Sustained Effects of a Mindfulness-Based Stress-Reduction Intervention in Type 2 Diabetic Patients

Design and first results of a randomized controlled trial (the Heidelberger Diabetes and Stress-Study)

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OBJECTIVE—To determine whether a mindfulness-based stress reduction (MBSR) intervention is effective for reducing psychosocial distress (i.e., depression, psychosocial stress) and the progression of nephropathy (i.e., albuminuria) and for improving the subjective health status of patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS—Patients with type 2 diabetes and microalbuminuria were randomized to a mindfulness-based intervention (n = 53) or a treatment-as-usual control (n = 57) group. The study is designed to investigate long-term outcomes over a period of 5 years. We present data up to the first year of follow-up (FU).

RESULTS—At FU, the MBSR group showed lower levels of depression (d = 0.71) and improved health status (d = 0.54) compared with the control group. No significant differences in albuminuria were found. Per-protocol analysis also showed higher stress reduction in the intervention group (d = 0.64).

CONCLUSIONS—MBSR intervention achieved a prolonged reduction in psychosocial distress. The effects on albuminuria will be followed up further.

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Several studies reported not only an increased incidence of depression among patients with type 2 diabetes (1), but also a putative causal role of psychological distress in the pathogenesis of diabetes (2) and its complications (3,4). As shown by our research group, psychological stress is linked to the activation of proinflammatory transcription factors known to be involved in late diabetes complications (5,6). Because previous studies in diabetes and other medical diseases indicate that mindfulness-based stress reduction (MBSR) or an MBSR component may be effective in reducing or preventing depression and stress as well as increasing health status (7–10), we initiated a 5-year trial with albuminuria progression as the primary end point and psychological distress, health status, mortality, cardiovascular events, and the activation of proinflammatory transcription factors as secondary end points.

RESEARCH DESIGN AND METHODS

—The Heidelberger Diabetes and Stress-Study (HEIDIS-Study) was developed as a 5-year prospective randomized controlled trial (RCT) within a group at high risk for diabetes complications. The main inclusion criterion (see Supplementary Table 1) was type 2 diabetes with albuminuria, which is a well-established risk factor for cardiovascular and microvascular diseases. These patients were also suspected to be at risk for developing high levels of (diabetes-related) distress and depression (3,4). Six hundred ninety-four patients were evaluated in the Diabetes Outpatient Clinic at the University of Heidelberg. A total of 110 patients fulfilled the inclusion criteria and provided written informed consent as follows: 57 patients were randomized to the control group, and 53 patients were randomized to the intervention group (Supplementary Fig. 1). Follow-up (FU) assessments were scheduled immediately postintervention and yearly for 5 years.

Interventions

MBSR (11) is an 8-week program based on body and meditation practices that aims to increase the openness to as well as the awareness and acceptance of all internal and external experiences. Such mindful attention is assumed to allow the patient to behave in a less reactive and more reflective manner when confronted with life stressors. Over time, this may result in less arousal, reduced emotional distress, and more effective health behaviors. For the purpose of our study, MBSR was adapted (12) by including practices for difficult thoughts and feelings related to diabetes. Participants met once weekly in groups of 6–10 and for a booster session after 6 months. The groups were led by a psychologist and a resident in internal medicine. To guarantee standardized medical treatment-as-usual according to diabetes guidelines in both arms, all patients were seen on a

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regular basis by a physician in our outpatient clinic.

Measurements

Albuminuria was determined using 24-h urine on 3 consecutive days. All routine blood parameters were analyzed in the Clinical Laboratory of the University of Heidelberg using standardized and certified methods; blood pressure was examined with a 24-h measurement.

Psychiatric comorbidity and levels of depression and stress were assessed using the Patient Health Questionnaire (PHQ) (13). Subjective health status was measured by the 12-item short-form health survey (SF-12) (14), which includes a physical and mental component summary score.

Statistical analysis

Covariance analyses with the baseline value of the respective variable, age, and diabetes comorbidity as covariates and gender as a possible moderator were used to compare the difference in change between the groups. In a sensitivity analysis, all calculations were redone with missing data imputed (using multiple imputation). Assuming a two-sided type I error rate of 5% and a power of 80%, the given sample size can detect high (Cohen $d > 0.8$) and medium ($0.5 < d < 0.8$) effect sizes, whereas small effects ($d < 0.5$) may not reach the level of significance. All statistical analyses were performed with SAS, version 9.2 (SAS Institute).

RESULTS—Patient characteristics are provided in Supplementary Table 2. There were no significant baseline differences between the groups, except for the history of myocardial infarction. No significant effect was found immediately after the intervention (Table 1 and Supplementary Fig. 2).

After 1 year, all patients were alive, and no cardiovascular event had occurred. An intent-to-treat analysis for 1-year FU showed no significant effect of MBSR for the progression of albuminuria. In the intervention group, a significantly lower level of depression (PHQ-9, $d = 0.71$) and an improved health status were found (mental component summary, $d = 0.54$), but no difference in physical health or the stress scale was observed. In addition, diastolic blood pressure was significantly lower in the MBSR group ($d = 0.78$); however, HbA_{1c} and systolic blood pressure were not significantly affected. Sensitivity analyses that included imputed data yielded similar results.

