Stress Management Improves Long-Term Glycemic Control in Type 2 Diabetes

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OBJECTIVE — There is conflicting evidence regarding the utility of stress management training in the treatment of diabetes. The few studies that have shown a therapeutic effect of stress management have used time-intensive individual therapy. Unfortunately, widespread use of such interventions is not practical. The aim of the present investigation is to determine whether a cost-effective, group-based stress management training program can improve glucose metabolism in patients with type 2 diabetes and to determine whether a particular subset of patients is more likely to get positive results.

RESEARCH DESIGN AND METHODS — Patients with type 2 diabetes were randomized to undergo a five-session group diabetes education program with or without stress management training. Participants ($n = 108$) were followed for 1 year, during which HbA_{1c} tests and questionnaires assessing perceived stress, anxiety, and psychological health were administered at regular intervals to evaluate treatment effects.

RESULTS — Stress management training was associated with a small (0.5%) but significant reduction in HbA_{1c}. Compliance with the treatment regimen decreased over time but was similar to that seen in patients receiving stress management for other reasons in the clinic. Trait anxiety (a measure of stable individual differences in anxiety proneness) did not predict response to treatment, showing that highly anxious patients did not derive more benefit from training.

CONCLUSIONS — The current results indicate that a cost-effective, group stress management program in a "real-world" setting can result in clinically significant benefits for patients with type 2 diabetes.

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It is widely recognized that stress may have negative effects on health and that patients with type 2 diabetes may be at increased risk. The experience of stress is associated with the release of counterregulatory hormones and energy mobilization, often resulting in elevated glucose levels (1,2). In addition, stress can disrupt diabetes control indirectly through effects on diet, exercise, and other self-care behaviors. Several studies have demonstrated a relationship of stress to glycemic control in samples of patients with type 2 diabetes (3,4). Stress can be managed through the use of behavioral stress management programs or through the administration of anxiolytic medications. Both types of interventions have been reported to improve glycemic control in patients with type 2 diabetes (5–7).

Stress management training typically includes progressive muscle relaxation (PMR) with or without electromyography biofeedback, mental imagery, diaphragmatic breathing, and instructions on how to modify the physiologic, cognitive, and behavioral responses to stress. Stress management and PMR have been shown to be very effective in the treatment of disorders with a psychophysiological component such as migraine (7,8). Surwit and Feinglos (9) conducted the first controlled investigation of PMR on a sample of 12 patients with type 2 diabetes who had reported frequent stress hyperglycemia. The intervention group showed a reduction in incremental glucose area from preintervention to postintervention, whereas this change was not seen in the control group. However, because the PMR training and the evaluations were conducted during a single week-long hospitalization, the generalizability of these findings to outpatient treatment was not known. Furthermore, in a follow-up study, these investigators were unable to find similar effects in a sample of patients with type 1 diabetes (10).

Since that study, several investigations have examined the effects of stress management training or discrete components of stress management training in an outpatient setting, but the findings have been inconclusive. Positive effects on blood glucose have been reported in two case studies (11,12) and in a randomized trial of 18 adults undergoing individualized stress management including biofeedback-assisted PMR (5,13). However, other studies have failed to demonstrate a therapeutic effect of stress management on diabetes control (14,15).

There may be several explanations for these mixed results. First, there may be a particular subset of diabetes patients who benefit from stress management training. For example, this intervention may be particularly suited to individuals who are stress-responsive or highly anxious. Lane et al. (5) showed that highly anxious patients with type 2 diabetes benefited more from PMR or benzodiazepines than low-anxious patients with type 2 diabetes. In contrast, two recent studies observed that low-anxious and stress-unresponsive subjects improved more after stress management training (15,16) than highly anxious patients. Therefore, the question

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Abbreviations: DASI, Duke Activity Status Index; GHQ, General Health Questionnaire; PMR, progressive muscle relaxation; PSS, Perceived Stress Scale; STAI, Spielberger State-Trait Anxiety Inventory.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

remains whether such training is helpful for all diabetic patients and, if not, who is more likely to benefit. Second, the mixed results may also be due to differences in treatment methods. Many of the behavioral interventions that have been used successfully were staff-intensive, using costly one-to-one techniques (11–16), whereas the results of group training have been mixed (5,15). Individual training is not practical in the average clinical setting because of poor third-party reimbursement for psychotherapeutic interventions. The purpose of the present investigation is to examine the efficacy and feasibility of cost-effective outpatient group-stress management training. In addition, we will examine whether stress management is more effective in treating high-anxious than low-anxious diabetic patients.

