Standards of Care of Diabetics with regard to long-term Follow-up

S. S. Srikanta*(*Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow.)

INTRODUCTION

Goals for continuing medical care and education in a chronic illness are (1) to prevent acute complications, and (2) to reduce the risk of long term complications. Strategies for follow-up, and continuing care of chronic disease like diabetes mellitus depends upon (1) the known natural history and health burden of he disorders. (2) The availability of easy and effective screening methods for early detection of complications and associated medical conditions, and (3) feasibility of effective post-primary (or better-primary) interventions. Actual implementation of "standard care" depends upon cost-beneficial ratios and the socio-economic context (What is "ideal" versus "practical' varies from society to society).

STANDARDS OF CONTINUING MEDICAL CARES FOR PATIENTS WITH DIABETES MELLITUS: MODIFICATIONS OF ADA GUIDELINES

The guidelines recently published by American Diabetes Association (Diabetes Care 12: 365-368, 1989) for "CONTINUING CARE"/follow-up, are summarised below. These standards define basic/minimum medical care for diabetes [1].

Following are the recommendations for follow-up under headings of a) Physical examination, b) laboratory evaluation & c) management plan.

a) PHYSICAL EXAMINATION CONTINUING CARE: DM

* Comprehensive Physical Examination, Annually: (Ht), weight, BP, CVS, Peripheral pulses, feet, CNS, skin-injection site, previous/interim abnormalities
* Complete eye/visual examination: Annually (Ophthalmologist)
  > 30yr age - All Diabetics
  12 - 30 yr. age if - DM > 5 – yr. duration

b) LABORATORY EVALUATION CONTINUING CARE: DM

* Glycated Haemoglobin : q 3mo (for those on insulin
  q 6mo (all)
* Fasting blood glucose : NIDDM
* Random blood glucose : of SHBGM
* Lipid Profile : q 1 yr. (adult)
  (TG, T-C, HDL-C) : q 2 yr. (children)
* Urinalysis – routine : q 1 yr.
* Microalbuminuria : q 1 yr.
  (Proteinuria)
  > 30 yr. age
  12-30 yr. age
  < 12 yr.
* S Creatinine/
  BUN/GFR : if – UPE (+)

c) MANAGEMENT PLAN CONTINUING CARE

* **Review:** Goals, adherence and problems
* Nutrition, body weight exercise
* **Desired levels:** BG, GHb, Lipids,
* 'Hypo'/'Hyper': Intervention
* **Complications:** Follow-up referrals
* **Self care:** Knowledge, skills, behaviour - reassess annually.

STANDARDS HAVE CONTINUING MEDICAL CARES FOR PATIENTS WITH DIABETES MELLITUS: SCREENING FOR COMPLICATIONS:

DIABETIC NEPHROPAHY [2]

Natural History

Diabetic nephropathy develops in ~35% of patients with IDDM between 15-60% of NIDDM patients, depending on their ethnic origin. The vast majority of IDDM patients, with proteinuria eventually will progress to end-stage renal failure (ESRF) or die prematurely from cardiovascular complications. Without any medical intervention GFR falls at an average of 1 ml. min^{-1}. mo^{-1}, even though a large fivefold variation exists between individuals, leading to ESRF in mean period of 7 yr. In addition, this group of proteinuric patients displays a 20-to 40-fold increased risk for cardiovascular mortality compared with age, sex, and duration of disease-matched diabetic patients without proteinuria.

