A Psychoeducational Program to Restore Hypoglycemia Awareness: The DAFNE-HART Pilot Study

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OBJECTIVE

To develop and pilot a novel intervention addressing motivational and cognitive barriers to avoiding hypoglycemia in people with type 1 diabetes and persistent impaired awareness of hypoglycemia (IAH) despite training in flexible insulin therapy.

RESEARCH DESIGN AND METHODS

A 6-week intervention using motivational interviewing and cognitive behavioral techniques was designed. Diabetes educators were trained and supported in its delivery to 23 people with IAH (Gold score ≥4).

RESULTS

Twelve months postcourse, hypoglycemia awareness had improved ($P < 0.001$). Median (range) rates of severe hypoglycemia (SH) fell from 3 (0–104) to 0 (0–3) per person per year ($P < 0.0001$) and moderate from 14 (0–100) to 0 (0–18) per person per 6 weeks ($P < 0.001$). Worry and behavior around hyperglycemia improved. HbA_{1c} was unchanged.

CONCLUSIONS

A pilot intervention targeting motivation and cognitions around hypoglycemia engaged patients with resistant IAH and recurrent SH and was associated with significant improvement, supporting the hypothesis that these factors underpin problematic hypoglycemia.

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Hypoglycemia and fear of hypoglycemia remain major barriers to achieving optimal glucose control and quality of life for people with type 1 diabetes. Structured education in flexible insulin therapy (e.g., the U.K.'s Dose Adjustment for Normal Eating [DAFNE]) and/or use of insulin pump therapy reduces severe hypoglycemia (SH) (1), but some continue to experience impaired awareness of hypoglycemia (IAH) with high rates of SH, their problematic hypoglycemia resistant to intervention. We hypothesized that many such people have motivational and cognitive barriers to hypoglycemia avoidance and resolution of IAH. We designed and piloted an intervention using motivational interviewing and cognitive behavioral theory targeting these barriers.

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RESEARCH DESIGN AND METHODS

An intervention, teaching aids, curriculum, and manual (DAFNE-Hypoglycemia Awareness Restoration Training [DAFNE-HART]) were designed by a clinical psychologist, doctors, educators, and patient representatives. It revised relevant sections from DAFNE and interventions targeting problematic hypoglycemia (2,3). Participants were taught to look for hypoglycemia cues and consider their own causes and consequences of IAH and how to reduce hypoglycemia exposure. The educational material was presented within a motivational interviewing framework to support behavior change and minimize resistance. Cognitive behavioral techniques were used to identify and restructure unhelpful thoughts such as needing to "soldier on" through episodes, underestimating the consequences of hypoglycemia, and worrying excessively about intermittent hyperglycemia. In three weekly full-day group sessions, theories about hypoglycemia and awareness were reviewed, the concept of a "body scan" (a structured guide to find subjective cues to blood glucose concentration) was taught, insulin action was revised, and theories linking thoughts with behavior were explored, supporting patients to recognize and challenge their own cognitions around hypoglycemia. "Homework" used home glucose monitoring to test the learning and, during weeks 4 and 5, try newly learned skills/strategies, with scheduled individual face-to-face and telephone support. A final full-day group session focused on relapse prevention.

Twenty-four people (12 male) with type 1 diabetes, using DAFNE principles for insulin self-adjustment, with persistent IAH assessed clinically and scoring $\geq$4 on the Gold score, in which patients rate their awareness of hypoglycemia from 1 ("I am always aware of my hypoglycemia") to 7 ("I am never aware of my hypoglycemia") (4), were recruited. Hypoglycemia experience, including self-report of SH (hypoglycemia [$<$63 mg/dL/3.5 mmol/L] that could not be self-treated, requiring assistance), over the preceding 12 months and moderate hypoglycemia ($<$63 mg/dL/3.5 mmol/L, self-treated but disrupting daily activity) over the last 6 weeks, hypoglycemia awareness and burden (Gold, Clarke, and Ryan scores) (4–6), and mood and self-care behaviors around glucose control were documented by questionnaires, including the Hospital Anxiety and Depression Scale (HADS) (7), the Problem Areas In Diabetes (PAID) Questionnaire (8), the Hypoglycemia Fear Survey II (9), and the Hyperglycemia Avoidance Score (courtesy of L. Gonder-Frederick, University of Virginia, Charlottesville, VA), and glycated hemoglobin (HbA_{1c}) was measured. At baseline and 3 months postcourse, up to 6 days continuous glucose monitoring (CGM) (Medtronic, Inc.) was performed. Participants were reassessed 12 months postcourse.

