

The UKPDS: a diabetes nursing perspective

Marilyn Gallichan

ARTICLE POINTS

1 The UKPDS followed up more than 5000 patients from 23 centres for a median of 10 years.

2 The findings provide a powerful demonstration of the benefits of tighter blood pressure and blood glucose control in type 2 diabetes.

3 Evidence suggests that about 600,000 type 2 patients in the UK require more intensive treatment, closer follow-up and more frequent review.

4 The UKPDS is likely to have more impact on the nursing profession than any other professional group.

5 Several questions concerning diabetes care, however, remain unanswered.

KEY WORDS

- UKPDS
- Type 2 diabetes
- Diabetes nursing

Introduction

After 21 years of research, and an expenditure of £23 million, the findings of the United Kingdom Prospective Diabetes Study (UKPDS) have finally been released (UKPDS Group, 1998a,b). The publicity surrounding the announcement of the results of the world's largest and most comprehensive study of type 2 diabetes ensured that news of the UKPDS reached everyone working in the field of diabetes care, even if they had not heard of it before. But what difference will it make? This article outlines the UKPDS and summarises its main findings. It reflects upon them and discusses their possible impact upon diabetes care, especially in relation to diabetes nursing.

The United Kingdom Prospective Diabetes Study (UKPDS) was a randomised controlled trial of different therapies in type 2 diabetes, involving more than 5000 patients from 23 centres. Patients were allocated to the various treatment groups and followed from diagnosis for a median of 10 years.

The original aims were to determine whether improved glucose control would reduce the risk of long-term diabetic complications, and whether treatment with a first- or second-generation sulphonylurea, insulin or metformin had any specific advantage or disadvantage.

As 39% of patients entering the study were found to be hypertensive, a hypertension study was added, to examine whether tighter blood pressure control would reduce the risk of microvascular and macrovascular complications, and whether treatment with

a beta-blocker or an angiotensin-converting enzyme (ACE) inhibitor had any specific advantage or disadvantage.

The main findings

The main findings of the study are summarised in Table 1 and their implications for diabetes nursing are discussed below.

Blood glucose control

Improved blood glucose control in type 2 diabetes substantially decreased the risk of microvascular complications (retinopathy and nephropathy), but not macrovascular disease (e.g. myocardial infarction, stroke). There was no difference in overall risk reduction among the different intensive treatment groups, suggesting that improved glycaemic control was the principal factor, rather than any specific treatment. Only 3% of the patients studied were able to achieve

Table 1. Summary of the main findings of the UKPDS

- Intensive blood glucose control reduced the risk of diabetic complications, the greatest effect being on microvascular complications
- Sulphonylureas and insulin were similarly effective in reducing HbA_{1c}
- Tighter blood pressure control (144/82 mmHg) reduced the risk of both microvascular and macrovascular complications
- ACE inhibitors and beta-blockers were equally effective in lowering mean blood pressure in hypertensive patients and in reducing the risk of diabetic complications

Marilyn Gallichan is Diabetes Specialist Nurse at East Cornwall Hospital, Bodmin.

Table 2. Diabetes-related endpoints

- Sudden death
- Death from hyperglycaemia or hypoglycaemia
- Fatal or non-fatal myocardial infarction
- Angina
- Heart failure
- Stroke
- Renal failure
- Amputation (of at least one digit)
- Vitreous haemorrhage
- Retinopathy requiring photocoagulation
- Blindness in one eye
- Cataract extraction

satisfactory glycaemic control with dietary treatment alone.

Apart from the well-known risks of hypoglycaemia and weight gain, insulin and sulphonylureas were found to be safe treatments. There had been fears in the past that sulphonylureas might cause cardiac arrhythmia, and that insulin treatment could contribute to atheroma formation, but the study found no evidence to support either of these theories.

Although the glycated haemoglobin (HbA_{1c}) in the more intensively treated group was only approximately 1% lower, over 10 years, than in the group treated conventionally, this improvement was associated with a 25% reduction in the risk of microvascular complications and a 12% reduction in the risk of any diabetes-related endpoint (Table 2). All intensive treatments increased the risk of hypoglycaemia.