RESEARCH DESIGN AND METHODS

Subjects

Patients with type 2 diabetes were recruited through local advertisements, Duke University Outpatient Clinics, general medical facilities, and diabetes education and support groups. The study was advertised as a study of stress and diabetes. Subjects were men and women aged ≥30 years with diabetes currently managed with diet, exercise, and/or oral medications. Exclusion criteria included prior training in relaxation or stress management, current use of a psychoactive drug, current psychiatric treatment, use of insulin, inability to read and write English, pregnancy or lactation, and significant ongoing acute or chronic illness or other conditions that would preclude the donation of the required amount of blood. A total of 113 volunteers were enrolled and completed the initial assessment. Five subjects were excluded due to normal glucose tolerance at baseline. Their data are not included in the analyses (see Table 1 for sample characteristics). From the sample of 108 patients, 72 completed the study (38 treatment and 34 control subjects). The greatest attrition occurred during the treatment phase, when 26 patients dropped out or were terminated (5 control and 11 treatment subjects were terminated for missing classes, the remaining 6 treatment and 4 control subjects withdrew for other reasons, including illness, work commitments, and need to begin insulin therapy).

Table 1—*Sample characteristics at baseline*

	Control group (n = 48)	Intervention group (n = 60)
Sex		
Male	27 (56.2)	36 (60)
Female	21 (43.8)	24 (40)
Race		
Caucasian	42 (87.5)	51 (85)
African-American	5 (10.4)	9 (15)
Asian	1 (2.1)	0
Age (years)	58.33 ± 11.33	56.53 ± 10.15
BMI (kg/m^2)	30.40 ± 7.74	29.49 ± 5.85
HbA_{1c} (%)	7.54 ± 1.34	8.14 ± 2.11*
STAI-trait	43.73 ± 12.59	42.55 ± 9.98
STAI-state	33.98 ± 8.99	36.58 ± 11.47
GHQ	51.25 ± 10.07	52.58 ± 9.49
PSS	23.98 ± 9.67	24.67 ± 8.35
DASI	40.67 ± 16.29	39.23 ± 14.72
Daily caloric intake	1,872.96 ± 487.23	2,172.95 ± 669.90*

Data are n (%) or means ± SD. *$P < 0.05$

Measures

The main outcome variable in this study is HbA_{1c} as an indicator of metabolic control over the previous 3 months. In addition, perceived stress, anxiety, and psychological health were assessed by self-reported instruments as indicators of the effectiveness of stress management training in reducing stress and anxiety or improving psychological health. Additional data were collected on weight, physical activity, and diet because changes in these variables could potentially confound an improvement in HbA_{1c} otherwise attributed to stress management training. Data were collected with the following instruments and techniques.

HbA_{1c}. Over the course of the study, HbA_{1c} was measured by three different methods: *1*) affinity chromatography (17), *2*) radioimmunoassay (reference range 4.1–5.7 [Hitachi 911 chemistry analyzer; Roche Diagnostics, Branchburg, NJ], and *3*) ion exchange high-performance liquid chromatography (reference range 4.3–6.0 [A_{1c} 2.2 Plus; Tosoh Medics, Foster City, CA]). All tests were conducted in a standard clinical laboratory that has met the requirements to be certified by the National Glycohemoglobin Standardization Program. The results determined by the high-performance liquid chromatography method were mathematically converted to the immunoassay equivalents before data analysis. Because no mathematical conversion was available for the results obtained with affinity chromatography, all analyses were rerun, excluding the patients in whom HbA_{1c} levels were assessed with chromatography (n = 10). No major differences in results were found, and it was decided to leave these patients in the analyses that are reported.

Spielberger State-Trait Anxiety Inventory. The Spielberger State-Trait Anxiety Inventory (STAI) (18) is a well-known tool used to measure current level of tension and apprehension (Y-1 form-state anxiety) as well as relatively stable anxiety proneness (Y-2 form-trait anxiety). The 20 items are scored on a scale of 0–3; higher scores indicated higher anxiety.

Perceived Stress Scale. The Perceived Stress Scale (PSS) (19) is a 14-item self-report tool used to provide a global measure of perceived stress in daily life. Responses range from "never" to "very often" on a 5-point scale. The PSS has adequate reliability and correlates well with life-events stress measures and social anxiety.