Five DAFNE educators (specialist nurses and dietitians) were trained in the curriculum and relevant psychological skills in a 2-day workshop. They delivered four courses with weekly supervision (face-to-face, telephone, and e-mail) from a clinical psychologist.

The protocol was approved by the National Research Ethics Committee London. King's College Hospital NHS Foundation Trust sponsored the protocol. Participants provided written informed consent. Data were compared using Student *t*, Wilcoxon signed rank (nonparametric variables), and χ^2 or related samples McNemar (categorical variables or when including episodes of no incidence) tests, using IBM SSPS version 4. Hypoglycemia in valid CGM data was defined as $<$3 mmol/L for $\geq$20 min. $P < 0.05$ was considered significant.

RESULTS

All participants completed courses. One missed follow-up and two returned only SH and HbA_{1c} data at 12 months. Mean ($\pm$SD) age for the 23 completers was 54.4 $\pm$ 7.9 years; diabetes duration 30.7 $\pm$ 11.9 years; time since DAFNE 7.1 $\pm$ 4.1 years. Fifteen were using twice-daily background and premeal quick-acting insulin injections, and eight were using insulin pumps. None had renal impairment, hypoadrenalism, hypothyroidism, or growth hormone deficiency. All described themselves as having "impaired awareness," not experiencing symptoms with a blood glucose $<$54 mg/dL (3 mmol/L) when awake. Their SH in the year before, defined above, included 14 participants reporting unconsciousness (0–30/participant, median 1), 3 attending emergency departments (one 24 times), and 3 admissions. Nineteen people answering the question reported an additional six ambulance call-outs.

Twelve months postcourse, rates of severe and moderate hypoglycemia fell (Table 1). Seventeen participants reported no further SH ($P < 0.0001$). Measures of awareness improved (Table 1), with 9 of 20 regaining awareness with Gold and/or Clarke scores $<$4 ($P <$ 0.04 vs. baseline for either) and 8 of 20 reporting no episodes of hypoglycemia ($<$54 mg/dL) without symptoms vs. none precourse (Table 1). Behavior scores around hyperglycemia avoidance improved and worry scores about hyperglycemia reduced significantly. Worries around hypoglycemia tended to reduce. PAID scores improved. HbA_{1c} did not deteriorate.

At 3 months postcourse, the duration of daytime hypoglycemia on CGM fell and hypoglycemia burden (Ryan score) fell from equivalent to people registering for islet transplantation toward that of routine clinic populations (6).

CONCLUSIONS

The main defense against hypoglycemia during insulin treatment of type 1 diabetes is subjective awareness of a falling blood glucose, impaired awareness being associated with a sixfold increase in SH (10). Awareness can be improved by hypoglycemia avoidance (e.g., 11). Retraining patients in insulin self-adjustment (1), training in hypoglycemia recognition and avoidance, as provided by Blood Glucose Awareness Training (BGAT) and Hypoglycemia Anticipation, Awareness and Treatment Training (HAATT) (2,3), and insulin pump therapy (12) all reduce SH. DAFNE restores awareness to 43% of people with IAH (1). Continuous glucose sensing reduces SH without restoring awareness (13). A group of people remain resistant to interventions to restore hypoglycemia awareness and continue to experience SH.

Table 1—Pre- and postcourse demographic and biomedical data and anxiety, depression, and behavioral scores

