Diabetes mellitus DM.

CHRONIC COMPLICATIONS

Chronic complications include ***microvascular complications*** (*nephropathy*, retinopathy, *and neuropathy*) and ***macrovascular or cardiovascular complications*** (*hypertension, coronary artery disease, peripheral vascular disease, and cerebrovascular disease*).

MICROVASCULAR COMPLICATIONS

The incidence of microvascular complications is significantly higher in patients with T1DM than in those with T2DM.

Nephropathy

Diabetic nephropathy is the most common cause of ESRD in developed countries (about 30% of cases). About 20% to 30% of people with T1DM and T2DM develop nephropathy, and the incidence increases with duration of diabetes.

Fewer people with T2DM than with T1DM progress to ESRD (20%versus 75%, respectively, after 20 years).

Initially, increased glomerular filtration rate (GFR) and renal blood flow occur in all patients and are not associated with any histologic changes. This condition progresses to glomerular hypertrophy, renal enlargement, expansion of the mesangial matrix, and thickening of the glomerular basement membrane, resulting in glomerulosclerosis.

Subsequently, the GFR returns to normal, with an associated increase in intraglomerular pressure and the appearance of microalbuminuria (20 to 200 mcg per minute, 30 to 300 mg per 24 hours) 10 to 15 years after the diagnosis of diabetes (present in 30% of middle-aged patients with T1DM or T2DM).

This incipient or preclinical diabetic nephropathy is followed by a decline in GFR as the albumin excretion rate increases.

By about 15 years after the onset of diabetes, macroalbuminuria (>200 mcg per minute, >300 mg per 24 hours; dipstick positive) is generally present. Continued blood pressure control is essential, and some dietary protein restriction (0.6 to 0.8 g/kg per day) is probably helpful, but meticulous blood glucose control is unlikely to prevent the inexorable progression of overt diabetic nephropathy to ESRD. The rate of decline in GFR, however, may be slowed, but not halted, by blood pressure and glucose control with protein restriction.

Measurement of serum creatinine is an inaccurate guide to the degree of GFR impairment. Within 5 years of the appearance of macroalbuminuria, GFR will have declined by 50% in about 50% of patients; within a further 3 to 4 years, one half of these patients will have ESRD. Dialysis (hemoperitoneal or peritoneal) or renal transplantation is initiated when the GFR is less than 15 mL per minute ***(serum creatinine ≥10 mg/dL)***.

Screening for proteinuria should be performed annually in all patients, starting at the time of diagnosis in patients with T2DM and 5 years after the diagnosis in patients with T1DM.

Management

The optimal therapy for diabetic nephropathy is prevention by control of glycemia. As part of comprehensive diabetes care, microalbuminuria should be detected at an early stage when effective therapies can be instituted.

The recommended strategy for detecting microalbuminuria includes annual measurement of the serum creatinine to estimate GFR.

Interventions effective in slowing progression from microalbuminuria to macro albuminuria include (1) normalization of glycaemia, (2) strict blood pressure control, and (3) administration of ACE inhibitors or ARBs. Dyslipidemia should also be treated.

Once macro albuminuria exists, it is unclear whether improved glycemic control will slow progression of renal disease. During the phase of declining renal function, insulin requirements may fall as the kidney is a site of insulin degradation. Furthermore, many glucose lowering medications (sulfonylureas and metformin) are contraindicated in advanced renal insufficiency.

Many individuals with type 1 or type 2 DM develop hypertension. Numerous studies in both type 1 and type 2 DM demonstrate the effectiveness of strict blood pressure control in reducing albumin excretion and slowing the decline in renal function. Blood pressure should be maintained at <130/80 mmHg in diabetic individuals without proteinuria. A slightly lower blood pressure (125/75) should be considered for individuals with microalbuminuria or macro albuminuria.

Either ACE inhibitors or ARBs should be used to reduce the progression from microalbuminuria to macro albuminuria and the associated decline in GFR that accompanies macro albuminuria in individuals with type 1 or type 2 DM.

After 2–3 months of therapy in patients with microalbuminuria, the drug dose is increased until either the microalbuminuria disappears or the maximum dose is reached. If use of either ACE inhibitors or ARBs is not possible, then calcium channel blockers (nondihydropyridine class), beta blockers, or diuretics should be used. However, their efficacy in slowing the fall in the GFR is not proven. Blood pressure control with any agent is extremely important, but a drug-specific benefit in diabetic nephropathy, independent of blood pressure control, has been shown only for ACE inhibitors and ARBs in patients with DM.

