

Editorial

Coronary heart disease in UK Indian Asians: the potential for reducing mortality

The latest census data confirm that coronary heart disease (CHD) mortality in Indian Asians living in the UK remains 38% higher in men and 43% higher in women compared to Europeans.¹ However, the burden of CHD in UK Indian Asians is greatest in young men in whom the relative risk is at least twofold higher compared to Europeans. There is also some loss of immunity from CHD in Indian Asian women. Recent reports of a reduction in CHD rates among Indian Asians and Europeans provide encouragement that accurate diagnosis, novel and effective treatment strategies, and control of risk factors in the past decade have benefited both groups.¹

Coronary risk factors in Indian Asians

The prevalence of classic risk factors such as smoking, hypercholesterolaemia, and hypertension are generally lower in Indian Asians than in Europeans,² implying that classic risk factors do not account for the excess CHD mortality in Indian Asians.³ However, this view is based on the inherent assumption that reference levels of risk factors in Europeans apply equally to UK Indian Asians. Comparisons between migrant Indian Asians and their non-migrant siblings indicate significantly higher serum cholesterol, blood pressure, smoking rates, and body mass index in the former. Although, the extent to which classic risk factors contribute to CHD remains unclear, they undoubtedly have important influences on excess CHD rates in UK Indian Asians. Insulin resistance, and its metabolic consequences, are increasingly recognised as risk factors for CHD.⁴ Insulin resistance, characterised by glucose intolerance, raised plasma insulin, increased triglycerides, decreased high density lipoprotein (HDL) cholesterol, and central obesity, is more prevalent in UK Indian Asians than Europeans.³

In European populations the risk of myocardial infarction (MI) may be increased by 10-fold with a family history of premature CHD.⁵ In Indian Asians, part of the increased risk in susceptible families may be mediated by insulin resistance and central obesity.⁶ The findings of defective insulin action in UK Indian Asian survivors of premature MI and their asymptomatic non-diabetic first degree relatives, suggest that a component of insulin resistance is inherited in Indian Asians.⁶ Serum Lp(a) lipoprotein concentrations, influenced primarily by genetic factors,⁷ are also higher in Indian Asians than in Europeans.⁸ Previous studies have shown that CHD risk is increased up to ninefold in the presence of raised Lp(a) and low density lipoprotein (LDL) cholesterol.⁹ The latter is increased in UK Indian Asians compared to non-migrants.⁸

Reducing CHD mortality in Indian Asians

The priorities are patients with established CHD; asymptomatic subjects with risk factors and first degree relatives of patients with premature CHD.

POSTMYOCARDIAL INFARCTION

The six month mortality after acute MI is twofold higher in UK Indian Asian compared to Europeans, despite similar use of thrombolysis, β blockers, and aspirin,¹⁰ and is attrib-

uted to a higher prevalence of diabetes.¹⁰ Although formal studies have not been undertaken in Indian Asians, hyperglycaemia may have deleterious effects. The immediate antiplatelet effect of aspirin is reduced in hyperglycaemia,^{11,12} and may explain the reduced benefit in diabetic patients in ISIS-2 after 150 mg of aspirin.¹³ Many Indian Asian MI patients will have hyperglycaemia and should therefore receive higher initial doses of aspirin (300 mg). Mortality from acute MI is reduced after β blockers, but there is often concern among admitting physicians that β blockers may prolong hypoglycaemia or mask hypoglycaemic symptoms in diabetics. The approximate 37% reduction in the odds of dying in diabetic patients, compared with 13% in all treated patients,¹² and a similar benefit in reinfarction, are compelling reasons for early and routine use of β blockers in Indian Asians. The problem of hypoglycaemia is infrequent and can be minimised further by using cardioselective β blockers. Optimum blood glucose control, using glucose-insulin-potassium (GIK), is known to reduce mortality in diabetic patients with acute MI,¹⁴ partly through reduced non-esterified fatty acid utilisation, known to have adverse effects on cardiac rhythm, oxygen consumption, and mechanical performance.¹⁴⁻¹⁶ GIK should therefore be considered as adjunctive treatment in Indian Asians with acute MI, many of whom will have insulin resistance or diabetes. There is additional concern with regard to increased risk of cardiac events in diabetics on treatment with sulphonylureas.