Blood pressure control

Tight blood pressure control in patients with hypertension and type 2 diabetes was shown to be even more beneficial than blood glucose control, in that it was associated with a significantly reduced risk of both microvascular and macrovascular complications.

It reduced the risk of any microvascular or macrovascular diabetes-related endpoint (Table 2) by 24%, compared with the 12% risk reduction obtained by improved blood glucose control. It reduced the risk of

diabetes-related death, complications related to diabetes, progression of diabetic retinopathy, and deterioration in visual acuity. Every 10mmHg reduction in systolic blood pressure was associated with a 12% reduction in risk.

The UKPDS found no evidence that either antihypertensive agent had any advantage or disadvantage, suggesting that blood pressure reduction in itself may be more important than the treatment used. This is particularly useful to know since ACE inhibitors are contraindicated in patients with renovascular disease which is not uncommon in type 2 diabetes.

Disease progression

The UKPDS also provided a striking demonstration of the relentless disease progression in type 2 diabetes in both the conventionally and the intensively treated groups.

Unanswered questions

Despite the enormous size and long duration of this study, some questions remain unanswered.

● **Will older patients benefit from improved blood pressure and blood glucose control?** The peak incidence of type 2 diabetes occurs between the ages of 65 and 69 years in men, and between 70 and 74 years in women (Stout, 1991). However, the patients recruited to the UKPDS were aged between 25 and 65 years, with a mean age of 53 years. Although it is reasonable to extrapolate the results, there is no clear evidence that the benefits of improved blood pressure and blood glucose control seen in the younger minority of patients with type 2 diabetes will apply to the older majority.

● **Will patients who are not overweight benefit from the addition of metformin to their treatment?** Metformin was shown to be a very advantageous primary treatment in obese patients, in that fewer diabetes-related endpoints occurred among those treated with this agent. However, the study did not show whether the same benefits would apply to patients who are not overweight.

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1 There was no evidence that sulphonylureas caused cardiac arrhythmias or that insulin contributed to atheroma formation.

2 A 1% reduction in HbA_{1c} reduced the risk of microvascular complications by 25%.

3 In hypertensive patients, tight blood pressure control was even more beneficial than blood glucose control.

4 The study findings highlighted the relentless progression of type 2 diabetes.

5 Only 3% of the study patients achieved satisfactory glycaemic control with diet alone.

PAGE POINTS

1 A significant shift in diabetes care from primary to secondary care has been predicted.

2 A national survey of general practices, however, found 'enormous enthusiasm' for diabetes care in this setting.

3 With appropriate resources and support, it should be possible to provide intensified treatment for type 2 diabetes in primary care.

4 The standard of diabetes care between individual practices varies widely at present.

5 The establishment of Primary Care Groups will provide the opportunity for standardising care within a group of practices, enabling all to reach the same high standard.

● **Is it safe to prescribe metformin and sulphonylureas in combination?** An unexpected and worrying finding was an increased risk of diabetes-related death in one small group, namely those in whom there was early addition of metformin to sulphonylurea treatment.

The study's chief investigators acknowledge that the addition of metformin in patients already being treated with sulphonylureas requires further study, but have reassured us that this unexpected finding was probably due to differences in the patients studied and the short follow-up period (5 years or less), and that there is no need to stop prescribing the two agents in combination.

● **How do the newer oral hypoglycaemic agents compare with each other and with older agents?** The UKPDS found differences in outcome between the different sulphonylureas. Patients treated with chlorpropamide had a significantly lower HbA_{1c} than those receiving glibenclamide; nevertheless, their systolic and diastolic blood pressures were significantly higher throughout the study, and there was significantly more progression of their retinopathy.

Outside the study newer, shorter-acting sulphonylureas (such as gliclazide) with a lower risk of hypoglycaemia have largely superseded these older agents. We do not know how the newer sulphonylureas and other new agents compare with each other or with older agents.

What difference will the UKPDS make?