The ADA suggests modest restriction of protein intake in diabetic individuals with microalbuminuria (0.8 g/kg per d) or macro albuminuria (<0.8 g/kg per d, which is the adult recommended daily allowance, or ∼10% of the daily caloric intake).

Nephrology consultation should be considered when the estimated GFR is <60 mL/min per 1.743 m2. Once macro albuminuria ensues, the likelihood of ESRD is very high. As compared to nondiabetic individuals, hemodialysis in patients with DM is associated with more frequent complications, such as hypotension (due to autonomic neuropathy or loss of reflex tachycardia),more difficult vascular access, and accelerated progression of retinopathy. Survival after the onset of ESRD is shorter in the diabetic population compared to nondiabetics with similar clinical features. Atherosclerosis is the leading cause of death in diabetic individuals on dialysis,and hyperlipidemia should be treated aggressively.

Renal transplantation from a living-related donor is the preferred therapy but requires chronic immunosuppression.

Retinopathy

The presence and severity of diabetic retinopathy are related to age at diagnosis and the duration of diabetes; 100% of patients with T1DM and 60% to 80% of those with T2DM are affected by 20 years. Retinopathy is the most common cause of blindness in persons between the ages of 20 and 74 years in the developed world. About 25% of patients with T2DM may already have evidence of retinopathy at the time of diagnosis. Diabetic retinopathy is a progressive condition of increasing severity, accelerated by poor glycemic control.

Clinical features of diabetic retinopathy

- Microaneurysms .
- Retinal haemorrhages (dot and blot) .
- Exudates .
- Cotton wool spots .
- Venous changes.
- Neovascularisation (retina and iris) .
- Pre-retinal/subhyaloid haemorrhage .
- Vitreous haemorrhage .
- Fibrosis/gliosis .

Annual dilated funduscopic examination by an ophthalmologist should be performed in all patients with diabetes, starting 5 years after diagnosis in patients with T1DM.

Improvement of glycemic control may transiently worsen retinopathy, before ultimately improving it over a longer period.

Other causes of visual loss in people with diabetes

Around 50% of visual loss in people with type 2 diabetes results from causes other than diabetic retinopathy. These include cataract, age-related macular degeneration, retinal vein occlusion, retinal arterial occlusion, non-arteritic ischaemic optic neuropathy and glaucoma. Some of these conditions are to be expected in this group as they relate to cardiovascular risk factors (e.g. hypertension, hyperlipidaemia and smoking), all of which are prevalent in people with type 2 diabetes.

Neuropathy

Occurring in up to 70% of people with diabetes, any part of the peripheral or autonomic nervous system may be affected.

Peripheral polyneuropathy occurs most commonly, which usually presents as a bilaterally symmetrical, distal, primarily sensory (with or without motor) polyneuropathy, with a glove-and-stocking distribution. Pain, numbness, hyperesthesias, and paresthesias progress to sensory loss.

This condition, together with loss of proprioception, leads to an abnormal gait, with repeated trauma and fractures of the tarsal bones, sometimes resulting in the development of Charcot joints. These changes lead to abnormal pressures in the feet that, together with the soft tissue atrophy related to peripheral arterial insufficiency, result in foot ulcers that may progress to osteomyelitis and gangrene.

Detailed, regular neurologic examination of all patients is essential, to elicit the early loss of light touch, reflexes, and vibratory sensation. Painful neuropathies are difficult to treat, and, although they are self-limited, they may persist for years.
Analgesia should start with aspirin, acetaminophen, and nonsteroidal anti-inflammatory agents before codeine and addictive drugs such as pentazocine or narcotics are prescribed.
Anticonvulsants, including phenytoin, carbamazepine, gabapentin, and pregabalin, as well as the antidepressant amitriptyline, may provide moderate relief.
Mononeuropathies usually present acutely, may involve any nerve in the body, and are generally self-limiting. The cranial nerves most commonly involved are the third, sixth, and fourth, in that order.
Radiculopathies are self-limited painful sensory syndromes of one or more spinal nerves, usually of the chest or abdomen.
Diabetic amyotrophy causing muscle atrophy and weakness commonly involves the anterior thigh muscles and pelvic girdle and may also be self-limited, resolving after several months.
Autonomic neuropathy of the sympathetic and/or parasympathetic systems has numerous presentations. Most commonly involved is the gastrointestinal tract, with gastric dysmotility (30% to 50%), gastroparesis, and small bowel bacterial overgrowth, responsible for delayed gastric emptying, early satiety, postprandial nausea, abdominal fullness, bloating and discomfort, constipation, and diarrhea (usually nocturnal).
Gastropathy is frequently responsible for erratic and unpredictable blood glucose levels, with hyperglycemia itself exacerbating the dysmotility, even in people without diabetes. Gastroparesis may respond to treatment with metoclopramide or domperidone (dopamine D2 antagonists), erythromycin (motilin agonist) for bacterial overgrowth, cisapride (cholinergic agonist), or mosapride (selective serotonin 5-HT4 receptor agonist). Diarrhea may respond to loperamide or diphenoxylate and atropine.
Orthostatic hypotension can be treated by attention to mechanical factors such as elevation of the head of the bed, gradual rising from a lying to standing position, use of support stockings, and sometimes use of fludrocortisone.
Cardiac rhythm disturbances can result in syncope and cardiorespiratory arrest.
Bladder involvement may result in urinary retention or incontinence. In men, erectile dysfunction is multifactorial and may also be related to vascular insufficiency or venous leaks. Arousal is the main problem in the sexual dysfunction of women with diabetes.

