nephrologists and renal replacement therapy
- Diabetic foot with severe infection
- Diabetic foot amputation requiring artificial limb

LEVEL 4: AT100 OR MORE BEDDED DISTRICT HOSPITAL

Clinical Diagnosis : Usually severe/ complicated cases referred from level 3**.** Diagnostic criteria same as in earlier level.

Investigations:

Same as level 3 for the fresh case reporting directly

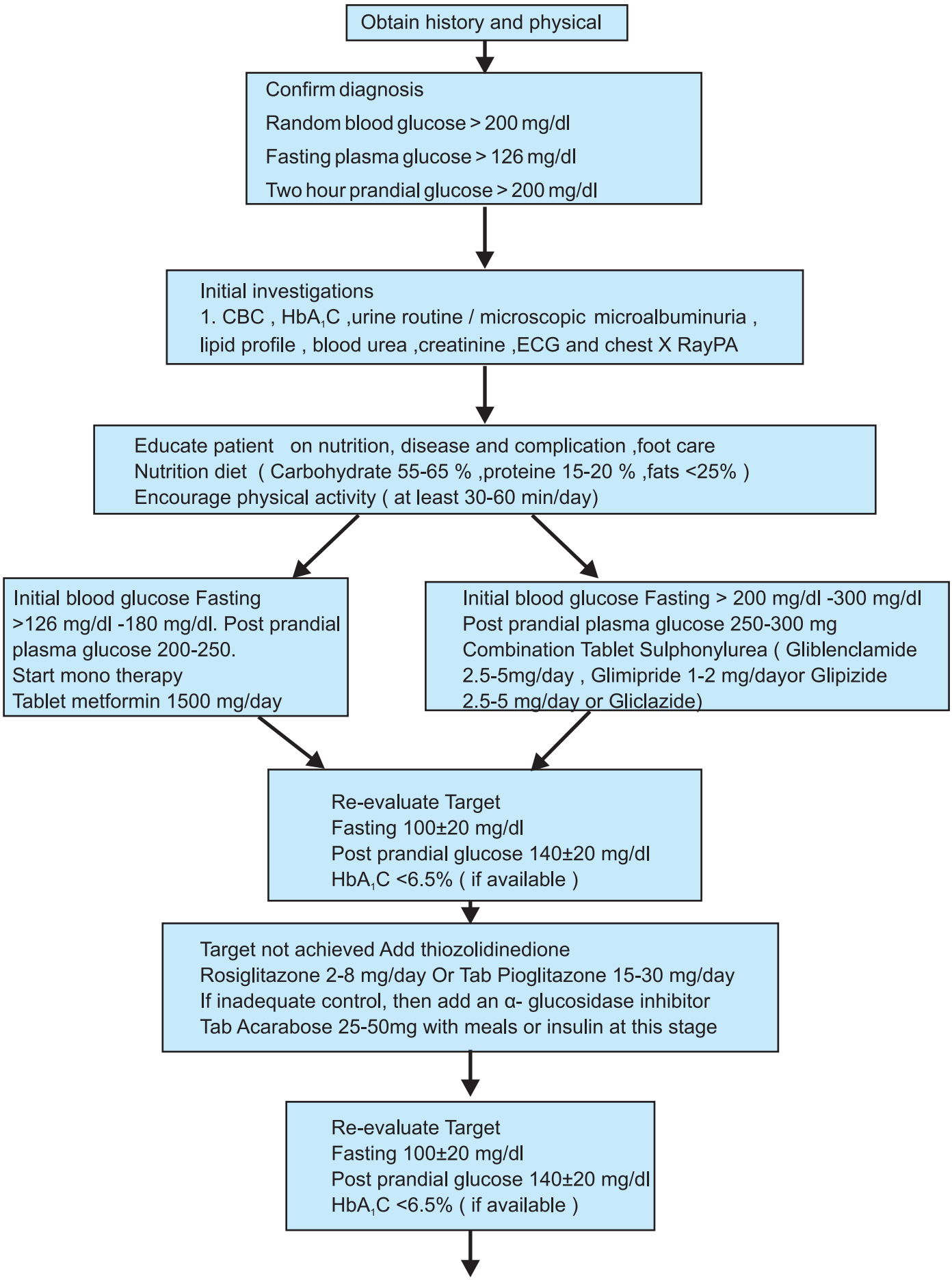
Treatment :

