Diabetes and cardiovascular disease: impacts from the NSF and GMS

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ARTICLE POINTS

1 Evidence shows that control of metabolic and risk factors in people with diabetes reduces acute symptoms and chronic complications.

2 The NSF for CHD requires actions to reduce risk factors and risk inequalities, and manage CHD. The NSF for diabetes built on these targets, adding glycaemic control and attention to microvascular risk.

3 The GMS contract advocates integrated care, with substantial points (and income) available for meeting targets. Patient involvement is crucial.

4 Important targets for microvascular disease are blood pressure and glycaemic control, and for macrovascular disease LDL-cholesterol and blood pressure.

KEY WORDS

- Guidelines
- Evidence
- Management
- Cardiovascular disease
- Targets

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Introduction

The National Service Framework guidelines and General Medical Services contract incorporated a much-needed review of the evidence available from randomised-controlled trials and current implementation of treatment in coronary heart disease (CHD), focusing on risk factor reduction and prevention of CHD development. In this article, John Reckless considers the evidence for the treatment of various risk factors, the impact these documents have had in practice for people with diabetes, and future implications.

Diabetes is a chronic inflammatory disorder which underlies long-term microvascular and macrovascular complications. The prevalence of diabetes is increasing and is currently around 3% of the UK population, with as many undiagnosed. With burgeoning obesity – 21–23% having body mass index (BMI) >30 kg/m^2 – type 2 diabetes has doubled in a decade (Amos et al, 1997) and consumes 10% of the health service budget. Diabetes is the most common cause of blindness in people of a working age and the major reason for renal failure. Amputation rates are increased 20-fold in people with diabetes. Coronary heart disease (CHD) is increased two- to four-fold in men and three- to five-fold in women.

The expectation that control of metabolic and risk factors might reduce chronic complications and not just acute symptoms was confirmed by evidence found in many randomised controlled trials controlling glycaemia, blood pressure and lipids. This research has led to the publication of *Guidelines for the Prevention of CHD* (Joint British Societies, 1998), the National Service Framework (NSF) for CHD (Department of Health, 2000) and the NSF for diabetes (DoH, 2002).

Evidence for glycaemia

The development and progression of microvascular complications is reduced by improved glycaemia (UK Prospective Diabetes Study group, 1998). Tight targets are set for fasting blood glucose levels (<7 mmol/l) and HbA_{1c} levels (7% without hypoglycaemia; American Diabetes Association, 2000) although only 50% achieved and 25% maintained these in the UKPDS intensive group (Turner et al, 1999). Reaching these goals is challenging early after the diagnosis of diabetes, and after having diabetes for five years, HbA_{1c} is usually >8% despite insulin (Diabetes UK, 2001). If achieved HbA_{1c} is considered (rather than intention-to-treat) there is no safe glycaemic threshold (Stratton et al, 2000); microangiopathic complications occur even with excellent blood glucose levels. In the UKPDS trial there was a trend towards fewer myocardial infarctions (-16%; p=0.052), but the epidemiological relationship between HbA_{1c} and CHD was strong (p<0.001), with no safe sugar level in diabetes, risk continuing down into glucose intolerance.

Evidence for hypertension

Hypertension is recognised as a risk factor for microvascular and macrovascular disease (including stroke and heart failure). Both are reduced by treatment (UKPDS study group, 1998). Those with diabetes who achieved low blood pressure had the best outcomes in the Hypertension Optimal Treatment (HOT) trial (Hasson et al, 1998), leading to targets of <140/<90 mmHg or even <130/<80 mmHg: currently around 50% of treated patients remain >160/95 mmHg (Colhoun et al, 1999). Many patients need two to four sets of hypotensive agents, and highest risk individuals (with nephropathy) are harder to control. Their polypharmacy poses many problems.

