Suggested Intervention Strategy for Early Complications of Diabetes Mellitus

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The recommendations of the American Diabetes association on intervention-strategy regarding complications of diabetes are summarized in this article.

INTERVENTION STRATEGY FOR NEPHROPATHY

Glycemic Control: Tight glucose control using CSII therapy is effective in reducing AER in micro-albuminuric IDDM patients; progression to overt clinical proteinuria (6 years) is reduced or prevented; reduction of GFR to within the normal range is observed. These results suggest that strict blood glucose control may have a renal protective effect.

Blood Pressure Control: Reduction of elevated BP slows the rate of loss of GFR and halts the increasing albuminuria in IDDM patients with overt as well as incipient nephropathy. A variety of antihypertensive agents, including angiotension converting enzyme inhibitors (ACEI) have been used. ACEI have been the focus of attention because of the possible specific renal protective effect. Micro-albuminuric IDDM patients receiving ACEI show significantly lower BP and a lower rate of progression of AER; development of clinical proteinuria in normotensive micro-albuminuric IDDM patients is postponed (independently of a reduction in systemic BP). In addition to lowering intraglomerular pressure, ACEI may improve glomerular selectivity.

Low, Vegetarian Protein Diets (VPD): Reduction of animal protein in the diet to ~0.6 g/kg body wt/day significantly slows the rate of GFR decline (3-5 yr.), independent of BP, in IDDM patients with overt nephropathy. In micro-albuminuric IDDM patients, restriction of dietary protein lowers AER and possibly delays the onset of clinical proteinuria (no long-term detrimental effects on nutritional status). In healthy, non-diabetic control subjects, a VPD with a normal protein content (~1 g/kg body wt/day) induced similar renal hemodynamic changes, like those obtained by LPD. (Mechanism of action of LPD and VPD:? effect on the intrarenal synthesis of PGEs and kinin). Whether any of these factors which are successful in reducing micro-albuminuria, will lead to an amelioration of the abnormal glomerular morphology already detectable in these patients and prevent ESRF is currently unknown.

Primary Prevention (Normoalbuminuria to micro-albuminuria): Hemodynamic determinants of glomerular hyperfiltration contribute significantly to glomerulopathy in diabetes. Initial glomerular hyperfiltration may be associated significantly with the development of micro or macro-albuminuria. Hyperfiltration is related to the degree of blood glucose control, and intensified insulin treatment reduces GFR towards normal levels (with decrease in renal size). Excess renal production of PGEs and kinins is an important mediator of glomerular hyperfiltration. The predictive value of glomerular hyperfiltration remains to be established, and whether a reduction of supranormal GFR by whatever means confers any long-term renal benefit is known.

INTERVENTION STRATEGY FOR RETINOPATHY:

Laser photocoagulation Surgery: The threrapeutic benefit of laser photocoagulation surgery is now established. Scatter (panretinal) photocoagulation surgery could improve the prognosis of proliferative retinopathy. Severe visual loss was seen in 15.9% of untreated eyes (2years) vs. 6.4% of treated eyes. The benefit is greatest among patients whose baseline evaluation revealed high-risk charactreristics (HRC; chiefly vitreous hemorrhage with any retinal neovascularization or disc neovascularization). Twenty-six percent of control eyes with HRC progressed to severe visual loss versus 11% of treated eyes. The absolute benefit of photocoagulation was much smaller for eyes that did not have HRC. Given the risk of a modest loss of visual acuity and of contraction of visual field from panretinal laser therapy, such therapy has been primarily recommended fir eyes approaching or reaching HRC.

The value of argon laser surgery in early proliferative (PDR), moderate to severe non-proliferative diabetic retinopathy (NPDR), and diabetic macular edema (a complication seen in the presence of both PDR and (NPDR) has also been

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assessed. The benefit of focal laser photocoagulation in eyes with macular edema, has been established.

Laser photocoagulation is beneficial in preventing further visual loss, but generally not beneficial in reversing already diminished acuity. Patients with proliferative retinopathy or macular edema may be asymptomatic; a screening program to detect diabetic retinopathy is this essential.

INTERVENTION STRATEGY FOR CARDIOVASCULAR DISEASE

Lipid Abnormalities: Reductions of total cholesterol and LDL-chol are associated with significant reductions of fatal and nonfatal coronary artery disease events. Correction of lipid abnormalities can halt progression and possibly further cause regression of atheromatous lesions in native and bypass-graft coronary arteries (general population). [Also refer to section on "lipid disorders"].