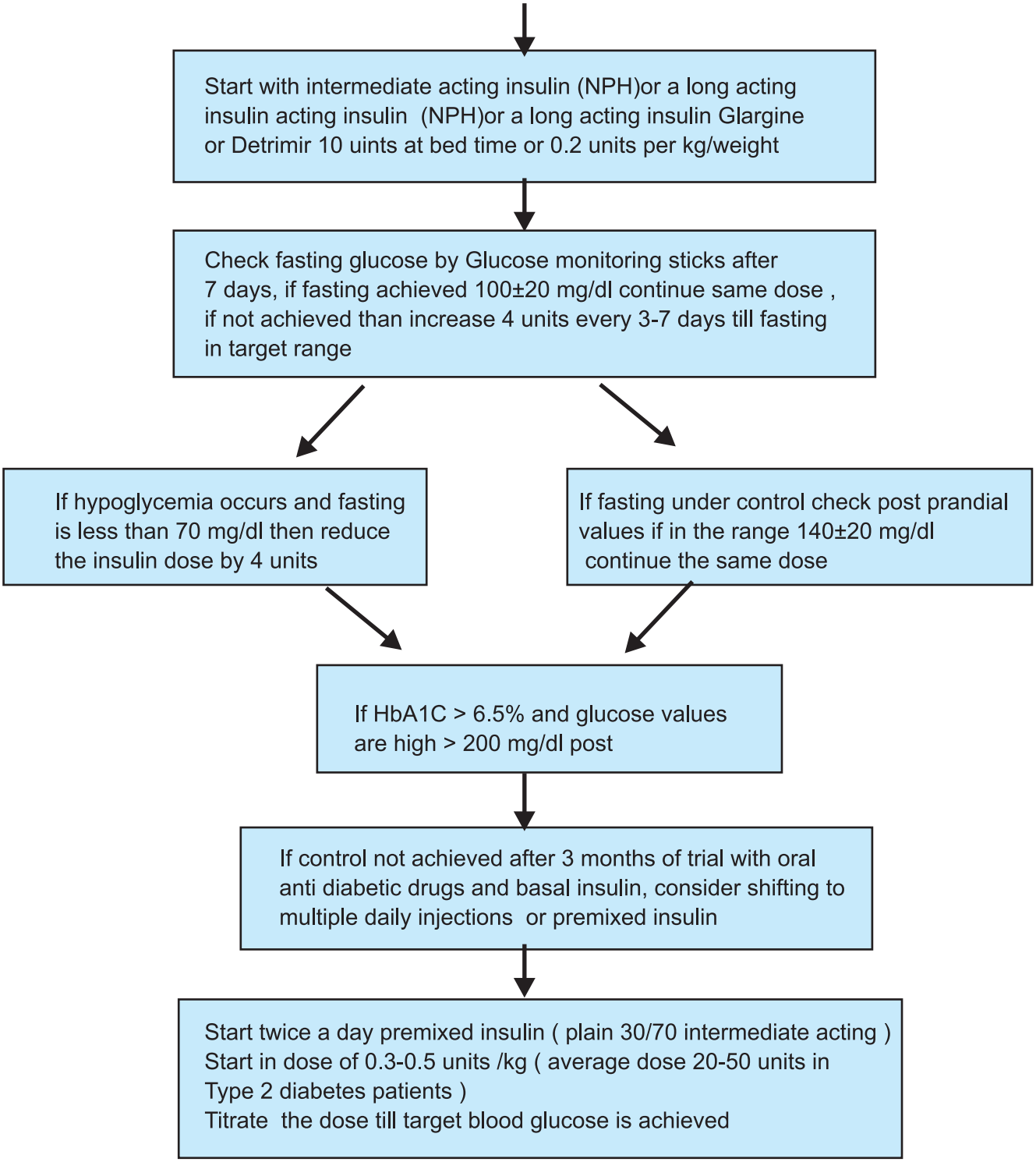
- A detailed assessment of the complications preferably by an endocrinologist.
- Every year the patient should be evaluated by an eye specialist for retinal involvement. The patients should be treated for diabetic retinopathy.
- The patients with renal failure should be evaluated by a nephrologists, patients with coronary artery disease should be referred to the cardiologist.

SUGGESTED READING

1. Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy. A consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes .Diabetes care 2006; 29: 1963-1972
2. Wyne KL, Drexler AJ, Miller JL, Bell DS, Braunstein S, Nuckolls JG. Type 2 diabetes management A postgraduate medicine special report. Postgrad Med. 2003; 5 : 63-72.
3. Sara Meltzer, MD; Lawrence Leiter, MD; Denis Daneman, MD; Hertzel C. Gerstein, MD, MSc; David Lau, MD, PhD; Sora Ludwig, MD; Jean-François Yale, MD; Bernard Zinman, MD; Donna Lillie, RN, BA; Steering and Expert Committees*1998 clinical practice guidelines for the management of diabetes in Canada .CMAJ 1998 ; 20:10; 159 (8 Suppl) 1-33
4. The American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus .Endocrine practice 2007 ;13 (suppl 1):1-66
5. Medical Guidelines for the Management of Diabetes Mellitus: The AACE System of Intensive Diabetes Self-Management Endocrine practice 2002; 8) (Suppl. 1)1-44
6. G C Chan Type 2 diabetes mellitus with hypertension at primary healthcare level in Malaysia: are they managed according to guidelines? Singapore Med J 2005; 46 :(3):127-131

ALGORITHM FOR TREATEMT OF PATIENTS OF TYPE 2 DIABETES




Start with intermediate acting insulin (NPH)or a long acting insulin acting insulin (NPH)or a long acting insulin Glargine or Detrimir 10 uints at bed time or 0.2 units per kg/weight
Check fasting glucose by Glucose monitoring sticks after 7 days, if fasting achieved 100±20 mg/dl continue same dose , if not achieved than increase 4 units every 3-7 days till fasting in target range
If hypoglycemia occurs and fasting is less than 70 mg/dl then reduce the insulin dose by 4 units
If fasting under control check post prandial values if in the range 140±20 mg/dl continue the same dose
If HbA1C > 6.5% and glucose values are high > 200 mg/dl post
If control not achieved after 3 months of trial with oral anti diabetic drugs and basal insulin, consider shifting to multiple daily injections or premixed insulin
Start twice a day premixed insulin (plain 30/70 intermediate acting)
Start in dose of 0.3-0.5 units /kg (average dose 20-50 units in Type 2 diabetes patients)
Titrate the dose till target blood glucose is achieved