* *Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow*

Screening

Micro-albuminuria and incipient diabetic nephropathy: Approximately 20% of NIDDM and 25% of IDDM and 25% of NIDDM patients with urine negative to dipstick test for protein excrete higher than normal amounts of albumin in their urine. This sub-clinical elevation of urinary albumin excretion rate (AER) has been termed micro-albuminuria and is defined conventionally as AER between 30-300 mg/24h. Prospective longitudinal studies (10-15 years) indicate that patients with micro-albuminuria were ~ 20 times more likely to develop clinical proteinuria than patients with normoalbuminuria. Micro-albuminuria has a predictive power of > 80%. Also more recently micro-albumiuria has emerged as a significant predictor of premature cardiovascular mortality, conferring a relative risk of 2.9. In NIDDM, micro-albuminuria is not only a predictor for proteinuria, but also a prognostic indicator of early mortality, mostly from cardiovascular disease (CVD). (Micro-albuminuria has also been predictive of cardiovascular mortality in middle-aged and elderly non-diabetic subjects).

Dyslipidaemia, (considered primarily a consequence of advanced renal disease) has been described increasingly in both IDDM and NIDDM patients with micro-albuminuria. Elevated levels of total and very-low-density lipoprotein triglycerides, total and low-density lipoprotein-cholesterol, apolipoprotein B, and reduced levels of high-density lipoprotein 2 cholesterol have been found. More recently, lipoprotein (a) and plasma fibrinogen (independent risk factors for atherosclerosis in the general population), have been shown to be elevated in micro-albuminuric IDDM patients. Such atherogenic lipid profiles may be important contributors to the excess cardiovascular mortality described in-patients with micro-albuminuria. In IDDM patients with micro-albuminuria, an increase in whole-body transcapillary escape of albumin has been described.

Micro-albuminuria displays a consistent association with higher levels of arterial pressure. Although the rise in arterial pressure often falls within the accepted normal range, on an average, micro-albuminuric patients display BP values that are about 10mmHg above that of age-, sex-, and duration-matched IDDM patients with normoalbuminuria. The relation to BP is independent of other variables, such as blood glucose control. Poorer blood glucose control is another independent association of micro-albuminuria. Significant glomerular abnormalities (renal biopsy) are already discernible at the stage of incipient diabetic nephropathy (although the vast majority of patients still enjoy a normal, or even supranormal GFR) - thickening of glomerular basement membrane, expansion of mesangial volume, and increased matrix volume fraction. Micro albuminuria is extremely uncommon in the first 5 yr. after diabetic onset and in children < 15 yr. of age.

DIABETIC RETINOPATHY [3]

Natural History

Prevalence of retinopathy is strongly related to the duration of diabetes. After 20 yr. of diabetes, nearly all patients with type I diabetes and 60% of patients with type II diabetes have some degree of retinopathy. Overall, diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20-74 yr. Vision-threatening retinopathy usually does not appear in type I patients in the first 5yr of diabetes, nor before puberty. Upto 21% patients with type II diabetes have retinopathy at the time of first diagnosis of diabetes.

In general, the progression of retinopathy is orderly, advancing from mild background abnormalities characterised by increased vascular permeability, to perproliferative retinopathy characterised by vascular closure, to proliferative retinopathy characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous.

Vision loss with diabetic retinopathy results from several mechanisms (macular oedema or capillary nonperfusion, tractional retinal detachment, preretinal or vitreous haemorrhage). Potential risk factors for retinopathy include poor glucose control, high blood pressure, serum lipid levels, and pregnancy.

Screening

The standard screening procedure for diabetic retinopathy is careful funds examination - indirect ophthalmoscopy through a dilated pupil. The most sensitive screening technique is stereofunds photography (seven field; fundus camera) and this might provide the basis for more efficient screening strategies in the future. The earliest sign of retinal change is an increased capillary permeability that is evidenced by leakage of dye into the viterous humor after fluorescein injection (fluorescein angiography).