Faced with an Indian Asian patient with significant obstructive coronary disease the cardiologist should give special thought to the question whether mechanical revascularisation is really desirable or necessary. The difficult anatomical and biological substrate present in these patients can present a formidable challenge. In clinical practice, the initial procedural success rate of coronary angioplasty in Indian Asians is similar to that of Europeans. However, the more extensive and diffuse disease in Indian Asians means that complete revascularisation is less readily achieved with coronary angioplasty. Although little is known of outcomes of balloon angioplasty in Indian Asians, transcatheter interventions are probably the treatment of choice in young patients with symptomatic obstructive coronary disease, and may help delay surgical revascularisation and redo surgery until later life. However, restenosis rates may be higher, silent, and perhaps more hazardous because of diabetes. Coronary surgery is the preferred revascularisation option in patients with multi-vessel disease particularly when it is accompanied by left ventricular dysfunction and diabetes.

RISK FACTORS

CHD has a multifactorial aetiology and coronary risk factors have a combined effect. Effective prevention therefore requires identification and treatment of the total burden of risk, rather than single risk factors. The data from basic, clinical, and epidemiological studies indicate that CHD is largely preventable by reduction of modifiable risk factors. Ideally, on a population basis, total cholesterol should not exceed 4.0 mmol/l beyond which CHD risk increases

progressively.¹⁷ In this regard, “normal” cholesterol, often based on a range between 4.0 and 6.5 mmol/l, is misleading. Ideally, in UK Indian Asians, the lipid profile should be similar to non-migrants; total cholesterol should not exceed 4.5 mmol/l, LDL cholesterol 2.5 mmol/l, triglycerides 1.5 mmol/l, and HDL cholesterol should be higher than 1.0 mmol/l. These values are acceptable because they are similar to rural populations at low risk of CHD. Generally, Indian Asian CHD patients have high triglyceride and low HDL cholesterol concentrations, and may have additional metabolic consequences including a shift from large and buoyant to small and dense LDL cholesterol subclasses, which are highly atherogenic. The evidence from clinical and metabolic studies linking mild to moderate hypertriglyceridaemia and low HDL cholesterol to CHD is too compelling to be ignored, and favours treatment of this atherogenic phenotype in high risk groups including UK Indian Asians. Statins should be used to treat hypercholesterolaemia and mild triglyceridaemia. Patients who have a more severe increase in plasma triglycerides, or very low HDL cholesterol, can be treated with fibrates as an initial choice, despite the less conclusive randomised trial data on their use. Although not adequately evaluated, combination treatment using a statin and fibrate may provide optimum control of the dyslipidaemia observed in Indian Asians.

Cigarette smoking is one of the most important predictors of MI in Indian Asians.¹⁸ For individuals currently smoking 10 or more cigarettes per day the odds ratio is estimated at 6.7. Smoking cessation may help to reduce CHD rates in Hindu and Muslim men whose smoking rates are similar to the national average.² Often, success on smoking cessation is greatest after the event. It is estimated that total elimination of cigarette smoking may reduce CHD by about 25% in Indian Asians. Sikh men and Indian Asian women have very low smoking rates. Health promotion measures must ensure that smoking rates do not rise in second generation UK Indian Asians.

Raised blood pressure is a strong predictor of CHD and randomised trials indicate that antihypertensive treatment is effective in reducing CHD and stroke rates.¹⁹ In middle aged UK Indian Asians, blood pressure should probably not exceed the non-migrant blood pressure of 140/85 mm Hg in men and women. Blood pressures are higher in Punjabis (Sikh and Hindu) than in Europeans.³ Active attempts should be made to detect and control hypertension in these subgroups. Lowering blood pressure will preserve renal function, and angiotensin converting enzyme inhibitors will have additional benefit on the rate of progression of proteinuria in diabetics. Few studies have compared the efficacy of different classes of antihypertensive drugs and their metabolic side effects in Indian Asians. Thiazides may have an adverse effect on glycaemic control and increase total cholesterol and triglyceride concentrations, and decrease HDL cholesterol. Cardioselective β blockers have few metabolic side effects and particular advantages in patients with coronary disease.

