Diabetes control and beyond

A report from the Second National Conference for Intermediate Diabetes Care Teams – with a special focus on the role of GPSIs, which took place on 25 June 2008 at the National Motorcycle Museum, Birmingham. The event was supported by unrestricted educational grants from Accu-Chek and Novo Nordisk.

Introduction

Good glycaemic control is the cornerstone of diabetes management. Achieving this takes time and effort on the part of both the individual with the condition and their healthcare professional. In order to optimise glycaemic control, the right regimen must be employed and, more importantly, the right diagnosis must be made so that treatment can be as effective as possible. Confounding factors such as fatty liver disease also need to be taken into account. This conference, presented in association with the Primary Care Diabetes Society and *Diabetes & Primary Care*, provided a forum for discussion of the different types of diabetes, how the condition affects different individuals, and the practical realities of providing intermediate care in light of the revised NICE guidelines for type 2 diabetes.

The conference comprised three sessions looking at: clinical priorities in intermediate care; how to set up and organise a successful service; and what the future holds for diabetes care in the UK. Below follows a summary of each session.

Clinical priorities: what intermediate care needs to know

Insulin initiation and intensification in type 2 diabetes

Stephen Gough, Consultant Physician and Professor of Medicine, Birmingham

When considering the data from Wing's and Mitchell's (2007) review of the financial costs of diabetes, the message seems to be that the real cost comes when we don't get the treatment regimen quite right. Of all medications for the condition, insulin is responsible for approximately half of the costs (The Information Centre, 2007).

The UKPDS (United Kingdom Prospective Diabetes Study) showed that a one percentage point lowering of HbA_{1c} produces a significant reduction in micro- and macrovascular events, mortality, and complications – whatever the baseline HbA_{1c} level (Stratton et al, 2000). More is achieved by a reduction in HbA_{1c} from 12%–10% in a poorly controlled individual than by a reduction from 7.9%–7.5% in someone who is better controlled.

In the UK, despite a large number of individuals with type 2 diabetes who will eventually require insulin, initiation of the drug is delayed for 5 years in approximately 50% of these individuals (Rubino et al, 2007). Perhaps initiating insulin earlier in diabetes' natural history for these individuals may not only prevent future complications, but also prove more cost-effective in the long term.

There have been significant improvements in insulin treatment since 1922 (when animal insulins began to be used) through the human and analogue insulins, to inhaled insulin in 2006 – whose removal from the market was described by Professor Gough as a "tragedy". Improving adherence to treatment regimens is implicit in improving glycaemic control; and improving patient choice and lifestyle could lead to this.

Typically, when using insulin therapy, people with diabetes will gain weight (Diabetes Control and Complications Trial Research Group, 1988; UKPDS Group, 1998). However, data from the Treat-To-Target and PREDICTIVE (Predictable Results and Experience in Diabetes through Intensification and Control to Target: an International Variability Evaluation) studies indicate less weight gain with insulin detemir compared with NPH insulin (Hermansen et al, 2006; Lüddeke et al, 2007).

The joint ADA/EASD (American Diabetes Association/ European Association for the Study of Diabetes) guidelines on managing hyperglycaemia in type 2 diabetes (Nathan et al, 2006) suggest adding basal insulin as the first insulin therapy; however, this may not be best for all individuals. Indeed, Riddle et al's 2003 data show that 65% of patients fail to achieve HbA_{1c} targets and further intensification of therapy is needed. Perhaps, if the individual is likely to eventually end up on a mixture, then maybe starting them on it is best. Professor Gough recommends adding a suitable insulin for the individual, rather than basal insulin specifically.

Data from Monnier et al's 2003 study suggests that postprandial levels have a greater effect on HbA_{1c} than fasting plasma glucose. The ongoing 4-T (Treating To Target in Type 2 Diabetes) trial's primary aim was to compare the effect of a variety of insulin regimens on glycaemic control (Holman et al, 2007). The study's 1-year results indicated that most people would need more than one type of insulin to achieve their target HbA_{1c} level.

