The 12th Conference on Health Care of the Chinese in North America

Treatment of Diabetes in Chinese

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Diabetes mellitus and its complications are major and increasing health problems worldwide. The number of Chinese patients with Type 2 diabetes has been increasing significantly with over 12% of the Chinese population age 20 to 79 in Hong Kong having Type 2 diabetes[1].

Although the World Health Organization Consultant Report still recommends that Obesity be defined as Body Mass Index (BMI) of 30 or above even in the Asians due to the difference of body size variation[2], they have recommended that cut point of 23 and 27.5 be used as increased trigger points in Asians. Similarly the Asian criteria of abdominal obesity of male over 35 in. and female over 31 in. in waist circumference instead of the 40 in. in male and 35 in. in female by National Cholesterol Educational Program Adult Treatment Program (ATP) III guideline may more appropriate for the Asians[3].

The best prevention of diabetes is by diet and exercise. This was shown in the Da Qing study in China where 577 patients with glucose intolerance were randomized to 4 groups of treatment in 1986. When comparing the diet alone, exercise alone and combination with the diet and exercise group with the control group, there was a 31% (p < 0.03), 46% (p < 0.0005) and 42% (p < 0.005) in risk of developing diabetes respectively 6 years later[4]. These data have now been confirmed with the larger Finnish Diabetes Prevention Study[5] and Diabetes Prevention Program[6] showing a 58% decrease in diabetes progression with moderate weight reduction and exercise program.

So for all patients diagnosed to have glucose intolerance, the initial treatment should be with diet and exercise program. Telling the patient to consume less Western food will not help the patient to lose weight or control the glucose levels. A consult with a dietitian that is familiar with Chinese diet is helpful. It is preferred to have less rice and more vegetable in the diet. Several excellent diet books are now available in both English and Chinese. There is good reference for diabetes management in Chinese at the Joslin Diabetes Center website.

Since the major complications of diabetes are mainly cardiovascular, it is now inadequate to control hyperglycemia alone. There appears to be no difference of cardiovascular events between the Chinese, Asians and the Caucasians with diabetes[7]. The Steno II study have shown that there can be significant decrease in diabetic complications in the Scandinavian population with aggressive treatment of hypertension, hyperlipidemia and glycemic control even though over 80% of the patients still have A1c > 6.5%[8]. Aspirin have significantly decreased the cardiac mortality[9]. Multivitamin with folate, B12 and chromium may also be helpful even though recent studies have demonstrated vitamin E not to be useful. Patients doing home blood glucose monitoring are more active in self diabetes

management[10]. Many patients with diabetes have depression and may benefit with anti-depressants[11].

Based on the recent prospective studies with lipid lowering agents showing decreased cardiovascular complications in the high risk group with "normal" cholesterol levels, the American Diabetes Association and ATP III Guideline have now considered diabetes mellitus as cardiac disease equivalent. A statin should be started in all Type 2 diabetics even if the LDL-cholesterol is < 100 mg/dl or the non HDL-cholesterol < 130 mg/dl. The goal is to lower the LDL-cholesterol level by more than 30 to 40% or even to LDL-cholesterol < 70 mg/dl in very high risk patients[12].

The same goes for hypertension management. The United Kingdom Prospective Diabetes Study (UKPDS) has shown that hypertension management lower cardiovascular mortalities better than glycemic control[13]. The Joint National Committee (JNC) 7 report has recommended that we keep the B.P. < 130/80 or even lower < 120/75 in patients with established renal disease[14]. Although the JNC 7 report have recommended use of thiazide or beta blocker as the first line of treatment, I still prefer to use an ACE inhibitor or Angiotensin Receptor Blocker initially as these drugs have been shown to be decrease cardiovascular mortalities and renal failure in the HOPE[15] and LIFE[16] studies. Frequently, multiple medications are needed to control the hypertension[17].

