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Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial

DAFNE Study Group

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Abstract

Objectives To evaluate whether a course teaching flexible intensive insulin treatment combining dietary freedom and insulin adjustment can improve both glycaemic control and quality of life in type 1 diabetes.

Design Randomised design with participants either attending training immediately (immediate DAFNE) or acting as waiting list controls and attending "delayed DAFNE" training 6 months later.

Setting Secondary care diabetes clinics in three English health districts.

Participants 169 adults with type 1 diabetes and moderate or poor glycaemic control.

Main outcome measures Glycated haemoglobin (HbA_{1c}), severe hypoglycaemia, impact of diabetes on quality of life (ADDQoL).

Results At 6 months, HbA_{1c} was significantly better in immediate DAFNE patients (mean 8.4%) than in delayed DAFNE patients (9.4%) ($t=6.1$, $P<0.0001$). The impact of diabetes on dietary freedom was significantly improved in immediate DAFNE patients compared with delayed DAFNE patients ($t=-5.4$, $P<0.0001$), as was the impact of diabetes on overall quality of life ($t=2.9$, $P<0.01$). General wellbeing and treatment satisfaction were also significantly improved, but severe hypoglycaemia, weight, and lipids remained unchanged. Improvements in "present quality of life" did not reach significance at 6 months but were significant by 1 year.

Conclusion Skills training promoting dietary freedom improved quality of life and glycaemic control in people with type 1 diabetes without worsening severe hypoglycaemia or cardiovascular risk. This approach has the potential to enable more people to adopt intensive insulin treatment and is worthy of further investigation.

Introduction

Self management is essential to successful treatment of type 1 diabetes, yet few patients alter their insulin from day to day or achieve the degree of glycaemic control known to be ideal.¹ The diabetes control and complications trial showed the long term benefits of strict glycaemic control.² However, the intensive approach used in the trial involved frequent outpatient visits with close supervision of insulin dose adjustment and has not been incorporated into general diabetes practice. The increased risk of severe hypoglycaemia in the diabetes control and complications trial may be unacceptable, and the staffing ratio of around three patients to each healthcare professional is beyond the scope of most healthcare systems.

Other reasons why intensified treatment has not been widely adopted may exist. Clinicians usually propose treatment goals formulated from the medical perspective, focusing on biomedical outcomes, whereas patients are more concerned about the immediate demands of treatment and how to integrate these into daily life.³ Diabetes and its treatment have a negative impact on quality of life, particularly in terms of dietary restrictions imposed by traditional treatment regimens.^{4,5} It has been argued elsewhere that an approach in which intensive insulin management is used to increase dietary freedom is likely to improve quality of life,⁶ as well as biomedical outcomes, and may result in its wider adoption.

For over 20 years, a team from Düsseldorf has used a five day structured inpatient training programme in intensive insulin treatment, producing sustained improvements in glycaemic control without increasing severe hypoglycaemia.⁷ Participants are taught to match insulin doses to their food choices, while keeping their blood glucose close to normal. Patients maintain this behaviour with minimal support from healthcare professionals. We tested this approach in a UK multicentre randomised controlled study, the dose adjustment for normal eating (DAFNE) trial.

Methods

Participants and protocol—We recruited patients attending hospital diabetes clinics in Sheffield, Northumbria, and London. We considered patients to be eligible if they were aged over 18 years with clinical features of type 1 diabetes, moderate or poor glycaemic control (HbA_{1c} 7.5-12%), and duration of diabetes of more than two years without advanced complications. We randomised volunteers either to attend a five day training course delivered in groups of six to eight participants in each centre (immediate DAFNE) or to continue to receive usual care for six months as controls and then attend a course (delayed DAFNE) (see bmj.com for details).

The skills course—The course provided the skills to enable patients to replace insulin by matching it to desired carbohydrate intake on a meal by meal basis. This was taught as a five day (Monday to Friday) outpatient programme (see bmj.com for details).