Diagnosing and understanding different types of diabetes

Simon Page, Consultant Physician and Endocrinologist, Nottingham

"There is more to diagnosing diabetes than simply deciding whether the individual has

type 1 or type 2 diabetes, or is insulin dependent or non insulin-dependent," began Dr Page.

With the changing demographics of the population, it will become more challenging to diagnose which type of diabetes a presenting individual may have. Increasing levels of obesity mean that type 2 diabetes will become more commonly diagnosed in younger individuals than previously; the emerging understanding of the natural history of monogenic forms of diabetes leading to beta-cell dysfunction (for example HNF1α and glucokinase MODY) and insulin action (for example type A insulin resistance or Rabson–Mendenhall Syndrome) will help doctors to consider such diagnoses in selected cases.

However, the decreasing age at which people are getting type 2 diabetes does not mean that this should be the immediate diagnosis. It is important to remember that type 1 diabetes can manifest at any age, as can latent autoimmune diabetes of adults (LADA). If an individual presents with a history of organ-specific autoimmune disease, then this could potentially indicate LADA rather than type 1 or type 2 diabetes.

The ADA's aetiological classification of diabetes lists over 60 of the most common forms of the condition (ADA, 2007). It is, therefore, quite apparent that there needs to be a greater awareness of the various types of diabetes, and other conditions which may cause similar symptoms, and it is important that these are kept in mind when an individual presents.

These different types can be identified, but only with careful and thorough investigation of an individual's personal and family history, circumstances and lifestyle, and if this does not provide a satisfactory diagnosis then refer for further investigation. "Never stop questioning", Dr Page ended.

Non-alcoholic fatty liver disease: Its management in type 2 diabetes

Mike Allison, Consultant Hepatologist, Cambridge

Non-alcoholic fatty liver disease (NAFLD) should be considered as part of the metabolic syndrome. Given this and the increasing prevalence of obesity and type 2 diabetes, fatty liver is now the most common cause of abnormal liver function tests. Equally, the presence of fatty liver is a predictor of the subsequent development of diabetes.

NAFLD can lead to progressive liver disease, with cirrhosis and, in some cases, primary liver cancer. The known risk factors for progressive liver disease in this context are obesity and diabetes. Commonly, liver enzymes are only mildly abnormal and individuals with NAFLD are usually asymptomatic, but may have fatigue, malaise and right upper quadrant discomfort.

Data from the Verona Diabetes Study (Muggeo et al, 1995) showed that 2.5 times more people with diabetes died from liver disease than people without diabetes. The vast majority of deaths in diabetes linked to liver problems are from NAFLD.

Investigating minor abnormalities of liver blood tests is, therefore, important, as the diagnosis of NAFLD can have prognostic implications; and other, significant and treatable, liver diseases can be uncovered.

Fortunately, treatments that benefit the metabolic syndrome and diabetes may also confer some benefits on NAFLD, for example weight loss (through diet, drugs or surgery), metformin, thiazolidinediones and statins. NAFLD should be managed by addressing all components of the metabolic syndrome.

If tests and examinations suggest NAFLD, referral for liver biopsy should be considered. In the event of advanced liver fibrosis, individuals will need hepatological surveillance.

Pre-pregnancy advice and counselling

Tristan Richardson, Consultant in Endocrinology and Diabetes, Bournemouth

"Based on the CEMACH [Confidential Enquiry into Maternal and Child Health] report, we are still not doing particularly well in terms of pregnancy care for women with diabetes in the UK," Dr Richardson began.

With increasing levels of obesity being responsible for a reduction in the age at which type 2 diabetes is occurring, increasing numbers of fertile women will be presenting with type 2 diabetes at a younger age – the Department of Health expects that 25% of girls between the ages of 11 and 15 years will be overweight by 2010 (Zaninotto et al, 2006). This worrying statistic also means that the number of women on blood glucose lowering therapies, and perhaps also on lipid-lowering and blood pressure lowering drugs, will increase, providing further complications to the pregnancy.