Table 1—*ANCOVA results for clinical and psychosomatic parameters in intent-to-treat and per-protocol analyses*

	Postintervention				1-year FU			
	Intervention	Control	*d**	*P* value	Intervention	Control	*d**	*P* value
Intent-to-treat analysis								
Albuminuria (mg/24 h)†	42.8 (21.1/42.8)	66.5 (20.2/204.5)	0.19	0.4238	43.3 (18.8/122.7)	54.6 (22.7/184.4)	0.40	0.134
HbA_{1c} (%)	7.2 ± 0.10	7.1 ± 0.11	0.09	0.7015	7.2 ± 0.14	7.5 ± 0.16	0.37	0.151
Systolic blood pressure (mmHg)	137.6 ± 1.95	140.8 ± 2.14	0.29	0.2669	138.7 ± 2.18	143.6 ± 2.24	0.42	0.116
Diastolic blood pressure (mmHg)	77.7 ± 1.09	80.7 ± 1.20	0.49	0.0605	77.8 ± 1.18	82.7 ± 1.22	0.78	0.004
SF-12 mental composite score‡	47.9 ± 1.39	46.0 ± 1.53	0.22	0.3691	48.4 ± 1.51	43.6 ± 1.70	0.54	0.033
SF-12 physical composite score‡	38.8 ± 0.89	39.0 ± 1.00	0.03	0.9115	38.9 ± 0.97	40.2 ± 1.12	0.23	0.366
PHQ-9 Depression score	5.7 ± 0.53	5.8 ± 0.58	0.03	0.9090	5.3 ± 0.48	7.3 ± 0.56	0.71	0.007
PHQ Stress score	4.9 ± 0.47	5.1 ± 0.58	0.08	0.7514	5.0 ± 0.42	6.2 ± 0.52	0.48	0.071
Per-protocol analysis								
Albuminuria (mg/24 h)†	42.2 (19.3/88.2)	66.5 (20.2/204.5)	0.19	0.4463	34.0 (16.8/115.7)	54.6 (22.7/184.4)	0.44	0.100
HbA_{1c} (%)	7.2 ± 0.12	7.1 ± 0.12	0.07	0.7959	7.1 ± 0.17	7.5 ± 0.17	0.47	0.087
Systolic blood pressure (mmHg)	137.7 ± 2.17	140.6 ± 2.13	0.27	0.3387	138.5 ± 2.51	143.2 ± 2.32	0.39	0.171
Diastolic blood pressure (mmHg)	77.8 ± 1.21	80.7 ± 1.18	0.48	0.0869	78.2 ± 1.37	82.6 ± 1.26	0.68	0.018
SF-12 mental composite score‡	49.2 ± 1.45	46.2 ± 1.43	0.39	0.1340	49.2 ± 1.69	43.5 ± 1.69	0.65	0.018
SF-12 physical composite score‡	38.3 ± 1.00	38.9 ± 1.01	0.11	0.6581	39.2 ± 1.11	40.3 ± 1.12	0.19	0.480
PHQ-9 Depression score	5.4 ± 0.59	5.8 ± 0.57	0.13	0.6328	5.0 ± 0.55	7.3 ± 0.57	0.79	0.005
PHQ Stress score	4.7 ± 0.53	5.0 ± 0.56	0.12	0.6527	4.6 ± 0.48	6.2 ± 0.52	0.64	0.023

Data are presented as adjusted means ± SE unless otherwise indicated. *Effect sizes were calculated as the ratio of difference of adjusted means and the square root of mean squared error. †Albuminuria data were log-transformed prior to the analysis in order to attain sufficient normality of distribution. Descriptive results are presented as unadjusted medians (25th/75th percentiles). ANCOVA results are reported with log values. ‡A higher number indicates improved functioning.

Because nine patients in the intervention group did not attend the training sessions as required (less than five sessions; for reasons, see Supplementary Fig. 1), a per-protocol analysis was performed. The findings confirm the abovementioned results and show consistently higher effect sizes, including a significantly lower level of stress in the MBSR group ($d = 0.64$).

CONCLUSIONS—The HEIDIS-Study is the first RCT to assess whether an MBSR intervention is effective in reducing stress and depression as well as late diabetes complications (i.e., nephropathy) in patients with type 2 diabetes. In agreement with our hypothesis, we found that MBSR led to better health status and lower levels of depression. Among regular attendees, psychological stress also decreased significantly. However, at baseline, the patients had rather low rates of depression compared with previous reports (1); the effect of the intervention on depression, therefore, is largely based on preventing progression rather than a true reduction in the level of emotional distress. In accord with previous studies on MBSR in medical patients (10), our results suggest that effects may even accumulate over time.

However, although the effect sizes were remarkable, no significant effect could be demonstrated for the main outcome (albuminuria) or other physical parameters, with the exception of diastolic blood pressure.

Psychosocial stress activates proinflammatory transcription factors, which mediate micro- and macrovascular disease (6,7). Therefore, a sustained reduction in the distress induced by MBSR may lead in the future to an effect on long-term diabetes complications. To further assess the influence of psychological distress on late diabetes complications, FU over a total period of 5 years is essential. The HEIDIS-Study takes this approach.

Despite the limitations of the study due to the small number of participants, this study adds to the sparse literature on stress and late diabetes complications and emphasizes the potential of psychosocial interventions. The specific advantage of MBSR is its preventive nature and broad applicability for a variety of symptoms.

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