CARDIOVASCULAR DISEASE [4]

Natural History

Diabetes mellitus is major risk factor for morbidity and mortality due to coronary heart disease, cerebrovascular disease, and peripheral vascular disease. The prevalence of these macro-vascular complications is increased about two to fourfold in diabetic populations. Multiple risk factors for macro-vascular disease are frequently found in individuals with diabetes. (Major: increased prevalence of hypertension and lipid abnormalities, smoking; other factors include obesity, impaired glucose tolerance (IGT), hyperglycaemia, hyperinsulinaemia, micro-albuminuria elevated fibrinogen levels, altered platelet function, and qualitative lipoprotein abnormalities). The prevalence of coronary artery disease, stroke, peripheral vascular disease, and total mortality are substantially increased in diabetic individuals, even in the absence of hypertension. In diabetic as in non-diabetic subjects, CVD risk is directly proportional to low-density lipoprotein cholesterol (LDL -chol) inversely proportional to high-density lipoprotein cholesterol (HDL-chol). Whereas hypertriglyceridaemia is common in NIDDM, it is uncertain whether triglycerides have independent predictive value for macro-vascular disease. The three major risk factors (hypertension, hyperlipidaemia, smoking) appear to be additive in their adverse impact on cardiovascular events in diabetic individuals.

With respect to obesity, it is recognized that the distribution of adiposity has a significant impact on cardiac risks. Hypertension, hyperinsulinaemia, diabetes, elevated very-low-density lipoprotein cholesterol (VLDL-chol) and low HDL-chol are highly associated with upper-body (abdominal) obesity, measured as an increased waist-to-hip ratio. In contrast, lower-body (femoral and gluteal) obesity appears to have less impact on these risks. Besides obesity a sedentary life style/inactivity appears to be a risk factor for macro-vascular events.

Screening

Screening ECGs will yield a high proportion of abnormal tracings. Newly diagnosed diabetics above the age of 45 years should have baseline ECGs. ECGs will clearly be necessary in-patients who have hypertension, angina or other symptomatic cardiac disease. Exercise ECGs, echocardiography, and other new non-invasive tests should be confined to patients with symptoms and/or signs and/or risk factors in whom the investigations will aid management.

DIABETIC NEUROPATHY [5]

Natural History

Diabetic neuropathy is a descriptive term meaning a demonstrable disorder, either clinically evident or subclinical, that occurs in the setting of diabetes mellitus without other causes for peripheral neuropathy. The neuropathic disorder includes manifestations in the somatic and/or autonomic parts of the peripheral nervous system.

While it is rarely a direct cause of death, it is a major cause of morbidity. Some lesions, such as the acute cranial nerve palsies and diabetic amyotrophy, have been attributed to ischaemic infraction of the involved peripheral nerve. The much more common symmetric sensory and motor peripheral neuropathies (may be present at the time of initial diagnosis of NIDDM) and autonomic neuropathy (common in patients with diabetes of long duration) are felt to be due to metabolic or osmotic toxicity somehow related to hyperglycaemia.

Screening

To fully classify diabetic neuropathy, at least one measures from each of the following categories: clinical symptoms, clinical examination, electro-diagnostic studies (EDX), and autonomic function testing (AFT) must be utilised.

ELECTRODIAGNOSIS: The electro-diagnostic examination id useful in evaluating various disorders, including mononeuropathy, mononeuritis multiplex, plexo-pathy, polyradiculopathy, and sensorimotor neuropathy. In a diffuse generalized poly-neuropathy, testing a few nerves suffices to indicate the functional state of the peripheral nervous system. In multiple mononeuropathies, affected nerves should be tested to characterize the abnormalities.

Conventional nerve conduction studies: Analysis of action potential amplitude allows estimates of the total number of active fibers. Nerve-conduction studies primarily reflect functional status of large myelinated sensory and motor nerve fibres in the upper and lower extremities.

Electromyography: It may reveal partial denervation in intrinsic foot muscles as an early sign of diabetic neuropathy. Needle studies also elucidate focal or

asymmetric clinical findings not detectable by conduction studies.

Distal lower-extremity responses are more commonly abnormal than upper-extremity responses, and sensory abnormalities are more frequent than motor abnormalities.