Many women with diabetes are unaware of the potentially lethal complications of becoming pregnant – fatal hypoglycaemia, hypoglycaemia unawareness, higher risk of diabetic ketoacidosis and accelerated progression of retinopathy and nephropathy. Furthermore, the risks to the foetus are increased as HbA_{1c} levels increase (in women with HbA_{1c}>8.5%, 22.4% of live births result in foetal malformation [Miller et al, 1981]); and preconception HbA_{1c}, rather than HbA_{1c} on presenting with pregnancy, is the predictor of congenital malformations as the woman may not discuss the pregnancy for some weeks following conception.

The CEMACH report (2007) indicated that 60% of women with type 1 diabetes and 75% of women with type 2 diabetes had not had pre-pregnancy counselling. Pre-pregnancy advice and counselling should start in the early teenage years in order to address this worrying statistic. Of those who had received counselling, 75% of women with type 1 diabetes and 60% of those with type 2 diabetes had sub-optimal diabetes control.

Organisation and training – making things work better?

Organisation and support of intermediate care in diabetes

Brian Karet, GPSI in Diabetes, Bradford

What is intermediate care and what does it do? It is a service that delivers high-quality care to individuals in the community who do not require secondary care resources but who do require more than can be provided solely by primary care. Dr Karet explained that intermediate care, above all, must be patient-centred and provided close to the patient. It also requires clear leadership, effective communication, a clear point of access, delivery by the multidisciplinary team and must be accreditable and auditable.

One-third of all diabetes centres have less than 2.0 whole time equivalent consultants (Royal College of Physicians, 2003). According to the Royal College of General Practitioners, these centres should be closed as this does not meet the recommended standards – "this clearly should not be the case," said Dr Karet.

Setting up an intermediate care team requires careful consideration and planning. A baseline audit needs to be conducted in order to assess satisfaction with the current service and whether it meets the ideal of 85% of individuals with type 2 diabetes and 50% of those

with type 1 diabetes being seen in primary care. Primary care would also ideally conduct all annual reviews. If primary care is found to be providing a good service then there may be no need for an intermediate service (or, "if it ain't broke, don't fix it"). If a service is needed then all stakeholders should be involved and the Diabetes Commissioning Toolkit used to set it up (Department of Health, 2006).

There are several benefits to setting up an intermediate care service. It improves continuity of care, communication between primary and secondary care, satisfaction and positive outcomes. Crucially, it also helps to individualise diabetes care. It can be difficult to maintain quality, hence a need for regular audit; there is also a risk of patients becoming political 'pawns' and there is an obvious risk of destabilisation of existing systems, said Dr Karet.

The key message is that if change is being considered, everyone needs to be involved, including the patient. The service being set up must be better than the previous service, it has to be auditable, securely funded and provide individualised care close to the patient.

Shared records – IT that can really work

John Parry, GP, Bradford

In 1998, Dr Parry and his colleagues agreed that they required a GP information-technology (IT) system that would enable all of the clinicians in the PCT to have access to a shared record, between primary and secondary care, to support each person with diabetes. The provision of such a record enables streamlined care to be delivered across a larger area.

The integrated system promotes electronic communications between primary and secondary care through the use of a shared clinical record with both structured data entries and free text. Dr Parry hopes that around 50% of referrals could be managed via this 'e-consultation' route, and that the system will reduce the number of full referrals to secondary care, in cases where a face-to-face consultation would not be more suitable for the patient.

Care is needed to ensure that patient consent to have their data stored in such a manner is properly obtained and the system is designed to accommodate patient wishes regarding sharing of sensitive data. Currently, Dr Parry has only had one individual refuse to have their data shared in this way. The long-term goal of this IT system is to provide a lifetime record for a lifetime condition.

Practice-based commissioning

Mark Davis, GP, Leeds

Dr Davis has had an instrumental role in setting up the Leodis Healthcare Limited Liability Partnership Commissioning Organisation. This organisation represents 130 GPs, serving approximately 200 000 individuals across over 28 practices. The board is made up of six GPs and two practice managers who are elected, plus a lay member and a chief executive who are appointed. Diabetes care is one of the priorities for Leodis Care, the provider arm of the organisation that went live in June. Leodis Care is also clinically led and has 91 shareholders.

