Management & prevention of type 2 diabetes

Pills as pals: Improving adherence in type 2 diabetes

Kenneth MacLeod, Consultant Physician, Exeter Postgraduate Medical Centre/ Senior Lecturer in Medicine, University of Exeter

The evidence-basis for effective prescribing in type 2 diabetes has grown steadily in recent years. We now have a fairly good idea what works best and why. We also know that the target of our interventions is, in most cases, more important than the method by which it is achieved. Blood pressure, LDL-cholesterol, triglyceride and HbA_{1c} are powerful independent risk factors for the vascular complications of diabetes and the more effectively we lower these variables the better the outcome. Any drug-specific benefits are largely dwarfed by the benefit associated by risk factor reduction per se.

The rigorous targets of modern therapy, however, are not easily achieved and combination therapy is the order of the day. Two or three drugs working together are required to achieve blood pressure targets of 140/85 mmHg or less in approximately 29 % of middle-aged patients with type 2 diabetes (UKPDS Group, 1998). Add to this the common need for a statin, an antiplatelet agent and two or more oral hypoglycaemic agents and the pill tally grows. The UKPDS 49 study (Turner et al, 1999) demonstrated that newly diagnosed patients followed for nine years had an increased requirement for multiple medical therapies over time in order to achieve an HbA_{1c} of <7 %. After three and nine years, only 50 % and 25 % of study subjects respectively achieved the goal of therapy using a single oral hypoglycaemic medication. Multiple drugs in combination are the rule and the daily drug diet for patients with type 2 diabetes can amount to a big swallow. This itself results in a further problem.

Patients worry about becoming resistant to drugs, about drugs interacting to neutralise potential benefits and about drugs losing activity with time. Patients become despondent in the face of an increasing diet of pills and this leads to reduced adherence, which decreases further as the complexity of the regimen increases. In the study by Krapek et al, a short, simple easy-to-administer, four-item questionnaire scale proved a robust and useful tool for assessing adherence. Poor adherence was found in 27 % of patients with diabetes and good adherence was associated with a significant reduction in HbA_{1c} (8.82 vs 7.60 %, respectively).

This suggests that education and effort aimed at maximising adherence has a significant role to play in improving outcomes in type 2 diabetes. Pills need to be seen as pals delivering important health benefits or insurance policies which pay out for patients with diabetes rather than their dependents. When we are reviewing treatment plans aimed to optimise outcome, the four simple questions of the Morisky scale may help us decide whether it is time to add something extra or concentrate on improving adherence with current pharmacopia.

UK Prospective Diabetes Study Group (1998) UKPDS 38. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes *British Medical Journal* **317**: 703–13
Turner RC, Cull CA, Frighi V, Holman RR (1999) UKPDS 49. Glycaemic control with diet, sulphonylurea, metformin and insulin therapy in patients with type 2 diabetes: progressive requirement for multiple therapies. *Journal of the American Medical Association* **281**: 2005–12

DIABETES CARE

Nonadherence and hospitalisation

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 This study examined the effects of nonadherence with oral antihyperglycaemic agents and subsequent hospitalisation.

2 Nine-hundred enrollees with type 2 diabetes, taking antihyperglycaemic agents, but who did not use insulin were examined. A medication possession ratio of <80 % was used to define nonadherence to treatment regimens.

3 Participants who did not adhere to their oral diabetes medication regimen in 2000 were at a higher risk of being hospitalised in the subsequent year (odds ratio 2.53; 95 % CI 1.38–4.64).

Lau DT, Nau DP (2004) Oral antihyperglycaemic medication nonadherence and susequent hospitalization among individuals with type 2 diabetes. Diabetes Care **27**: 2149–53

ANNALS OF PHARMACOTHERAPY

Medication adherence and associated HbA_{1c}

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 In people with diabetes, tight blood glucose control is correlated to reduced complications, and control is affected by medication adherence.

2 This study aimed to assess the relationship between blood glucose control (as HbA_{1c} levels) and type 2 diabetes patients' adherence to prescribed stable medication regimens by using a Morisky survey.

3 The Morisky medication adherence survey uses four questions to predict drug therapy adherence. Three-hundred-and-one patients were interviewed using Morisky scale to assess the relationship between medication adherence and HbA_{1c}, and the relationship was evaluated controlling for other variables.

4 Patients with Morisky scores of 0 or 1, 2, 3 and 4 had respective unadjusted mean HbA_{1c} values of 8.92 %, 8.67 %, 7.74 % and 7.60 %.

5 A score of ≥3 showed good adherence and was associated with a 10 % lower total HbA_{1c} (p=0.0003), adjusted for all other factors. Of participants, 73.1 % had a score of ≥3.