AUTONOMIC NERVOUS FUNCTION TESTING: Diabetic autonomic neuropathy may manifest as dysfunction of several different organ systems, e.g., cardiovascular, gastrointestinal, genitourinary, sudomotor, and ocular. Objective measurements of autonomic function measure endorgan responses to activation of neural reflex arcs. They can be influenced by end-organ failure, inter-current illness, drugs and age.

Noninvasive tests: (For routine screening for autonomic dysfunction or for monitoring the progress of autonomic neuropathy).

1. Tests of heart-rate control (mainly parasympathetic). Heart-rate response to a. Valsalva manoeuvre b. Deep breathing c. Standing.

2. Tests of blood pressure control (mainly sympathetic). Blood pressure response to (a) standing or tilting (b) sustained handgrip 3 Tests of sudomotor control, i.e., (a) Temperature-induced sweating (b) Chemically induced sweating (e.g., acetycholine or pilocarpine)

Invasive tests of cardiovascular function, gastrointestinal motility, and bladder function are not suitable for routine screening or for monitoring progress.

Other biochemical, physiological, and pharmacological studies. Although useful, they may not be generally available. They include skin vasomotor reflexes, plasma norepinephrine response to standing, pupilometry, and pancreatic polypeptide response to hypoglycaemia or a meal.

FOOT PROBLEMS

Natural History

Foot ulcers and other foot problems are a major cause of morbidity, mortality and disability in people with diabetes. (Presence of neuropathy and/or ischaemia, minor trauma leading to cutaneous ulceration and wound-healing failure, lower-extremity amputations). Once the amputation of one limb has occurred, the prognosis for the contralateral limb is poor.

Patients are at high risk to develop foot ulcers or infection if they have any of the following conditions: neuropathy, vascular disease, structural deformities, abnormal gait, skin or nail deformities, or a history of previous ulcers or infections. All such patients should be seen by a physician at frequent intervals.

The increased incidence and early onset of PVD in the diabetic has been well documented. In living diabetic groups, PVD has been reported to occur in 16% to 58% of all groups ('west'). Many of the adult onset diabetic patients have evidence of PVD at the time of diagnosis (Diabetic peripheral vascular disease: present at onset = 8%; after 10 years = 15%; after20 years = 45%; diabetic foot ulcers = 15%; amputations 6/1000/y' USA).

Screening

Patients' legs and feet must be examined, including the skin between the toes and the posterior aspects of the heels. This examination should be performed by a qualified health-care professional at every regular visit. A comprehensive vascular, neurological, musculoskeletal, and skin and soft tissue evaluation should be done at least annually. The vascular evaluation should include palpation of the pulses in the lower extremities and inspection of the feet and legs for any gross ischaemic changes (significant peripheral vascular disease: vascular consultation). The neurological examination should include a sensorimotor examination of the lower extremities. If sensorimotor deficiencies exist, footwear modification should be considered. Musculoskeletal evaluation should include foot and ankle joint range of motion and inspection for bone abnormalities. The patient should be observed for abnormal gait or stance (with and without shoes) and abnormal wear patterns of his/her shoes).

LIPID DISORDERS [7]

Natural History

50% of all diabetic people, whether IDDM or NIDDM, are dyslipidaemic. (a) Poorly controlled IDDM: elevated levels of VLDL triglycerides and chylomicrons due to decreased lipoprotein lipase activity. NIDDM: elevated triglycerides (> 1.69mM (150 mg/dl) and reduced HDL cholesterol (< 1.16mM (45 mg/dl); less commonly, LDL cholesterol also elevated (> 3.36mM [130 mg/dl]). In the NIDDM patients, these dyslipidaemias may be independent of glucose control.

Hypertriglyceridaemia: Elevated triglyceride levels occur in most NIDDM patients (relatively increased hepatic production of VLDL, in part as the result of excessive caloric intake and hyperinsulinaemia, or defective clearance of VLDL triglyceride or chylomicrons, due to an absolute or relative reduction in activity of the insulin-dependent enzyme lipoprotein lipase, owing to insulin deficiency or resistance). Elevated triglyceride levels are a significant additional CHD risk factor inpatients with high ratios of total cholesterol to HDL cholesterol.