Leodis Care takes on the functions of both the acute trust and the PCT to provide enhanced primary care services (to level 3) and is accredited by the PCT as a provider. The Leodis Care service is in line with the agreed Leeds diabetes model, which enables the delivery of high volume, low cost treatments in the community setting.

Three new GPSIs have been appointed by Leodis Care – this follows its aim to make sure that there are competent practitioners at each level of care. These individuals are selected by a consultant diabetologist and an existing GPSI, and the job description includes time for mentoring and education. They are part of the Leeds GPSI network and will work with diabetes specialist nurses and dietitians commissioned by the provider arm.

Dr Davis believes that having clinical engagement, as Leodis Healthcare Limited Liability Partnership Commissioning Organisation does, means that it will be easy to make practice-based commissioning work, and that practice-based commissioning will be instrumental in providing the right care in the right place at the right time.

The future of diabetes care

Management, monitoring and motivation: Using our experience to help people control their diabetes

Martin Hadley-Brown, GP, Thetford

In providing diabetes care, clinicians are trying to achieve minimum morbidity and mortality for all people with the condition, and minimise the impact on quality of life that can occur with diabetes. Recognising the varying needs of individuals at different stages of their diabetes is an everyday challenge for healthcare professionals. Not only this, but the cost of monitoring and drugs has also to be considered.

Monitoring HbA_{1c} alone is not enough. The discussion of what the results mean, and how to apply them to diabetes management is of paramount importance when encouraging patients to monitor their blood glucose levels.

Self-monitoring of blood glucose (SMBG) has an important role in empowering people with diabetes and educating them about their condition and potentially improving their quality of life (provided they don't feel that the frequent testing impacts on this). Patient selection, however, has to be considered. "Will the individual simply do it because he or she is being told that it will help, or will they use the results to change their habits and improve their control?"

Dr Hadley-Brown found that, in his area, he was only being informed of one out of every ten hypoglycaemic episodes requiring paramedic attention. SMBG can help identify night-time hypoglycaemia, or when an individual may be more susceptible. SMBG can also indicate the efficacy of a treatment regimen.

Dr Hadley-Brown believes that the most effective way to use SMBG is in intense bursts to begin with or to take scattered readings over a couple of weeks and then discuss the results' implications. The individual would then do this a few weeks later to assess any progress or decline in treatment efficacy.

It is important to clarify the reasoning behind asking a patient to perform SMBG and to include advice and education when discussing the results.

Is insulin pump therapy a realistic option?

Peter Hammond, Consultant in General Medicine, Harrogate

Reducing HbA_{1c} levels in people with type 1 diabetes to the levels in those without the condition has been shown to reduce the risk of complications such as retinopathy, but at the risk of increasing the frequency of severe hypoglycaemic episodes (Diabetes Control and Complications Trial Research Group, 1993).

Due to the nature of the way insulin is absorbed into the bloodstream, continuous subcutaneous insulin infusion is a more reliable method of delivering exogenous insulin

than subcutaneous injection, irrespective of the type of insulin used. Insulin pump therapy also confers a reduction in rates of hypoglycaemia over multiple daily injections (20 episode per year versus 100 episodes per year, respectively [Pickup and Sutton, 2008]). Data from Rodrigues et al's study (2005) showed that insulin pump therapy reduces HbA_{1c} and hypoglycaemic episodes in individuals with varying levels of underlying comorbidities as well as those without.

Insulin pump therapy has moved on in the last few decades: the backpack infuser was a prototype used in the 1960s (and included venous glucose monitoring in a "closed loop" system), while the original pumps of the early 1980s were the size of the current syringe drivers used in palliative care. These have been improved so that insulin pumps are now the size of a small mobile phone, with considerably improved technology.