6 There was a significant association between HbA_{1c} and both duration of diabetes and related complications.

7 There was poor adherence in 26.9 % of patients.

8 Morisky score was related to HbA_{1c} – patients with a higher score had lower HbA_{1c} – therefore, the Morisky score may be useful for identifying patients with poor adherence.

Krapek K, King K, Warren SS et al (2004) Medication adherence and associated hemoglobin A_{1c} in type 2 diabetes. Annals of Pharmacotherapy **38**: 1357–62

'...inhaled insulin provides glycemic control comparable to a conventional insulin regimen in patients with type 2 diabetes...'

DIABETES CARE

Safety and efficacy of inhaled insulin vs s.c. insulin

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 This six-month randomised trial compared the effects of inhaled insulin with a conventional regimen on glycaemic control in people with type 2 diabetes previously managed with two or more daily injections of insulin.

2 One-hundred-and-forty-nine patients were randomised to premeal inhaled insulin plus a dose of Ultralente at bedtime, and 150 to subcutaneous insulin injections of mixed regular/NPH insulin at least twice daily.

3 HbA_{1c}, the primary end point, decreased from baseline levels similarly in both groups, -0.6 % with subcutaneous insulin and -0.7 % with inhaled insulin.

4 A greater number of patients on inhaled insulin achieved an HbA_{1c} <7.0 % compared to patients on subcutaneous insulin (46.9 % vs 31.7 % respectively; odds ratio 2.27, confidence interval 1.24–4.14).

5 There was a reduction in hypoglycaemic events, with slightly fewer events per month in patients taking inhaled insulin. There was no change in the number of severe hypoglycaemic events.

6 The inhaled insulin group experienced cough more frequently than the subcutaneous group.

7 Patient satisfaction was greater with inhaled insulin.

8 In this study of people with type 2 diabetes, inhaled insulin appears to be well tolerated and effective, with comparable glycaemic control to a conventional subcutaneous regimen.

Hollander PA, Hershon KS, Blonde L et al (2004) Efficacy and safety of inhaled insulin (Exubera) compared with subcutaneous insulin therapy in patients with type 2 diabetes. Diabetes Care **27**: 2356–62

'Half of those with diabetes still have have high cholesterol, a third have high blood pressure and a sixth smoke.'

DIABETOLOGIA

Stepwise screening is ineffective in general practice

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The reliability of population-based general practice screening algorithms for type 2 diabetes was examined in this study, as was the effectiveness of a proposed stepwise screening programme.

2 There were four steps in the screening programme: 1) a self-administered risk chart, posted to participants' GPs; 2) screening tests for HbA_{1c} and random blood glucose; 3) diagnostic procedure one, a fasting blood glucose; 4) and diagnostic procedure two, an oral glucose tolerance test.

3 World Health Organization 1999 criteria on abnormalities of glucose metabolism were used.

4 People (n=60 926) aged 40–69 years from 88 general practices participated and of these 11 263 had a high-risk risk score and attended screening tests (step 1 – positive).

5 Diagnostic tests were needed in 3390 (30.1%) of step 1 positive patients and of these 3390, 27.7 % (step 2 – positive) required an oral glucose tolerance test (step 3 – positive).

6 Positive test proportions matched those from data from a population-based survey from screening tests, thus the algorithms are reliable.

7 Only 19 % of prevalent undiagnosed diabetes was identified due to low participation of people at high-risk.

8 Screening for type 2 diabetes in general practice using population-based mail-distribution is ineffective even though algorithms are reliable because of the lack of participation from many people at high risk.

Christensen JO, Sandbæk A, Lauritzen T et al (2004) Population-based stepwise screening for unrecognised type 2 diabetes is ineffective in general practice despite reliable algorithms. Diabetologia **47**: 1566–73

AMERICAN JOURNAL OF EPIDEMIOLOGY

CV risk factor levels in diabetes over 30 years

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 This study looked at the 30-year trends in blood pressure, total cholesterol and smoking levels in adults with diabetes in America, using the National Health and Nutrition Examination Surveys from 1971–2000.

2 Mean changes per year were calculated for: blood pressure, total cholesterol, prevalence of high blood pressure (≥140/≥90 mmHg), high total cholesterol (≥5.17 mmol/l) and smoking.

3 Mean total cholesterol level decreased to 5.48mmol/l from 5.95mmol/l between 1971–1974 and 1999–2000 surveys and the decrease was greater in those aged 60–74 than 20–59 years.

4 During this time, mean blood pressure fell to 134/72 from 146/86 mmHg.

5 The percentage of people with high cholesterol decreased to 55 % from 72 %; percentage with high blood pressure decreased to 37 % from 64 %; and smoking decreased to 17 % from 32 %.
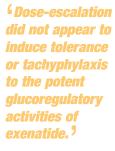
6 These trends are encouraging. However, half of those with diabetes still have high cholesterol, a third high blood pressure and a sixth smoke.