Reduced HDL cholesterol: Decreased HDL levels, particularly HDL-2 levels, are common in diabetic subjects. In general, the patient with diabetes mellitus demonstrates a 15%-25% reduction in HDL cholesterol levels relative to age, weight, and sex-matched non-diabetic people. About 20% of diabetic men and 25% of diabetic women have severely reduced HDL levels (< 0.80 and < 1.06mM [<31 and < 41 mg/dl]), respectively).

Dyslipidaemia related to insulin resistance may be present for many years before the onset of clinical diabetes. Thus, years before diagnosis of diabetes, patients destined to become diabetic can have observable lipoprotein metabolic abnormalities and pre-existing but related CHD risk factors.

Screening

Annual measurements of fasting total cholesterol, total triglyceride and HDL-cholesterol are recommended. Lipoprotein electrophoresis in-patients with raised total lipids identifies the underlying the lipoprotein abnormality. Other causes of secondary hyperlipidaemias should be excluded particularly hypothyroidism and impaired renal function. (Also drugs: betablockers, thiazides, oestrogens). Co-existent primary hyperlipidaemia should be identified and treated as in a non-diabetic.

CONCLUSION

Some aphorisms of the Belgian Physician Jean Pirart who has probably one of the largest follow-up of about 4,400 diabetics over 25 years [8]:

LOOKING AFTER PEOPLE WITH DIABETES [9]

* "Do not trust schemes and classifications too much. After all, a patient has a right to be himself regardless of the pattern he should fit in accordance with your theories.
* Be ambitious and always try to give the best of yourself for the cause of your patients, but remain realistic. Do not try to normalize all parameters.
* Do not talk in a scholarly way; high blood sugar or low blood pressure are as good as hyperglycaemia or hypotension. Speak to be understood, not to be admired.
* Be cautious in taking any decision to change something that is running well, however odd a treatment it seems to be.
* Listen to your patients. The key to a problem is more often found in their talk than in a laboratory test.
* Do not evade any question; if not appropriate for the time being put the question aside and answer it in due time some weeks later."

REFERENCES

1. Standards of medical care for patients with diabetes mellitus. Diabetes Care 1989; 12: 365-68 [Reprinted: Diabetes Care 1992; 15 (Suppl 2): 10-13]
2. Viberti G. C., Yip-Messent J, Morocutti A. Diabetic nephropathy: Future avenue. Diabetic Care 1992; 15: 1216-25.
3. Screening for diabetic retinopathy. Diabetes Care 1992; 15 (Suppl 2): 16-18.
4. Role of cardiovascular risk factors in prevention and treatment of macro-vascular disease in diabetes. Diabetes Care 1989; 12: 573-79 [Reprinted: Diabetes Care 1992; 15 (Suppl 2): 68-74.
5. Diabetic Neuropathy, Diabetes 1988; 37: 1000-04 [Reprinted: Diabetes Care 1992; 15 (Suppl 2): 62-67.
6. Foot Care in-patients with diabetes mellitus. Diabetes Care 1992; 15 (Suppl 2): 19-20.
7. Garber A. J., Vinik A. I., Crespin S. R. Detection and management of lipid disorders in diabetic patients: A commentary for clinicians. Diabetes Care 1992; 15: 1068-74.
8. Pirart J. Diabetes mellitus and its degenerative complications: A prospective study of 4,400 patients observed between 1947 and 1973. Diabetes Care 1978; 1: 168-88 (Part 1), 252-63 (Part 2).
9. Pirart J. What I have to say to young diabetes specialist after 35 years of experience. In: Assal J-Ph, Berger M. Gay N, Canivert J. eds. Diabetes education: How to improve patient education. Excerpta Medica Int. Congress 1983; Chapter 32:624.