	Baseline	12 months	*n* with paired data	*P* value
HbA_{1c} (%)	7.8 ± 1.2	7.8 ± 1.1	23	0.80
HbA_{1c} (mmol/mol)	62.0 ± 13.3	61.8 ± 11.7	23	0.861
SH, events per patient per year, median (range)	3.0 (0–104)	0 (0–3)		<0.0001[1]
Moderate hypoglycemia per patient per 6 weeks, median (range)	14 (0–100)	1 (0–18)	21	<0.001[1]
Gold score[4]	5.6 ± 1.4	4.5 ± 1.9	20	<0.029[2]
Clarke score[5]	5.4 ± 1.2	3.8 ± 1.8	20	<0.001[2]
HADS, anxiety[6]	5.9 ± 5.0	6.1 ± 5.7	21	0.82
HADS, depression[7]	5.2 ± 4.6	5.1 ± 4.7	21	0.87
PAID[8]	30.7 ± 22.6	24.7 ± 20.5	21	0.006
Adult low blood glucose score (behavior)[9]	2.7 ± 0.7	2.3 ± 1.0	21	0.39
Adult low blood glucose score (worry)[1,10]	2.7 ± 0.9	2.5 ± 1.0	21	0.1
Hyperglycemia avoidance score (behavior)[11]	2.51 ± 0.54	2.26 ± 0.52	21	0.037
Hyperglycemia avoidance score (worry)[12]	2.78 ± 0.80	2.31 ± 0.92	21	0.004
	Baseline	3 months		
Ryan score[13]	948 ± 831	372 ± 466	20	<0.001[3]
CGM mean duration episodes <3 mmol/L, day[14]	83 ± 59	32 ± 43	17	0.001[2]
CGM mean duration <3 mmol/L, min, night[14]	76 ± 106	123 ± 159	17	0.30[2]

[1]Wilcoxon signed rank test. [2]Related samples McNemar test. [3]χ^2 test. [4]Range 1 (always aware) to 7 (never aware). Score ≥4 indicates impaired awareness (4). [5]Score ≥4 indicates impaired awareness (5). [6]Score >8 indicates clinically relevant psychological distress (7). [7]Score >8 indicates clinically relevant psychological distress (7). [8]PAID score ≥40 indicates clinically relevant psychological distress (8). [9]Behavior subscore, mean ± SD in adult European population with type 1 diabetes: 0.98 ± 0.67 (from Hypoglycemia Fear Survey II, Adult Scoring Manual for adult versions, courtesy of L. Gonder-Frederick; also see reference 9). [10]Worry subscale, mean ± SD in adult European population with type 1 diabetes = 1.22 ± 0.84 (from Hypoglycemia Fear Survey II, Adult Scoring Manual for adult versions, courtesy of L. Gonder-Frederick; also see reference 9). [11]Behavior subscale, mean ± SD from 500 U.S. adult patients with type 1 diabetes = 1.95 ± 1.04, data from L. Gonder-Frederick. [12]Worry subscale, mean ± SD from 500 U.S. adults with type 1 diabetes = 1.48 ± 1.06, data from L. Gonder-Frederick. [13]Ryan score, hypoglycemia burden <423 considered to indicate hypoglycemia not a major clinical concern. Median score in patients with unawareness 850 (25th to 75th interquartile range [IQR] 485–1,228) and in those with awareness 91 (25th to 75th IQR 23–203). Score in patients presenting for islet transplantation 722 (25th to 75th IQR 432–1,980) (6). [14]CGM: day, 6:00 A.M. to midnight; night, midnight to 6:00 A.M.

We hypothesized that these patients have cognitive and motivational barriers to hypoglycemia avoidance, based on neuroimaging showing different activation in reward pathways during hypoglycemia in people with IAH, qualitative research describing patient beliefs about hypoglycemia awareness, and clinical audit (14–16). Although we cannot attribute outcomes to particular elements of the intervention from this uncontrolled pilot, the preliminary evidence of reduced hypoglycemia and increased awareness suggests that addressing beliefs and motivation is very relevant to this population.

The novelty of our intervention lies in the following: first, in training diabetes educators in motivational interviewing to address resistance around behavior change that might have occurred and did occur; second, in providing educators with basic cognitive behavioral therapy skills to provide patients with an explicit model of how thoughts can influence behavior; and third, in offering accessible visual metaphors (e.g., the ostrich burying its head in the sand for underestimation of the impact of hypoglycemia) by which patients could identify their own "thinking traps" and explore alternatives. Although additional technologies addressing hypoglycemia, such as pumps, sensors, and islet transplantation, were available at our centers, few of our patients had accessed them; some were more open to these after DAFNE-HART. This, together with the evidence of behavior change described above, suggests that people may be more ready to use additional technologies to address problematic hypoglycemia if motivational factors to regain awareness are addressed.