Primary outcomes—A central laboratory measured glycated haemoglobin (HbA_{1c}). The top of the reference range for people without diabetes was 6.1%. Patients recorded severe hypoglycaemic episodes (episodes causing coma or requiring the assistance of another person) in diaries. We used the audit of diabetes-dependent quality of life (ADDQoL) questionnaire to measure the impact of diabetes on quality of life. This tool produces a diabetes impact rating



See web extra for details of study group members

Table 1 Primary outcomes: differences between immediate DAFNE and delayed DAFNE groups at six months. Values are means (standard deviations) unless stated otherwise

Group	Glycated haemoglobin (HbA _{1c} , %)	Proportion of participants experiencing severe hypoglycaemia in previous six months* (No (%))	Audit of diabetes-dependent quality of life (ADDQoL)		
			Weighted impact of diabetes on "freedom to eat as I wish"†	Average weighted impact of diabetes on quality of life†	Present quality of life‡
Immediate DAFNE:					
Baseline	9.4 (1.2)	15/68 (22)	-4.8 (2.9)	-2.0 (1.6)	1.0 (0.9)
Six months	8.4 (1.2)	12/67 (18)	-1.8 (2.3)	-1.6 (1.6)	1.3 (0.9)
Delayed DAFNE:					
Baseline	9.3 (1.1)	8/72 (11)	-4.0 (2.9)	-1.9 (1.3)	1.1 (0.8)
Six months	9.4 (1.3)	11/72 (15)	-4.0 (2.8)	-1.9 (1.4)	1.0 (1.1)
Difference between groups at six months					
Mean (95% CI)	1.0 (0.5 to 1.4)	-	2.2 (1.3 to 3.1)§	0.4 (-0.1 to 0.9)§	0.3 (-0.1 to 0.6)§
Statistical values	t=4.4, P<0.0001	χ ² =0.17, P=0.68	t=-5.4, P<0.0001	t=2.9, P<0.01	t=1.7, P=0.095

*Percent of participants; χ² test performed for differences between groups at six months.

†Scored from -9 (maximum negative impact) to +9 (maximum positive impact).

‡Scored from -3 (extremely bad) to +3 (excellent); 0=neither good nor bad, 1=good, 2=very good.

§Confidence interval should be interpreted with caution as variables were transformed before parametric analysis was performed but natural data are reported.

weighted by importance for 18 potentially applicable domains of life, including dietary freedom.⁵ Scores for single domains and the composite average weighted impact can range from -9 (maximum negative impact of diabetes) to +9 (maximum positive impact of diabetes). The questionnaire also includes a single item measuring "present quality of life," with scores ranging from -3 (extremely bad) to +3 (excellent).

Secondary outcomes—We measured satisfaction with treatment and perceived frequency of hyperglycaemia and hypoglycaemia⁸ and psychological wellbeing.⁹ We also measured weight, blood pressure, serum cholesterol, triglycerides, and high density lipoprotein cholesterol. Patients recorded in their diaries the number of insulin injections, total insulin dose, and blood glucose monitoring.

Results

Participant flow and follow up

One hundred and sixty nine patients were randomised, but 29 dropped out (27 before participating in a course) (see bmj.com). Thus we analysed data from 140 participants at six months and data from 68 immediate DAFNE participants at 12 months.

Participants' mean age was 40 (SD 9) years, and the mean duration of diabetes was 16.6 (9.6) years. Seventy six (56%) participants were women. Fifty two (37%) participants had retinopathy, 19 (13%) had peripheral neuropathy, and two had nephropathy. No significant differences existed between the two groups at baseline in terms of participants' characteristics or primary or secondary endpoints or between the immediate DAFNE group at baseline and the delayed DAFNE group at six months (that is, immediately pre-course).

Primary endpoints

Table 1 shows the primary outcome data. At six months, HbA_{1c} was significantly improved in the immediate DAFNE group compared with the delayed DAFNE group (clinically important mean improvement of 1%). We found no significant difference in the proportion of the immediate DAFNE group who experienced severe hypoglycaemia compared with the delayed DAFNE group. For the quality of life measures, the immediate DAFNE group showed significant improvements in the negative impact of diabetes on dietary freedom in particular ("freedom to eat as I wish score") and the impact on quality of life in general

Table 2 Secondary outcomes: differences between immediate DAFNE and delayed DAFNE groups at six months. Values are means (SDs) unless stated otherwise