General Health Questionnaire. The 20-item version of the General Health Questionnaire (GHQ) (20) is a widely used self-report psychiatric screening instrument that covers all aspects of adjustment and feelings of distress.

BMI. BMI was calculated as body weight (kg) divided by height (m) squared.

Dietary intake. Total daily energy and macronutrient intake was assessed and analyzed by a research nutritionist (regis-

tered dietitian) using 24-h recall methodology and the nutrient analysis program Nutritionist IV (First Data Bank, San Bruno, CA). The recall methodology was supplemented by questioning and a professional estimate of the validity of the data using the previous day's intake. In cases in which the intake was determined to be atypical, the recall focused on the most recent typical day.

Duke Activity Status Index. The Duke Activity Status Index (DASI) (21) is a 12-item scale that was developed as a brief self-report measure to assess exercise capacity using questions about activities of daily living. This tool has been validated against a physiologic measure of functional ability and addresses activities that encompass the major aspects of physical function: ambulation, personal care, sexual function, recreation, and household tasks. The tool allows for estimates of change in exercise ability and physical limitations.

Procedures

For all procedures of this year-long study, patients visited Duke University Medical Center. During the trial, subjects remained under the care of their personal physicians. At baseline, informed consent was obtained; HbA_{1c}, STAI, PSS, GHQ, DASI, diet, and weight were measured; and subjects were randomized to either the control or treatment group. In the first 2 months of the study, subjects were required to attend five weekly small-group class sessions that provided general diabetes education (control group) or stress management plus diabetes education (treatment group). Missing more than one session (treatment) or more than two sessions (control) resulted in study termination. At 2, 4, 6, and 12 months after baseline, subjects returned for the assessment of HbA_{1c}, STAI (state only), PSS, GHQ, DASI, diet, and weight. All study procedures were approved by the Duke University Medical Center Institutional Review Board.

Diabetes education. Diabetes education consisted of five 30-min sessions focusing on general diabetes facts (such as physiology, prevalence, signs, and symptoms), complications (including foot, eye, and dental care), healthy eating, and generic information about treatments for diabetes. The classes were developed to match the nonspecific factors of treatment but also as a control intervention, the goal of which was to avoid influencing the subjects' routine diabetes care. There was no discussion of specific recommendations or glycemic goals.

Stress management program. The stress management program included *1*) PMR training, *2*) instruction in the use of cognitive and behavioral skills to recognize and reduce physiological stress levels (such as recognition of major stressors in life, guided imagery, thought-stopping, and deep breathing), and *3*) education on the health consequences of stress. PMR training consisted of consecutively tensing and relaxing a prescribed set of muscle groups in the body, starting with the feet and progressing through the head, with specific attention paid to tense regions of the body. This was combined with techniques such as deep breathing and mental imagery to produce a deeply relaxed state of mind and body.

Participants learned PMR in part by listening to an audiotape during each group session. They also were instructed to practice muscle relaxation at home twice daily with the aid of the tape, first using a longer exercise to achieve relaxation and then advancing to a shorter version. After some skill was developed, mini-practices were introduced. Mini-practices are a brief, 30-s version of a PMR session using deep breathing and imagery. Incorporation of mini-practices into daily life to maintain a relaxed body and mind is the eventual goal of PMR training. Participants were instructed to engage in mini-practices at least two times per hour. During the last session, patients were encouraged to keep practicing their acquired skills during the remainder of the study. This included incorporating frequent mini-practices into daily life as well using the relaxation tape during more stressful periods or when their skills needed enhancement. During the follow-up assessments at 2, 4, 6, and 12 months, patients in the treatment group were asked how many times they listened to the audiotape in a typical week and how frequently they used mini-practices in a typical day.

RESULTS

— Preliminary analyses (Student's *t* test) compared the treatment and control groups at baseline. These comparisons revealed that, despite random assignment to group, there was a significant difference between treatment and control in baseline levels of the primary outcome variable, HbA_{1c}. The two groups also differed in total caloric intake at baseline. However, treatment and control groups did not differ at baseline in BMI or in scores for the STAI-trait, STAI-state, GHQ, DASI, or PSS. Group means and standard deviations are presented in Table 1.

Given the baseline difference in HbA_{1c}, the decision was made to use covariance analysis to test the effects of treatment on glucose regulation. The repeated measures of HbA_{1c} collected at 2, 4, 6, and 12 months of study were analyzed with treatment group and time included as the two factors and with baseline levels included as a covariate to adjust for initial differences. Heterogeneity of regression was tested to ensure the validity of the covariance adjustment. Statistical analysis was accomplished using SAS Proc Mixed (version 8.0; SAS Institute, Cary, NC).