Evidence for lipid lowering

While a clear causal role of LDL-cholesterol for CHD is well accepted, treatment uptake had been poor (unlike treatment uptake for hypertension). After the pivotal Scandinavian Simvastatin Survival Study (4S) trial, treatment improved, but in 78 600 CHD patients (from a 2.4 million population) only half had cholesterol measured, half of these only being on treatment, and only a further half achieving cholesterol < 5 mmol/l (de Lusignan, 2003). Results in the 202 diabetes subset patients in the 4S trial (Pyorala et al, 1997) and in the extended numbers after applying revised American Diabetes Association diabetes and impaired fasting glucose criteria, were as good as in the population as a whole. The 6 000 people with diabetes in the Heart Protection Study (2003) had similar relative risk benefits as the whole group but at higher absolute risk. Similar benefits occurred in females, elderly people (80 years old at entry), and people with low initial cholesterol (3.5–5.0 mmol/l).

In the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm (ASCOT-LLA) there was a 36 % event reduction (p=0.0005) at 3.3 years in a low-risk population (placebo rate of 9 % at 10 years), also seen in people with diabetes (Sever et al, 2003).

In the GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study, 1600 patients were randomised to hospital or primary care for lipid management. Nearly all hospital patients reached the ATP-III LDL-cholesterol of < 2.6 mmol/l, achieving 50 % endpoint reductions compared to primary care patients (Athyros et al, 2002). Of the 313 diabetes patients, 30.3 % of those treated in primary care experienced a vascular event or died compared to 12.5 % in the structured care group; relative reductions of 52–68 % (Athyros et al, 2003).

We now have the results from the Collaborative AtoRvastatin Diabetes Study (CARDS) placebo-controlled trial of atorvastatin 10mg daily in the primary prevention of cardiovascular disease in 2838 patients aged 40–75 years with type 2 diabetes (Colhoun et al, 2004). They did not have raised cholesterol levels, but had at least one risk factor. The study was stopped over a year early because of clear benefit. Median baseline cholesterol and LDL-cholesterol levels were 5.4 and 3.0 mmol/l respectively. They fell by 26 and 40 % (1.4 and 1.2 mmol/l) respectively. The primary endpoint of cardiovascular events was reduced by 37 %, and stroke by 48 % on an intention-to-treat basis. The benefit was the same whether patients had higher or lower initial LDL-cholesterol levels, supporting the view that lowering LDL-cholesterol well below 2 mmol/l is appropriate.

Guidelines for management: National Service Frameworks

The NSF for CHD set out a 10-year programme for the prevention and management of CHD (DoH, 2000). Many of its aims apply also to atherosclerotic cerebrovascular disease. The

PAGE POINTS

1 CHD patients require ACE inhibitors, beta-blockers, warfarin or aspirin, as appropriate.

2 Substantial GMS contract points reflect the importance of improving cardiovascular, diabetes and metabolic care.

3 Intergrated team approaches, and patient education and empowerment are essential for best outcomes.

4 When risks have been reduced into normal ranges, further reductions will benefit high-risk individuals.

5 A CHD 'polypill' is attractive but due to potential, perceived or real side-effects, compliance may be limited.

NSF requires actions to reduce CHD risk factors and risk inequalities, and for GPs and primary care trusts to find, advise and treat cardiovascular disease patients and those at high risk.

For primary CHD prevention in patients >30% at 10 year risk (>15% at 10 year risk 'as resource allows') the following are required:

- smoking advice and nicotine replacement treatment
- information about modifiable risks (exercise, diet, alcohol, weight and diabetes)
- blood pressure <140/85 mmHg
- statins and diet: cholesterol <5 mmol/l (or 25% reduction, whichever is the greater), or LDL <3 (or 30% reduction, whichever is the greater)
- meticulous control of blood pressure and blood glucose in diabetes.

For patients with cardiovascular disease the following are additionally required:

- ACE inhibitors if a person has left ventricular dysfunction
- beta-blockade after acute myocardial infarction
- warfarin or aspirin if >60 years old with atrial fibrillation.

Various service models were proposed, and aspirin, beta-blocker and statin use were to reach 80–90% post myocardial infarction by April 2002.

The NSF for diabetes (DoH, 2002) built on these targets, adding glycaemic control and attention to microvascular risk.

Guidelines for management: General Medical Services contract

The General Medical Services (GMS) contract is practice-based, not GP-based. Team approaches in primary care that extend to secondary care to provide integrated care packages are already reflected in diabetes care. This has led to DoH recommendations on diabetes service design and roles of practice staff (DoH, 2002) while GMS documents (National Primary and Care Trust Development Programme, 2003) look at extending nursing roles.