Hypertension: Lowering blood pressure reduces total and cardiovascular mortality in general populations; whereas the incidence of stroke kidney failure, and congestive heart failure are reduced by antihypertensive therapy, the incidence of myocardial infarction is not affected. Although increased cardiovascular risk has been demonstrated in adult diabetic subjects with pressures > 125/80mmHg, in the absence of specific data demonstrating clinical efficacy in diabetic subjects with mild hypertension, the indications for initiating antihypertensive treatment should be the same as for non-diabetic hypertensive patients. The decision to treat mild hypertension must be made on clinical grounds in individual cases, depending on age of the patient and presence or absence of other risk factors, e.g., impaired renal function and congestive heart failure. Isolated systolic hypertension is more common in diabetic than non-diabetic people and is a risk factor for the development of macro-vascular disease. Benefits of routine treatment have not been established. Because obesity is frequently associated with hypertension in NIDDM and because calorie restriction, weight loss, and exercise frequently have a beneficial effect on blood pressure, these nonpharmacological modalities should be fully pursued in all cases.

The selection of an appropriate drug regimen for the treatment of hypertension in diabetic patients entails special consideration. Thiazide diuretics may have adverse effects on glucose levels and lipid profiles; B-blockers may also adversely affect lipid profiles and may present special problems with counter regulation in-patients treated insulin. Therefore, drugs of these classes cannot be considered first-line agents in the treatment of hypertensive diabetic patients. Although long-term studies are lacking, preliminary evidence indicating a beneficial effect of angiotensin-converting enzyme inhibitors on proteinuria and renal function in diabetic subjects, in conjunction with demonstrated antihypertensive efficacy, suggest a primary role for this class of agents in the treatment of hypertension. Renal function and serum potessium levels must be monitored carefully during treatment with angiotensin converting, enzyme inhibitor. Calcium channel-blocking agents may beneficial as well but more data on the long-term effects of these agents are required. The addition of other agents in refractory cases should follow the guidelines used in the treatment of non-diabetic hypertension.

Smoking: Reduced cigarette smoking in association with dietary modification leads to reduction in fatal and nonfatal myocardial infractions and sudden death (general population). The treatment of cigarette smoking is to stop; and young people must be prevented from smoking (physiological, psychological, and social dependency components.)

Platelet abnormalities: The effects of antiplatelet therapy, with aspirin and dipyridamole indicate a modest reduction in strokes and transient ischemic attacks, but no beneficial effect on opposite-leg amputation and cardiovascular death. After a cardiovascular event, antiplatelet treatment appears to have protective effect on subsequent cardiovascular mortality and morbidity in non-diabetic subjects. Therefore (in view of increased platelet aggregability), antiplatelet therapy may have a significant role in diabetes.

INTERVENTION FOR DIABETIC NEUROPATHY AND FOOTCARE

NEUROPATHY: Unfortunately there is no consistently effective treatment for any of the neuropathies. It remains to be demonstrated definitively whether normalisation of blood glucose levels can prevent development and progression of this devastating complication. Peripheral neuropathy: aspirin, non-steroidal anti-inflammatory drugs, codeine, phenytoin, amitryptiline plus fluphenazine, local capscaisin. Autonomic neuropathy: symptomatic treatment for visceral dysfunction.

FOOT CARE:

Patient Education: Patients with diabetes must be educated and understand proper foot care. Low-risk patients should be instructed about 1) foot hygiene, 2) proper footwear, 3) avoidance of foot trauma, 4) the need to stop smoking, and 5) actions to take if problems develop, which include when to see a health-care professional. In addition, high-risk patients and their family members should be taught to perform daily foot inspections. Neuropathic and vascular complications and their relationships to foot problems should be explained.

SURGERY:

Clinical grading: A quick clinical Grading of the severity of foot lesion can now be done (Wagner).

G 0: No open lesion, skin intact, may be bony deformities e.g. (a) Claw toes. (b) Depressed meta-tarsal head: Surgical correction of bony deformity, patient education.

G 1: Full thickness loss of skin, prominent bony deformities ± . (a) For skin loss: Debride, primary closure/skin grafting. (b) For bony lesion: Excise dead tissue, correct bony lesion. Close by a skin graft. (c) If no healing and condition worsens: Amputation.

G 2: Penetration of ulcer to bone/tendon/joint (a) Debridement: If heals-Prophylactic shoes. (b) If no healing: Bone resection. If heals:-fine, if not: Amputate & prosthesis.

G 3: Plantar abscess, pyoarthrosis, osteomyelities. Medical Treatment (a) Response: Debride, dressing & skin grafting-Healing. (b) No response: Amputation & prosthesis.