DIABETIC FOOT

Care of the feet of patients with diabetes is extremely important to prevent foot ulcers and amputations. Risk factors include distal symmetrical polyneuropathy, peripheral arterial insufficiency, areas of increased pressure, limited joint mobility and bony deformities, obesity, and chronic hyperglycemia.
Patient education about foot care includes advice on daily foot inspection, appropriate footwear, drying and nail cutting, and referral to a podiatrist when necessary.
Early detection and treatment of blisters, ulcers, trauma, and cellulitis may prevent progression to osteomyelitis and amputation. Treatment of ulcers may include débridement, antibiotics, growth-stimulating factors, reduction of weight bearing (elevation, casting), and improvement in arterial supply (surgical or medical).

MACROVASCULAR COMPLICATIONS

Seventy to 80% of people with diabetes die from a macrovascular event. The risk for such an event (2 to 4 times increased in patients with T2DM or 20% over 7 years) in people with diabetes is equivalent to that of nondiabetic patients with established cardiovascular disease (i.e., those who have already had a macrovascular event, e.g., post myocardial infarction). Thus, all patients with diabetes and no prior cardiovascular event are considered coronary heart disease, or cardiovascular disease, risk equivalents. Following a first cardiac event in people with diabetes, the chance of a second event increases dramatically to 45%. The pathogenesis of atherosclerosis (increasingly recognized as an inflammatory disease) and vascular thrombosis in people with diabetes is similar to that in people without diabetes, albeit markedly accelerated in the former. Tight glucose control, including acutely post myocardial infarction, results in improvement in cardiovascular disease. Women with diabetes have the same risk profile as men at all ages. Hypertension (50% of patients with T2DM), dyslipidemia (40% of patients with T2DM at diagnosis), obesity, hyperglycemia, and smoking are major risk factors. In people with diabetes, the risk for death from hypertension is greater than from hyperglycemia. Aggressive treatment of hypertension, to less than 130/80 mm Hg, reduces both macrovascular and microvascular complications and should preferably start with an ACE inhibitor or ARB, for added renal protection. All other classes of antihypertensive agents may be used, including selective B1-blocking drugs, which are also used in the secondary prevention of myocardial infarction. B-blockers may increase the severity of hypoglycemia by inhibiting glycogenolysis and gluconeogenesis and may mask the warning symptoms and signs of hypoglycemia by blunting the adrenergic response to hypoglycemia. However, the potential adverse effects of B-blockers in patients with diabetes have not been consistently observed in the clinical setting. Most hypertensive patients require combination antihypertensive therapy, using, on average, three different classes of agents, including diuretics. In hypertensive patients with microalbuminuria or macroalbuminuria, nondihydropyridine calcium channel blockers may be added to the list of other drugs.

The procoagulant state of the blood in patients with diabetes is caused by platelet hypersensitivity to the aggregating properties of thromboxane (synthesized in excess), as well as disordered fibrinolysis and increased levels of the prothrombotic mediator, PAI-1 (“Metabolic Syndrome,”). Low-dose aspirin (81 to 162 mg per day) is recommended as primary prevention in patients with diabetes who are at high risk for cardiovascular disease, as well as secondary prevention in those with evidence of large vessel disease. Additionally, smoking cessation and management of obesity, dyslipidemia, hypertension, and hyperglycemia, together with initiation of safe exercise, all decrease the risk and severity of macrovascular disease.

THANK YOU.....