These data are from a pilot: small patient numbers and not controlled for the impact of the educational element alone. The early evidence of success supports a key role for cognitive barriers in apparently intractable IAH. The intervention now requires refinement, based on participant (patients and educators) experiences, and testing in a randomized, controlled trial. It has potential to be delivered at scale by existing diabetes educators, trained and supported by clinical psychologists, rather than requiring referral to a new cadre of diabetes-experienced psychologists. Meanwhile, we conclude that motivational and cognitive barriers to hypoglycemia avoidance in people with significantly impaired hypoglycemia awareness are legitimate therapeutic targets.

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Author Contributions. N.d.Z. designed the intervention and supervised its implementation and drafted the manuscript. M.S. conducted the analysis of the 12-month data and assisted in its collection. H.R., P.C., and J.E. contributed to the protocol and the construction of the intervention and its delivery and analyzed data. C.G., S.B., and S.H. contributed to the protocol and the construction of the intervention and its delivery. E.B. analyzed data and created the database for the analysis. S.A.A. contributed to the protocol and the construction of the intervention and its delivery, created the database for the analysis, and drafted the manuscript. All the listed authors made substantial contributions to the study design, performance, and/or analysis and contributed to and/or reviewed and revised the final manuscript. S.A.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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References

1. Hopkins D, Lawrence I, Mansell P, et al. Improved biomedical and psychological outcomes 1 year after structured education in flexible insulin therapy for people with type 1 diabetes: the U.K. DAFNE experience. Diabetes Care 2012;35:1638–1642
2. Cox DJ, Gonder-Frederick L, Polonsky W, Schlundt D, Kovatchev B, Clarke W. Blood glucose awareness training (BGAT-2): long-term benefits. Diabetes Care 2001;24:637–642
3. Cox DJ, Kovatchev B, Koev D, et al. Hypoglycemia anticipation, awareness and treatment training (HAATT) reduces occurrence of severe hypoglycemia among adults with type 1 diabetes mellitus. Int J Behav Med 2004;11:212–218
4. Gold AE, MacLeod KM, Frier BM. Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia. Diabetes Care 1994;17:697–703
5. Clarke WL, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemic frequency and associated symptoms. Diabetes Care 1995;18:517–522
6. Ryan EA, Shandro T, Green K, et al. Assessment of the severity of hypoglycemia and glycemic lability in type 1 diabetic subjects undergoing islet transplantation. Diabetes 2004;53:955–962
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–370
8. Polonsky WH, Anderson BJ, Lohrer PA, et al. Assessment of diabetes-related distress. Diabetes Care 1995;18:754–760
9. Gonder-Frederick LA, Schmidt KM, Vajda KA, et al. Psychometric properties of the hypoglycemia fear survey-ii for adults with type 1 diabetes. Diabetes Care 2011;34:801–806
10. Geddes J, Schopman JE, Zammitt NN, Frier BM. Prevalence of impaired awareness of hypoglycaemia in adults with type 1 diabetes. Diabet Med 2008;25:501–504
11. Cranston I, Lomas J, Maran A, Macdonald I, Amiel SA. Restoration of hypoglycaemia awareness in patients with long-duration insulin-dependent diabetes. Lancet 1994;344:283–287
12. Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabet Med 2008;25:765–774
13. Ly TT, Nicholas JA, Retterath A, Lim EM, Davis EA, Jones TW. Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. JAMA 2013;310:1240–1247
14. Dunn JT, Cranston I, Marsden PK, Amiel SA, Reed LJ. Attenuation of amydgala and frontal cortical responses to low blood glucose concentration in asymptomatic hypoglycemia in type 1 diabetes: a new player in hypoglycemia unawareness? Diabetes 2007;56:2766–2773
15. Smith CB, Choudhary P, Pernet A, Hopkins D, Amiel SA. Hypoglycemia unawareness is associated with reduced adherence to therapeutic decisions in patients with type 1 diabetes: evidence from a clinical audit. Diabetes Care 2009;32:1196–1198
16. Rogers HA, de Zoysa N, Amiel SA. Patient experience of hypoglycaemia unawareness in type 1 diabetes: are patients appropriately concerned? Diabet Med 2012;29:321–327