Group	W-BQ12	Diabetes treatment satisfaction questionnaire (DTSQ)		Cardiovascular risk factors				
	Total wellbeing*	Total satisfaction*	Perceived frequency† of:		Weight (kg)	Total cholesterol (mmol/l)	HDL cholesterol (mmol/l)	Triglycerides (mmol/l)
			Hyperglycaemia	Hypoglycaemia				
Immediate DAFNE:								
Baseline	20.94 (5.8)	22.88 (6.2)	3.57 (1.4)	2.04 (1.2)	80.5 (16.7)	5.2 (0.9)	1.5 (0.4)	1.5 (0.9)
6 months	24.34 (5.7)	31.58 (3.9)	2.90 (1.4)	2.16 (1.3)	81.5 (16.9)	5.1 (0.8)	1.6 (0.4)	1.4 (0.7)
Delayed DAFNE:								
Baseline	21.09 (5.8)	23.21 (5.8)	3.60 (1.6)	2.12 (1.4)	77.4 (13.4)	4.9 (0.8)	1.5 (0.5)	1.5 (0.9)
6 months	21.37 (5.5)	22.82 (6.0)	4.03 (1.3)	2.40 (1.3)	77.3 (13.4)	5.0 (1.0)	1.5 (0.3)	1.5 (0.9)
Difference between groups at six months								
Mean (95% CI)	2.98 (1.06 to 4.89)	8.75 (7.02 to 10.48)‡	-1.13 (-1.59 to -0.67)	-0.23 (-0.68 to 0.21)	4.18 (-0.90 to 9.27)	0.15 (-0.16 to 0.45)	0.09 (-0.01 to 0.22)	0.12 (-0.41 to 0.17)
Statistical values	t=3.1, P<0.01	t=-10.3, P<0.0001	t=-4.88, P<0.0001	t=-1.0, P=0.31	t=1.6, P=0.11	t=0.95, P=0.34	t=1.46, P=0.14	t=0.83, P=0.41

HDL=high density lipoprotein; W-BQ12=12-item wellbeing questionnaire.

*Scored from 0 to 36; a higher score indicates greater wellbeing or satisfaction.

†Scored from 0 to 6; a higher score indicates greater perceived frequency of hyperglycaemia or hypoglycaemia.

‡Confidence interval should be interpreted with caution as variable was transformed before parametric analysis was performed but natural data are reported.

What is already known on this topic

Current treatment of type 1 diabetes fails to engage many patients in intensive self management and is associated with poor glycaemic outcomes and impaired quality of life

An approach to intensive insulin treatment in which participants match insulin dose to unrestricted food choices has been developed in Germany

This approach has been shown to lead to sustained improvements in glycaemic control but has not been widely adopted elsewhere

What this study adds

Training in flexible, intensive insulin treatment can improve glycaemic control in the United Kingdom

This approach also leads to significant improvements in treatment satisfaction, psychological wellbeing, and quality of life measures

(average weighted impact score) compared with the delayed DAFNE group.

The qualitative data collected illustrate the personal importance of these improvements to participants. Examples included “I now feel able to travel abroad without worry about not eating or eating on time” (change in average weighted impact score=0.28); “I have found my whole lifestyle and outlook on life has improved” (change=1.08); and “Because I now have better control than ever before I will hopefully cut back on any complications I may have incurred in the future” (change=2.74). The difference in “present quality of life” did not reach significance at six months.

Twelve months after training (assessed only in immediate DAFNE) HbA_{1c} remained significantly improved compared with baseline (mean difference 0.5%, 95% confidence interval 0.2 to -0.9; $t=3.5$, $P=0.001$). One quarter (16/67) of participants maintained a fall in HbA_{1c} of >1.5%, and four (6%) showed a rise of >1.5%. The number of participants experiencing severe hypoglycaemia did not increase significantly.

Improvements in the impact of diabetes on dietary freedom were maintained between six and 12 months (see bmj.com), as was the impact of diabetes on quality of life in general (average weighted impact score). “Present quality of life” also continued to improve and reached significance by one year.

Secondary outcomes

We found a significant improvement in psychological wellbeing and satisfaction with treatment at six months and a significant decrease in perceived frequency of hyperglycaemia (table 2). Cardiovascular risk factors and perceived frequency of hypoglycaemia did not change significantly in either group across the trial.

Discussion

Our data show that a structured training course (designed to maintain glucose control while enabling dietary freedom) teaching self management skills to patients with type 1 diabetes was effective over the short term in a British healthcare setting. DAFNE training significantly improved glycosylated haemoglobin, with no significant increase in severe hypoglycaemia.

The training also produced sustained positive effects on quality of life, satisfaction with treatment, and psychological wellbeing, despite an increase in the number of insulin injections and encouragement to increase blood glucose monitoring. Despite increased dietary freedom (as shown by responses to the “freedom to eat as I wish” item in the audit of diabetes-dependent quality of life), we observed no deterioration in cardiovascular risk factors. These results are encouraging and suggest that people with established diabetes, when taught appropriate skills, will intensify management of their diabetes and that this can be (and perhaps needs to be) associated with improved quality of life.