The initial mixed-model regression analysis included the four replicate measures as levels of a class variable to provide an omnibus test of differences among time points. This analysis revealed a significant interaction of treatment group and time $F(3,219) = 2.56$, $P = 0.05$), indicating that the effects of treatment varied over time. The regression analysis provided estimated values for HbA_{1c} for the two groups and the four follow-up points, and these values are shown in Fig. 1. A second mixed-design regression analysis was performed to test the linear effects of time after treatment and the interaction of time with treatment. This analysis also revealed a significant group-by-time interaction [$F(1,223) = 5.39$, $P = 0.02$], providing evidence that the linear component of HbA_{1c} changes over time differed in the treatment and control groups. Using coefficients provided in the solution of this regression equation, the linear effects of time were plotted in Fig. 1, which clearly shows the difference between groups, a general decrease in HbA_{1c} over time in the group receiving stress management treatment, and a gradual increase in the group receiving diabetes education alone. The plot of the linear effects shows the contrasting downward and upward trends of the treatment and control groups more clearly. The difference between groups becomes apparent only at the 12-month follow-up, when stress management and education control groups differ by ~0.5% in HbA_{1c}. At this

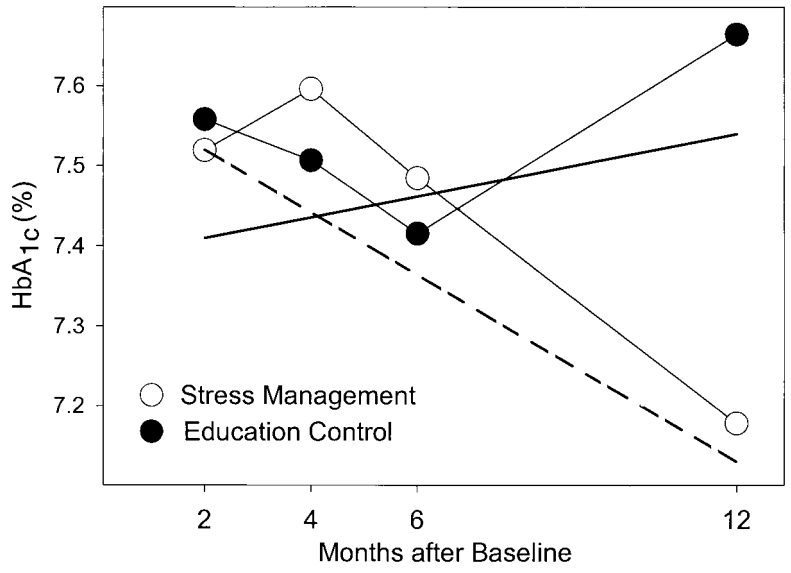

Figure 1—*Treatment-related changes in HbA_{1c} with statistical adjustment for baseline levels. The linear component of change is shown by the straight line.*

time point, 32% of the stress management subjects had HbA_{1c} levels that were lower than baseline by 1% or more. In contrast, only 12% of the control subjects had levels that were this much lower. This difference was statistically significant by χ^2 test ($\chi^2 = 4.08$, $P = 0.04$). These analyses support the hypothesis that stress management training would improve glycemic control over time, although data suggest that the benefits may take several months to appear and may be modest in size.

To test the hypothesis that stress management training would benefit subjects who had higher anxiety, we tested mixed regression models that included baseline levels of trait anxiety (STAI-trait) as a factor, along with factors for treatment group and time and baseline levels of HbA_{1c} as a covariate. However, neither the effect of baseline trait anxiety score nor any of the interactions with treatment and time was significant. These results provide no evidence to support the hypothesis that stress management training is of greater benefit to subjects who began the training with higher levels of anxiety. This analysis was repeated with data from the treatment group alone and, again, the effects of baseline trait anxiety and the interaction with time were not significant. Additional analyses examined the effect of treatment on measures of perceived stress, anxiety, and general psychological health. Although treatment and control groups did not differ at baseline on any of these measures, the covariance approach was again used to assess changes over time in these variables. Scores on the PSS, STAI-state scale, and the GHQ collected at 2, 4, 6, and 12 months were analyzed individually by mixed-design regression, with treatment group and time as experimental factors and baseline levels of each measure as a covariate. These collected analyses provided no evidence of effects attributable to stress management training. All of the main effects and interactions of treatment group were nonsignificant. The main effect of time was also nonsignificant.