With the Diabetes Control and Complication Trial (DCCT)[18] and UKPDS[19] demonstrating that lowering every 1% of A1c can decrease microvascular complications by 20 to 40%, we should aim for near normal glycemic control with the A1c less than 7% and preferably less than 6.5%. Early good glycemic control with multiple insulin injections for 7 years have continued to show benefit 5 years after off intensive treatment than the conventional treatment group in EDIC, the DCCT follow up study[20].

One should consider pharmacotherapy early if the A1c is over 8% or if the patient does not respond to diet or exercise over a 2 to 3 months period. There does not appear to be different response rate of the various medications between the races[21].

If the patient is overweight, then metformin may be a good candidate. One should start slowly at 500 mg daily with gradual increase to 1000 mg b.i.d. to prevent gastrointestinal discomfort. This drug should not be used if the patient has serum creatinine over 1.5 mg/dl as this suggests moderate renal disease as Chinese tend to less muscle mass[22].

Sulfonylureas have been used for over 40 years and can lower blood glucose values rapidly. However, they are associated with more hypoglycemia. The newer short acting insulin secretagogues such as meglitinide or nateglinide taken with meals are more physiologic but are more expensive[23].

Although the alpha-glucosidase inhibitors are quite popular in Japan, these products are not often prescribed in the U.S. due to common gastric side effects[24].

Since the Chinese have more insulin resistance compared with the Caucasian population, medications that lower the insulin resistance may be very useful[25]. The thiazolidinediones (TZDs) including rosiglitazone and pioglitazone are approved for both initial treatment or

in combination with other hypoglycemic agents. These TZDs have not been shown to have significant liver toxicity and have been used in patients with hepatitis C but care must be taken[26]. They are associated with more weight gain and edema. The serum insulin level, highly sensitive C reactive protein, plasminogen activator1-1 (PAI-1), fibrinogen are lower with treatment. Studies are being done to see if these drugs prevent the loss of beta cell function[27].

Many patients with type 2 diabetes present with both insulin deficiency and insulin resistance. Combination therapy with complementary modes of action is now the preferred course of treatment. Whether one should use up to 3 medications before adding insulin or to add insulin early after 2 medications are still being debated. The physicians should not scare the patients by telling them that they will be on injections if they don't behave as over 40% of the Type 2 patients will eventually need insulin treatment[28].

If the patient still has high A1c despite on diet, exercise and combination oral agents, then insulin should be added. Many primary care physicians are hesitant to start insulin early due to perceived patient resistance. However, I felt this is more due to physician resistance because of insulin treatment is more time consuming and there is always worry about hypoglycemia. There are many diabetic educators and endocrinologists available to assist the primary care physicians on insulin management.

Bedtime NPH usage has been shown to decrease A1c and fasting glucose values. However, there is increased nocturnal hypoglycemia prevalence. I prefer to add the long acting insulin glargine at bedtime with the oral agents as this insulin preparation lasts over 24 hours and has less nocturnal hypoglycemia[29]. Using 2 to 3 injections of premixed combination of NPH with Regular insulin can decrease postprandial hyperglycemia. The patient should give the insulin mixture 30 minutes before meals due to slow absorption of the Regular insulin. The rapid acting insulin such as lispro and aspart given separately or with the intermediate acting insulin can be given just before meals and are associated with less hypoglycemia than with Regular insulin. The patient should not use the same insulin bottle for more than 1 month after it is opened due to degradation[30]. The sulfonylurea should be tapered off after insulin is initiated to prevent hypoglycemia.

In summary, we need to treat patients with diabetes mellitus aggressively not just to manage the hyperglycemic symptoms but to decrease macrovascular and microvascular complications. Diet and exercise are the cornerstone of good management. Statin and ACE-inhibitor should be used early. Multivitamin and low dose aspirin are helpful. Combinations of hypoglycemic agents are needed to control the hyperglycemia. Insulin should be used early. Finally, patients should have retinal examination and microalbuminuria yearly and physicians should always check for cardiac disease, neuropathy and depression[31].

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