Imperatore G, Cadwell BL, Geiss L et al (2004) Thirty-year trends in cardiovascular risk factor levels among US adults with diabetes. American Journal of Epidemiology **160**: 531–39

'Hyperglycaemia is common in people with type 2 diabetes and may interfere with many daily activities though adverse effects on cognitive function and mood.'

DIABETES CARE

Mood and cognitive function altered by acute hyperglycaemia

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The effects of acute hyperglycaemia on mood and cognitive function were studied in 20 people with type 2 diabetes.

2 Patients were aged 53–72 years with average known duration of diabetes of 5.9 years, average HbA$_{1c}$ 7.5 %, average body mass index 29.8 kg/m^2 and on a variety of treatments from insulin to antidiabetic medication.

3 Patients were tested on information processing, working memory, immediate and delayed memory, and attention while their arterialised blood glucose was maintained at 4.5 mmol/l (euglycaemia) or 16.5 mmol/l (hyperglycaemia) on two occasions using a hyperinsulinemic glucose clamp. Patients also completed a mood questionnaire during these periods.

4 During periods of hyperglycaemia, working memory and some aspects of attention were impaired, and information processing was slowed.

5 Patients showed increased anxiety and sadness, reduced energetic arousal and were significantly more dysphoric when they were hyperglycaemic.

6 Cognitive function was impaired and mood depressed in people with type 2 diabetes when they had acute hyperglycaemia. As hyperglycaemia is common in this group, it may interfere with daily activities.

Sommerfield AJ, Deary IJ, Frier BM (2004) Acute hyperglycemia alters mood state and impairs cognitive performance in people with type 2 diabetes. Diabetes Care **27**: 2335–40

'Dose-escalation did not appear to induce tolerance or tachyphylaxis to the potent glucoregulatory activities of exenatide.'

DIABETES/METABOLISM RESEARCH AND REVIEWS

Dose-limiting effects of exenatide reduced with dose escalation

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 Dose escalation was used in this study to see if the dose-limiting side-effects of exenatide (nausea and vomiting at therapeutic dose) could be reduced by inducing tolerance.

2 Ninety-nine of the 123 people with type 2 diabetes participating completed this triple-blind, multicentre study.

3 Exenatide was started at 0.02 µg/ kg three times daily in those in the exenatide-primed arm and was then increased by 0.02 µg/kg every three days for 35 days. The exenatide-naïve patients received placebo three times daily for 35 days. All patients were then given 0.24 µg/kg exenatide three times a day for three days.

4 Nausea and vomiting was experienced by 27 % of people in the exenatide-primed arm and 56 % in the exenatide-naive arm (p=0.0018).

5 Over the 35 days before maximum exenatide dose (0.24 µg/kg), fasting serum glucose declined progressively in the exenatide-primed arm but was unchanged in those on placebo.

6 The proportion of patients reporting nausea and vomiting side-effects with exenatide use was reduced by gradual dose escalation.

Fineman MS, Shen LZ, Taylor K et al (2004) Effectiveness of progressive dose-escalation of exenatide (exendin-4) in reducing dose-limiting side effects in subjects with type 2 diabetes. Diabetes/ Metabolism Research and Reviews **20**: 411–17

ARCHIVES OF INTERNAL MEDICINE

Social and other risk factors for T2D: the Whitehall II study

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 This prospective occupational cohort study aimed to establish the relationship between social inequalities, psychosocial factors and health behaviours to type 2 diabetes incidence.

2 A questionnaire was used to ascertain diagnosis of diabetes in 10 308 civil servants, aged between 35 and 55, at phase 1 (baseline) and at follow-up phases. The dates of phases 1 to 5 were 1985–1988, 1989, 1992–1993, 1995 and 1997–1999 respectively. In phases 3 and 5, glucose tolerance tests were carried out.

3 There was a lower incidence of diabetes in civil servants in higher employment grades compared to lower grades.

4 Risk factors for diabetes and body mass index were as expected in this cohort.

5 Effort-reward imbalance was the only psychosocial risk factor examined that was related to diabetes incidence in men.

6 Depression, as determined by the General Health Questionnaire, was related to impaired glucose tolerance and incidence of diabetes, even after adjustments for confounding factors.

7 After adjustment for conventional risk factors, in men there was still a significant inverse relationship between social status and diabetes incidence, partly explained by health behaviours and other risk factors.

8 Effort-reward balance is associated with increased risk of type 2 diabetes.

Kumari M, Head J, Marmot M (2004) Prospective study of social and other risk factors for incidence of type 2 diabetes in the Whitehall II study. Archives of Internal Medicine **164:** 1873–80