Changes in diet and physical activity were evaluated by analyses of calorie consumption based on diet analysis and scores on the DASI. Mixed-design regressions testing the 2-, 4-, 6-, and 12-month follow-up data as repeated measures with the baseline value as a covariate revealed no effects of treatment group or group-by-time interactions. Therefore, neither diet nor physical activity changed in a way that could have produced the observed effect on glycemic control.

Consistent with standard stress management training, after subjects had successfully learned to relax, they were instructed to reduce formal practice with the relaxation tape. However, they were free to use the tape as often as they wished. They were instructed to use the "mini-practices" they had learned to induce the relaxation response whenever appropriate to manage stress in their daily lives. Self-reports collected at follow-up visits revealed that subjects did transition from formal practice. Shortly after completion of training, subjects in the stress management group reported using the cassette tape an average of 3.2 times per week, and one in five reported that they did not use the tape at all. At 12 months of follow-up, the group average was 0.7 times per week, and roughly three quarters of the subjects reported not using the tape at all. At 2 months, the average reported number of daily "mini-practices" was 4.3, and at 12 months, the average number had decreased to 0.8 per day. Therefore, evidence suggests that subjects did decrease formal practice over time, as they learned to use the techniques during daily life.

Comparisons were made to determine whether subjects who completed the 12-month study differed from those who dropped out at any time before completion, using Student's *t* test for continuous variables and the χ^2 test for categorical variables. The dropout group differed only in age (54.3 vs. 58.9 years for completers) and did not differ in duration of diabetes, baseline BMI, levels of HbA_{1c}, or scores on the STAI-trait, PSS, or GHQ instruments. Proportions by sex, race, and treatment group did not differ. Therefore, failure to complete the study was not related to any of the study variables.

CONCLUSIONS — The findings from this investigation support the efficacy of outpatient stress management training for the improvement of glycemic control in patients with type 2 diabetes. At the end of a 1-year follow-up period, patients who received training in stress management skills demonstrated approximately a 0.5% reduction in HbA_{1c} relative to control patients. Although this change was modest, improvements of $<0.5\%$ in HbA_{1c} have been associated with a significant reduction in risk of microvascular complications (22). Furthermore, by the end of 1 year, 32% of the stress management subjects had HbA_{1c} levels that were lower by $\geq 1\%$. In contrast, only 12% of the control subjects had levels that were this much lower. Although previous studies using more intensive one-to-one interventions have shown that stress management can improve glycemic control, this is the first demonstration that a

simple, cost-effective group approach can have a meaningful therapeutic impact.

It is interesting that the impact of stress management did not become evident before the 12-month data collection point. Control and experimental patients both showed decreased HbA_{1c} up to 6 months. However, after that point, the average blood glucose of control subjects deteriorated, while that of stress management subjects continued to improve. This effect was not due to changes in BMI, diet, or exercise in the stress management group, because the two groups did not differ on these variables over the 12-month course of the study.

Practice data from this study suggest that subjects complied with treatment instructions as patients in our other stress management programs. Subjects had been instructed to decrease formal practice with the tape as they gained proficiency in relaxation. Although we have no data to prove that patients began to internalize cues for relaxation as formal practice waned, a similar decrease in formal practice is seen in our clinic population undergoing stress management for other conditions. It does seem that clinical improvements may not require continued daily practice to be effective.

The second aim of this study was to examine whether patients with higher levels of anxiety would respond more to treatment. Remarkably, baseline trait anxiety did not predict treatment effects. This finding adds to controversial literature demonstrating that highly anxious (5), stress-responsive (9), and low-anxious individuals (13) benefit differentially from stress management training. Although these previous studies reported effects of individual differences in anxiety proneness, we could not replicate these findings in the current investigation.

Even though a modest group-based stress management program was successful in improving glycemic control in this study, stress management training may not be an option for every patient. Previous investigations have shown that anxiolytic therapy with benzodiazepines can also improve glucose metabolism in diabetes (5,6). Although chronic benzodiazepine therapy is not a desirable option for glucose control, diabetic patients who respond to benzodiazepines have been shown to be more likely to respond to relaxation training (5). Therefore, patients who have adverse metabolic control due to acute stress might be treated initially with benzodiazepines and then started on a behavioral stress management program. Nevertheless, this study, combined with previously published literature, suggests that stress management can be a meaningful addition to a comprehensive treatment program for patients with type 2 diabetes.

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