Substantial points in the GMS contract maximise practice income and reflect improving cardiovascular, diabetes and metabolic care.

Targets lead to resource problems. What is possible in a standard or extended consultation? Weight, height, urinalysis (albumin/creatinine ratio), blood pressure, venesection (glucose, HbA_{1c}, fasting lipids, creatinine), retinoscopy with mydriasis and foot examination are needed yearly, and augmented if adrift from targets. Furthermore, patient education and empowerment are essential for best outcomes.

Targets now: where are we?

Targets in diabetes are demanding, and blood pressures remain high even in well-organised practices. Joseph et al (2003) studied 220 people with type 1 diabetes and a mean blood pressure of 129/77 mmHg. Of the total participants 26% were >140/90 mmHg, of whom 95% were treated, and 76% reached <140/80 mmHg. Results were worse in 1411 people with type 2 diabetes with mean of 147/82 mmHg; 51% were hypertensive, 90% were treated but only 52% reached target.

EuroAspire showed significant lipid treatment gaps with improvement over time, although recent UK studies (e.g. de Lusignan et al, 2003) show significant gaps in high risk groups.

To reach a HbA_{1c} <7% in type 2 patients will mean that 50% will need insulin therapy and if asymptomatic are likely to resist this. Already 3% of the population with diabetes consume about 10% of the NHS budget, while a further asymptomatic 3% of the population are undiagnosed.

Targets in the future: how can we get there?

Management requires reduction of all risks. When risks have been reduced into normal ranges, further reductions will benefit high-risk individuals (thus moderate lipids need to be reduced in people with hypertension and diabetes; Law and Wald, 2002). People with diabetes often require a statin (and some a fibrate), two to three drugs for hypertension, two to three hypoglycaemic agents (or insulin), aspirin, and perhaps other cardiovascular-acting agents. Therefore a 'polypill' was advocated, and epidemiologically has attractions (Wald and Law, 2003). While many agents have low or very low side-effects, potential, real or perceived side-effects are likely to limit 'polypill' compliance, which is the major issue with polypharmacy. Patients need

education about treatment needs, benefits achievable, and requirement for long-term treatment in asymptomatic conditions. Having reached individual and sensible agreed treatments and targets, then rationalisations to one or more 'oligo-pills' may have merit to concordance.

What are the important targets in agreed protocols with each patient? Microvascular disease requires blood pressure and glycaemic control. For macrovascular disease, LDL-cholesterol is dominant, blood pressure next; glycaemia gives substantially smaller rewards. In type 2 diabetes, macrovascular disease gives the most (and most severe) morbidity and premature mortality. LDL-cholesterol lowering is usually straightforward and can be achieved with a single tablet in these patients (although some need a fibrate as well).

Conclusions

Diabetes is becoming a worldwide epidemic which reduces life expectancy by 30%, and results in microvascular and macrovascular morbidity. The NSF for CHD and the NSF for diabetes have set targets for the next decade. Substantial lessening of macrovascular risk can be achieved but treatment falls short of this potential. The GMS contract sets clinical and management targets in primary care with financial incentives. Standards are likely to tighten over time, and apply to all.

Unfortunately, diabetes, hypertension, hyperlipidaemia, smoking, obesity, and existing cardiovascular disease need multiple therapies. Patient education is essential for treatment concordance, and a compact with patients for sensible targets (perhaps short of ideal) established. For macrovascular disease prevention, LDL-cholesterol reduction needs to be high on the list, usually ahead of blood pressure with glycaemia third. ■

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PAGE POINTS

1 Microvascular disease requires blood pressure and glycaemic control; macrovascular disease LDL-cholesterol control, followed by blood pressure.

2 Substantial lesening of macrovascular risk can be achieved but treatment falls short of this potential.

3 Standards are likely to tighten over time and apply to all.

4 A compact with patients for sensible targets (perhaps short of ideal) should be established.

5 LDL-cholesterol reduction needs to be a high priority in preventing macrovascular disease.