Intensification of therapy

The UKPDS findings suggest that about 50% of patients with type 2 diabetes require intensification of their treatment. Based on the British Diabetic Association's estimated prevalence of type 2 diabetes (BDA, 1995), approximately 600,000 patients in the UK are currently in need of additional oral medication and/or insulin therapy, as well as closer follow-up and more frequent review.

The resource implications are enormous: who will provide this additional care and will there be a huge increase in the number of referrals to hospital diabetes teams?

Primary or secondary care?

Professor Rury Holman, one of the study's principal investigators, has predicted a significant shift of diabetes care from primary to secondary care (Legge, 1998). However, a recent national survey of general practices (Pierce, 1998) found 'enormous enthusiasm' for providing diabetes care in this setting.

Most general practices already have at least one GP and one practice nurse with a special interest in diabetes. With appropriate financial, educational and specialist nursing support, there is no reason why intensified treatment for patients with type 2 diabetes cannot be provided in primary care.

There is currently enormous variation in the standards of diabetes care between individual general practices. However, the formation of the new Primary Care Groups (PCGs) will provide an excellent opportunity for the standardisation of care within a group of practices, potentially enabling all of the practices to achieve the same high level of care.

Dr Mary Pierce, from the Department of General Practice and Primary Health Care, Imperial College School of Medicine (Pierce, 1998), has suggested that each PCG should nominate a GP and nurse who would be responsible for overseeing the delivery and audit of diabetes care.

Implications for nursing

The UKPDS is likely to have more impact on the nursing profession than on any other professional group. An essential component of intensified treatment, especially when insulin therapy is indicated, is one-to-one patient education, and this is almost exclusively the role of the nurse. There have been calls for the employment of more diabetes specialist nurses (DSNs) to cope with this immense workload (Sinclair, 1998); perhaps these additional nurses could be practice nurses with an interest in diabetes.

At present, supervision of the initiation of insulin treatment at home is usually the responsibility of the DSN. But even if they had sufficient time to cope with an increased workload, practice nurses and district nurses have traditionally had insufficient insulin-requiring type 2 patients

on their caseload to give them the necessary experience for competent practice.

However, as insulin therapy becomes more widespread, the situation may change, especially if the practice or district nurse sees patients from several general practices, as already happens in Bradford's local 'diabetes centres' (Hocking, 1999). The way forward may be for each PCG to be covered by one or two DSNs (depending on the size of the PCG) who would provide education, leadership and support to other nurses involved in diabetes care.

Changing role of the DSN

Since the introduction of DSNs, their role has gradually evolved so that, in general, their hands-on clinical role has diminished, and they have become more involved in the education of other healthcare providers. The publication of the UKPDS results has coincided with several other professional and government initiatives that will influence the changing role of the DSN (Table 3).

A joint working party was set up in 1998 to define the roles and educational requirements of diabetes nurses (Turner, Hicks and Padmore, 1998). The roles of nurses within PCGs is an issue that this group will need to consider.

DSNs are also eagerly awaiting the publication of Dr June Crown's second report which will examine:

'Whether health professionals other than existing prescribers might take on new roles in respect of... the arrangements under which medicines are prescribed, supplied and administered (not under group protocol)' (DoH, 1998a).

Many DSNs already make detailed prescribing recommendations to GPs and other physicians on a daily basis, concerning not only glucose monitoring equipment, but also the species, preparation, presentation and dosage of insulins, and the choice and dosage of oral hypoglycaemic agents. Some DSNs are even provided with pre-signed prescription pads (Cradock and Avery, 1998).

It is hoped that this report will recognise current practice, and open the way for DSNs with appropriate training and experience

to become legal prescribers of glucose monitoring equipment, oral hypoglycaemic agents, insulin, Hypostop, glucagon and, in light of the UKPDS, antihypertensive treatments. Perhaps a DSN with clinical, prescribing and educational roles, plus responsibility for audit of diabetes care, would conform to Tony Blair's vision of a nurse consultant (DoH, 1998b).