G 4: Gangrene of forefoot/toes, and, G 5: Gangrene of entire foot. If ischaemic index < 0.45: Try vascular repair. If ischaemic index > 0.45: Medical Treatment. (a) Good response: Trans metatarsal Amputation (Gr 4,) Symes Amputation (Gr 5) (b) Poor response: Guillotine amputation. (c) NO response: Higher amputation.

Prophylactic Surgery in Toe and Foot Deformities: This is important to prevent major morbidity in future. The indications are: (1) Failure of maintenance techniques, (2) Impending ulceration/ulceration despite adequate efforts, (3) Following unsuccessful revascularization procedures. The guidelines for surgical procedures are as follows: The procedures should be: (1) Early and simple e.g. excision of an exostosis, osteotomy and Ray amputation (amputation of a digit and its metatarsal) etc. (2) Definite and permanent. (3) Complex procedures to be avoided e.g. tendon transfers & Osteoplastic procedures. (4) Avoid muscle imbalances & plantar scars.

Treatment of Infection: Prompt control of infection is imperative in all grades of infections. The main guiding principles are: (1) Obtain Proper material for culture by curettage technique and do a proper debridement. (2) Start the antibiotic therapy based upon the seriousness of the infection and predicted spectrum of the bacteria.

Vascular surgery: The role of vascular reconstructive surgery is limited as in majority of the patients smaller vessels are involved. However, if cause for significant ischaemia is a bigger vessel, then after a vascular workup transluminal angioplasty, reconstruction using autogenous veins or grafts can be done with good results. Sympathectomy has no role and is contraindicated.

INTERVENTION FOR DYSLIPIDAEMIA:

The expert panel of the National Cholesterol Education Programme (USA) has proposed diagnostic and treatment guidelines for cholesterol levels in all adults. Because these guidelines focus on LDL and not triglycerides and HDL, thus neglecting mixed dyslipidamias, they may be of limited value in diabetic patients.

Diet, exercise, and successful glycemic control are first-line measures for managing dyslipidaemia in the diabetic patient.

Recommended dietary strategies include modest caloric restriction to attain desirable weight. The emphasis is on restriction of total fat (< 30% of total calories) and saturated fatty acids (< 10%) and dietary cholesterol (< 300mg/day) - consistent with the Step 1 diet of the American Heart Association - and upto 50-60% of calories from unrefined carbohydrates high in fiber. In IDDM, good glycemic control with often improve but not completely reverse dyslipidaemias. In the 20% of NIDDM patients who are lean, normoglycaemia will pay an important role in lowering lipids. In the obese patient with NIDDM, however, glucose control will often only partially correct lipid abnormalities. HDL levels may not increase with oral agent therapy, and intensive insulin therapy may increase HDL in some but not all patients. If routine anti-diabetic strategies including diet, weight loss, and glycemic control do not successfully normalize lipid levels within 3-6mo, pharmacological intervention seems necessary.

Intervention is recommended for the following: (a) The diabetic person without overt CAD who has persistent hypertriglyceridaemia (> 2.82mM or 250 mg/dl) and reduced HDL cholesterol (< 1.16mM [45 mg/dl]). (b) The diabetic person with established CAD who has elevated triglycerides (> 1.69mM or 150mg/dl) and reduced HDL cholesterol (< 1.16mM). (c) The diabetic person with LDL > 4.14mM (160 mg/dl).

Pharmacological therapies for treating hyperlipidaemia should be individualized and monitored closely.

1. Fibric acid derivatives increase lipoprotein lipase activity and decrease hepatic production of VLDL triglycerides; they may also enhance LDL receptor activity. These drugs significantly reduce triglycerides and raise HDL. They have a modest effect on total and LDL cholesterol.

2. HMG-CoA reductase inhibitors reduce the synthesis of cholesterol and increase the synthesis of hepatic LDL receptors, resulting in decreased production and increased clearance of LDL and VLDL remnants from plasma. HMG-CoA reductase inhibitors reduce total and LDL cholesterol, but have modest, non-dose-dependent, beneficial effects on triglycerides and HDL.

3 Bile acid sequestrants bind bile acids, sequestering cholesterol in bile and causing its excretion. They ultimately result in increased hepatic LDL-receptor synthesis. They reduce total and LDL cholesterol with little or no effect on HDL cholesterol; however, in hypertriglyceridemic (> 2.82 - 3.89mM or 250-300 mg/dl) patients, resins are not effective in lowering total cholesterol and cause increases in triglyceride levels and concomitant decrease in HDL.

4. Nicotinic acid reduces hepatic production of VLDL, resulting in reduced LDL, significant reduction in triglyceride levels, and significant increases in HDL. However, because this drug clearly worsens glycemic control, increases plasma uric acid levels, and produces an insulin resistant state, its use in diabetic or insulin-resistant patients is not advised.