Consideration for insulin pump initiation should be on an individual basis, as recommended by NICE (2008). The merits of individual versus group initiation should be considered and there should be 24-hour support and follow up available for all individuals. After a trial period of around 6 months there should be a discussion and decision on whether to continue insulin pump therapy. Education is also very important.

Staff initiating insulin pump therapy should be competent in the following:

- Assessing the individual's suitability.
- Providing education for pump therapy, including dietary advice.
- Enable an individual with diabetes to administer insulin using a pump.
- Provide ongoing support and dietary education to people on pump therapy.

It is estimated that approximately 20–30% of people with type 1 diabetes are suitable for insulin pump therapy, however, currently there is only an uptake of 1–2% in the UK.

Audit of the insulin pump service is difficult as there is, as yet, no centralised database of all insulin pump users. However, the standards for audit should include:

- Is NICE guidance followed?
- Is continuous subcutaneous insulin infusion considered for all eligible individuals?
- Are local clinical quality indicators for continuous subcutaneous insulin infusion met?
- Are side effects routinely measured?
- Is patient experience and satisfaction high?

Audit results from Dr Hammond's own clinic suggest a high level of satisfaction, with approximately 99% of insulin pump users wishing to continue with this treatment.

In order to provide an increase in the use of insulin pump therapy as NICE has recommended, there will need to be a considerable increase in the development of specialised insulin pump clinics and capacity to provide an insulin pump service.

New and emerging therapies

Neil Munro, GP and Associate Specialist in Diabetes, Surrey

Dr Munro summarised a number of existing and upcoming therapies for diabetes, as well as those in early investigational stages.

Important new classes of therapies are now available to clinicians in the UK (these will be the subject of a NICE rapid update due next year). The glucagon-like peptide-1 (GLP-1) analogues and dipeptidyl peptidase-4 (DPP-4) inhibitors act in different ways on the incretin system in order to stimulate insulin release and inhibit glucagon release.

Exenatide, a GLP-1 analogue, is resistant to degradation by DPP-4 and has been shown to reduce blood glucose levels while also reducing weight. It has been shown that over 26 weeks exenatide has a comparable blood glucose lowering effect to insulin glargine, but with an average reduction in weight of 4kg between the two agents. A weekly preparation of exenatide is being tested, with results suggesting a reduction in HbA_{1c} of nearly two percentage points.

Liraglutide, a GLP-1 analogue that is currently undergoing assessment for licensing, appears to reduce blood glucose and lipid levels and may potentially inhibit beta-cell death and possibly stimulate their growth. It is due to come to market in 2009.

The selective peroxisome proliferator-activated receptor modulators (SPPARMs) are currently in development and appear to be beneficial for lowering blood glucose levels and weight.

Dapagliflozin, a sodium-dependent glucose cotransporter is being studied for the treatment of both type 1 and type 2 diabetes.

The glucokinase activators are also being investigated as a possibile agent to reduce blood glucose levels in people with diabetes. These compounds stimulate beta-cells to increase their insulin secretion, and also increase hepatic uptake of glucose.

Gluconeogenesis is increased in people with diabetes, resulting in greater hepatic glucose production. The glucagon receptor antagonists are a novel class of compounds that block neogenesis, which should cause hepatic glucose production to slow down, but without decreasing hepatic glucose uptake, resulting in lower glucose levels in the blood.

Sirtuins may also be a novel treatment for diabetes (as well as an anti-ageing treatment). SIRT (silent mating type information regulation 2 homologue)-1 is found in the liver, muscles, white adipose tissue and regulates neogenesis. It may also stimulate beta-cell secretion in the pancreas.

Closely linked with the sirtuins are the STACS (SIRT-1 activating compounds). These polyphenols (including resveratrol, a substance found in red wine) activate sirtuin, resulting in reduced blood glucose. Studies have suggested that resveratrol may also be able to extend natural lifespan by 30%.

Another potential treatment for type 2 diabetes is a peptide that comes from the paradoxical frog – pseudin-2 – which may stimulate insulin secretion. ■

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