DIGAMI protocols post UKPDS

Since the UKPDS has shown sulphonylureas and insulin to be equally effective in reducing HbA_{1c} and in reducing the risk of complications, including myocardial infarction, there is a need to review the Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study protocols. The DIGAMI study, carried out in Sweden, recruited 620 post-myocardial infarction (post-MI) patients with diabetes (Malmberg, 1997). It demonstrated reduced long-term mortality in patients who received an insulin-glucose infusion followed by intensive insulin treatment, compared with a similar group receiving conventional treatment.

Despite flaws in the trial design (Frier, 1998), and recommendations to await the results of the second DIGAMI study, now in progress, many district hospitals have already instituted post-MI protocols involving the initiation of intensive insulin treatment (with major implications for nurses), even for those who already have excellent glycaemic control with oral agents.

In the UKPDS, which was a much larger study, there was no significant difference in the rate of fatal or non-fatal MI between those treated with insulin and those receiving oral hypoglycaemic agents. Indeed, the absolute risk (events per 1000 patient years) was slightly lower in the group treated with glibenclamide.

The UKPDS has provided strong evidence

PAGE POINTS

1 At present, supervision of initiation of insulin treatment at home is usually the DSN's responsibility.

2 Practice nurses and district nurses do not generally have enough experience of insulin-requiring type 2 patients to perform this role.

3 This situation may change as insulin treatment becomes more widespread.

4 It is suggested that one or two DSNs in each PCG could educate, lead and support other nurses involved in diabetes care.

5 It is hoped that DSNs will soon become legal prescribers of diabetic medicines and equipment.

6 DIGAMI protocols should be reviewed in the light of the findings of the UKPDS.

Table 3. Recent initiatives that will influence the DSN's role
● The Diabetes Nursing Joint Education Working Party
● The establishment of Primary Care Groups
● The Department of Health's review of prescribing, supply and administration of medicines
● The Department of Health's proposals to establish nurse consultant posts

PAGE POINTS

1 The finding that half the study patients already had tissue damage at diagnosis indicates a need for earlier diagnosis.

2 An international expert committee has recommended screening all adults at age 45, and every 3 years thereafter if results are normal.

3 Earlier and more frequent testing is recommended for high risk individuals.

4 The UKPDS has far-reaching implications for diabetes nursing.

for the benefits of improved control of blood glucose and blood pressure, but found no particular benefit in insulin compared with oral treatment.

Intensive, long-term insulin treatment for all post-MI diabetic patients has immense resource implications, especially for nurses. Is this the most effective use of DSN time?

Diabetes screening

The finding that about 50% of the patients recruited to the study already had diabetic tissue damage at diagnosis has emphasised the need for earlier diagnosis of type 2 diabetes.

In 1997, an international expert committee convened by the American Diabetes Association recommended that testing should be considered for all adults aged 45 years or over, and, if normal, repeated every 3 years (Shaw, 1997). The committee also suggested that earlier and more frequent testing should be considered for higher risk individuals, such as those listed in Table 4.

The British Diabetic Association has already begun a diabetes screening review, and will be involved in discussions with the National Screening Committee (BDA, 1998). The UKPDS will give added impetus to this project.

If these recommendations are implemented in the UK, as seems likely, this will also have implications for nursing, especially for practice nurses. The screening process will not simply be the collection of blood samples, but will also involve diabetes education for these higher risk patient groups.

Conclusion

Although the importance of control of blood glucose and blood pressure have been appreciated for many years, the results of this enormous study are a very powerful demonstration of the magnitude of the risks from hypertension and hyperglycaemia in type 2 diabetes, and the benefits of optimum treatment.

The UKPDS has provided a solid evidence base which will form the foundation for new policies and protocols, and has far-reaching implications for the organisation

Table 4. Groups at high risk of diabetes

- The obese
- People with first-degree relatives with diabetes
- Members of high-risk ethnic groups
- Women who have had gestational diabetes
- Those with hypertension or an abnormal lipid profile

and delivery of diabetes care, especially for diabetes nursing. ■

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