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)

Mechthild Hartmann, MSC¹
Stefan Kopf, MD²
Claudia Kircher, MD²
Verena Faude-Lang, MD¹,³
Zdenka Djuric, MD²
Florian Augustin²

Hans-Christoph Friederich, MD¹
Meinhard Kieser, PhD⁴
Angelika Bierhaus, PhD²
Per M. Humpert, MD⁵
Wolfgang Herzog, MD¹
Peter P. Nawroth, MD²

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 (3,6). 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.

From the ¹Department of Medicine II and Psychosomatics, University of Heidelberg, Heidelberg, Germany; the ²Department of Medicine I and Clinical Chemistry, University of Heidelberg, Heidelberg, Germany; the ³Department of Psychosomatic Medicine and Psychotherapy, University of Hamburg-Eppendorf, Hamburg, Germany; and the ⁴Institute of Medical Biometry, University of Heidelberg, Heidelberg, Germany. Corresponding author: Mechthild Hartmann, mechthild.hartmann@med.uni-heidelberg.de.

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**RESULTS**—Patient characteristics are provided in Supplementary Table 2. An intent-to-treat analysis for 1 year revealed no significant effect of MBSR on albuminuria. In the intervention group, a significant improvement in subjective health status was observed. In addition, a significant effect was found in the mental component summary (PHQ-9, d = 0.71) and SF-12 mental composite score (d = 0.54), whereas small effects (d = 0.5) may not reach the level of significance. All analyses that included imputed data yielded similar results. Sensitivity analysis that included imputed data yielded similar results.

**Statistical Analyses**—An ANCOVA analysis with SAS version 9.2 (SAS Institute) was performed to compare the difference in change between the intervention and control groups, adjusting for baseline covariates and other variables. Covariance analyses with the baseline value of the respective variable, age, and sex were performed as a possible moderator were used to compare the difference in change between the intervention and control groups. Assuming a two-sided type I error rate of 0.05 and a power of 80%, the given sample size can detect high (Cohen's d ≥ 0.8) effect sizes, medium (0.5 ≤ d < 0.8) effect sizes, or small effects (d < 0.5) with a power of 0.80.

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

| Measurements | Postintervention | 1-year FU |
|--------------|-----------------|-----------|
| **Intervention** | Control | d* | P value | Intervention | Control | d* | P value |
| **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 |
| **HbA1c (%)** | 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 |
| **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 ± 0.98 | 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 |
| **HbA1c (%)** | 7.2 ± 0.12 | 7.1 ± 0.12 | 0.07 | 0.7999 | 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 | 40.2 ± 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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