As with any randomised controlled trial, a crucial question is how readily the observed effects might be transferred to the wider population of adults with type 1 diabetes. The participants may have been atypical in the impact of diabetes on their quality of life, their dissatisfaction with current treatment, and their willingness to inject insulin five times a day. However, the fact that a third of patients attending routine hospital clinics expressed interest in participating after a single unsolicited advertisement is encouraging. Other studies have shown that current management of diabetes in the United Kingdom leads to negative effects on quality of life comparable to those seen in our participants at baseline, indicating that many patients with type 1 diabetes stand to benefit from a more flexible approach with increased dietary freedom.^{4,5}

The fall in HbA_{1c} at the six month analysis was comparable to that reported in similar interventions. The Dusseldorf group reported a lower HbA_{1c} (by 1.5%) one year after training, compared with group teaching of diabetes related information alone,¹⁰ and similar improvements have been maintained for three and six years.^{11,12} We did not see this in the immediate DAFNE group at one year; HbA_{1c} rose slightly from the six month value, although it remained statistically and clinically significantly lower than at baseline. The UK participants had a longer duration of diabetes than those in earlier studies and were discharged to a healthcare system unfamiliar with this approach. We avoided proactive follow up by DAFNE educators in order to evaluate the effects of the course alone. We might have expected some deterioration without specific reinforcement or feedback of HbA_{1c}.

As with any complex intervention, it is difficult to know which aspects contributed to its effect. Control participants received only usual care, and it is possible that the benefits were merely the result of patients spending five days intensively focusing on diabetes, receiving attention from enthusiastic educators. However, the diabetes control and complications trial was unable to show any improvements in quality of life,² and evidence in type 2 diabetes suggests that improvements in audit of diabetes-dependent quality of life scores and HbA_{1c} cannot be achieved by empowerment alone.¹³

Not everyone with type 1 diabetes will wish to undertake intensive insulin treatment, even without dietary restrictions; some will prefer a simpler regimen with routine meal timing and fewer injections. Such options will still be needed. Nevertheless, as the only way of reducing microvascular disease currently is by maintaining tight glycaemic control, we need better ways of enabling patients to intensify their insulin

treatment. This study builds on earlier work and shows that skills training and unrestricted food choices can be applied successfully across different healthcare systems. The follow up of our patients was, however, relatively short. We now need to establish whether similar results can be achieved in routine care and devise ways of sustaining improvement in glycaemic control.

Conclusion

We have shown, in a group of volunteers, that skills training in insulin adjustment that provides patients with the ability to fit diabetes into their lives rather than their lives into diabetes improves quality of life and glycaemic control in the short term. The DAFNE approach has the potential to reduce the incidence of microvascular complications and thereby protect quality of life in the long term, as well as the short term, and is worthy of further investigation.

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Association between psychological symptoms in adults and growth in early life: longitudinal follow up study

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Abstract

Objectives To test the hypothesis that birth weight for gestational age and weight gain in early childhood have a long term association with psychological distress in adults.

Design Longitudinal study of 1958 birth cohort followed to age 42 years.

Setting Population based birth cohort study.

Participants 9731 cohort members with valid perinatal, postnatal, and adult data.

Main outcome measures Malaise inventory scores measured at ages 23, 33, and 42 years. Generalised estimating equations approach used to analyse repeated measures.

Results Psychological distress score was inversely related to birthweight z score and weight gain from birth to the age of 7 years. A unit increase in birthweight z score or childhood weight gain was associated with a mean reduction in psychological distress score of 0.10 (95% confidence interval 0.05 to 0.14) and 0.06 (0.02 to 0.10), respectively. Birth weight

and weight gain were also inversely related to the odds of having a high level of psychological distress, with odds ratios being 0.90 (0.85 to 0.95) and 0.93 (0.89 to 0.98), respectively.

Conclusions Psychological health in adults is related to fetal growth and growth in early childhood.

Introduction

Although numerous studies have shown that fetal and postnatal growth can affect psychological and developmental outcomes in children, it is uncertain whether the influence persists into adulthood. We tested the hypothesis that small size at birth and slow growth in early childhood are associated with higher levels of psychological distress in adults.

Methods

Participants

The national child development study (NCDS) is a cohort study of about 17 000 people born in England, Wales, and Scotland in one week in March 1958. Data



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