INSULIN RESISTANCE

The absence of a simple, reliable, and reproducible marker of insulin resistance presents a major obstacle for the clinician in identifying and monitoring the clinical course of patients. The second limitation is the lack of solid evidence that insulin resistance is associated with risk of future CHD events, and that improved insulin sensitivity is associated with a reduction in CHD mortality. Nevertheless, clinical and epidemiological studies support an important role for insulin resistance in CHD, and in Indian Asians in particular. The combination of raised fasting triglyceride (> 1.5 mmol/l), low HDL cholesterol (< 1.0 mmol/l),

raised fasting glucose (> 7.0 mmol/l), central obesity (waist:hip ratio > 1.0 in men and > 0.85 in women), and hypertension may reliably identify patients with insulin resistance. As the metabolic syndrome may be present for many years before its manifestations become apparent, strategies aimed at improving insulin sensitivity and reducing CHD risk will be most successful when directed at high risk subjects, particularly first degree relatives of patients with premature CHD. Novel insulin sensitising agents, thiazolidinediones, have been demonstrated to improve insulin sensitivity and may reduce CHD risk in Indian Asians.

Weight loss improves insulin sensitivity. The principle for treatment is to achieve negative energy balance. A deficit of 500 kcal is often well tolerated and will enable normal activities. Weight loss can be achieved merely by reducing the fat content of the diet without the need to restrict food intake voluntarily.²⁰ In UK Indian Asians, the energy intake from fat is favourable compared to Europeans but twice that of non-migrants. Current targets aimed at reducing energy derived from fat to 33.5% of total energy intake are unlikely to have much impact in reducing obesity or CHD rates in UK Indian Asians. Fat intake should ideally be reduced to 21% of total energy intake (7% each from saturated, polyunsaturated, and monounsaturated fatty acids). In UK Indian Asians the most important practical measure is reducing the quantity of fat and oil used in cooking at home and reducing the consumption of Indian snacks and sweets. As most food is prepared at home involvement of the shopper and cook can be invaluable and have far reaching impact in other high risk members of the extended family. Physical activity levels in Asians are low. The principal aim should be to improve metabolic fitness and not circulatory fitness. Moderate activity including walking, swimming, and cycling will have energy expenditures of about 100 kcal/h and should be undertaken daily. It is important to maintain increased activity as effects on insulin resistance are short lived.

FIRST DEGREE RELATIVES

The majority of patients with CHD will have an inherited dyslipidaemia and this inherited trait will be expressed in their first degree relatives. Because these traits are often inherited in a Mendelian dominant fashion, screening of first degree relatives can be informative. This approach is ideally suited to extended Indian Asian families and enables large numbers of high risk individuals to be identified using structured programmes.

Implementation of measures

Prevention requires a multidisciplinary approach. Physicians should be motivated to translate available evidence from clinical studies into practice. The emphasis should be on reducing the burden of risk rather than single risk factors. Health authorities should ensure that clear policies are established and resources made available for clinicians to implement and audit accepted protocols. Hospitals with large numbers of Indian Asian patients should prioritise care and have the conviction to establish coronary risk prevention teams comprising clinicians, nurse practitioners, and dietitians. Prevention teams should be skilled, have a sound knowledge of benefits of interventions, and be equipped with suitable insights into methods of changing the varied Asian cultural lifestyles for the better. Most importantly, patients should have the information and education to make decisions, and be given ownership of their risk factors as incentive, feedback, and for regular reinforcement.

Personal perspective

CHD in UK Indian Asians is reducible and preventable. Greatest benefit will be obtained from early and accurate diagnosis and effective treatment strategies in young patients, those with risk factors, and first degree relatives of MI patients. Aggressive correction of classic risk factors including cigarette smoking, dyslipidaemia, and hypertension combined with intensive glycaemic control and control of obesity should be the mainstay of prevention. Reversal of insulin resistance is important, but not easily achieved or sustained. Until the magic bullet is at hand, systematic detection and correction of modifiable risk factors for CHD assumes even more importance in UK Indian Asians.

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