

OBSERVATIONS

Bodily Pain, Poor Physical Functioning, and Poor Glycemic Control in Adults With Diabetes

In the January issue of *Diabetes Care*, Krein et al. (1) reported that the presence of chronic pain was associated with poor diabetes self-management. Their study was performed in a primarily male veteran population, and glycemic control was not addressed. We examined psychosocial factors associated with poor glycemic control in a largely female population followed in an urban, underserved, primary care medical clinic and found that the presence of pain and poor physical functioning were associated with poor glycemic control.

Medical records of adults with diabetes ($n = 236$, 76% female, mean age 62 years) were reviewed. Mean HbA_{1c} was 8.1%, and 52.5% had HbA_{1c} levels of <8%. Patients were asked to complete the SF-36 Short Form Survey (2), the Appraisal of Diabetes Scale (ADS) (3), the Diabetes Quality of Life (DQOL) Measure (4), the Problem Areas in Diabetes (PAID) Scale (5), and the patient survey used by the American Diabetes Association for provider recognition. Bivariate analyses were conducted using correlation coefficients for continuous variables and one-way ANOVA to assess differences in means across groups. Alpha was set at 0.05, two-tailed. Odds ratios, 95% CIs, and χ^2 tests for trend were used to compare patients with HbA_{1c} <8% versus $\geq 8\%$ for various psychosocial measures. This project was approved by the Institutional Review Board for the Protection of Human Subjects at SUNY Upstate Medical University.

HbA_{1c} was negatively associated with the SF-36 Bodily Pain subscale score ($P = 0.012$). Those patients with HbA_{1c} $\geq 8.0\%$ were 5.6 times (95% CI 1.3–26.1) as likely to have more pain (as indicated by a low bodily pain subscore <30) compared with patients with less pain (high scores >70). HbA_{1c} was also negatively

correlated with physical functioning (SF-36 subscale, $P = 0.002$), with those having HbA_{1c} $\geq 8\%$ being 4.5 times (95% CI 1.1–20.3) as likely to have a low physical functioning subscale score (<30) as patients with high scores (>70). Patients with HbA_{1c} $\geq 8.0\%$ were 3.6 times (95% CI 0.8–18.8) as likely to report poor or fair overall health (American Diabetes Association Provider Recognition Patient Survey, Question 1). HbA_{1c} was not associated with the Mental Health subscales of SF-36, ADS, or DQOL, but those with HbA_{1c} $\geq 8.0\%$ had higher mean PAID scores ($P = 0.034$). As previously reported (6), as age increased, several psychosocial indicators improved (PAID total score, $P = 0.001$; PAID “worry,” $P < 0.001$; PAID “impact,” $P = 0.026$; Mental Composite Score from SF-36, $P = 0.005$; Mental Health Subscore from SF-36, $P = 0.017$).

Krein et al. (1) demonstrated that chronic pain limited the ability of patients with diabetes to self-manage their disease. We found that patients who reported more bodily pain, poorer physical functioning, and poorer self-assessment of overall health were more likely to have elevated HbA_{1c} levels. Whether measures to decrease pain and improve physical functioning would help to improve glycemic control is an area for future study.

CATHY SINNOTT, RN, MA¹

MARY A.M. ROGERS, PHD¹

DAVID LEHMANN, MD, PHARM¹

RUTH S. WEINSTOCK, MD, PHD^{1,2}

From the ¹Department of Medicine, SUNY Upstate Medical University, Syracuse, New York; and the ²Department of Veterans Affairs Medical Center, Syracuse, New York.

Address correspondence to Ruth S. Weinstock, MD, PhD, SUNY Upstate Medical University, 750 East Adams St. (CWB 353), Syracuse, NY 13210. E-mail: weinstor@upstate.edu.

M.A.M.R. is currently affiliated with the Division of General Medicine, University of Michigan, Ann Arbor, Michigan.

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Herbal Therapies and Diabetes Among Navajo Indians

In the treatment of chronic diseases like diabetes, many Native Americans value their ability to integrate traditional and western medicine (1). However, there are limited data from clinical trials about the efficacy of herbs, and health care professionals have been concerned that herbal treatments might be harmful or lead patients away from evidence-based therapies and self-monitoring of blood glucose (2).

Traditional medicines, including herbal therapies, are commonly used among the Navajo Indians (3). During a randomized clinical trial on the Navajo Nation, 203 participants recruited between 2001 and 2003 were asked about their use of traditional medicines for diabetes and their blood glucose-monitoring practices. Their most recent A1c values were abstracted from the medical record. The study, Effects of Navajo Interpreters

From the Division of Endocrinology, St. Luc University Hospital, UCL, Brussels, Belgium.

Address correspondence to O. Alexopoulou, MD, Endocrinologie, Cliniques Universitaires St. Luc, Avenue Hippocrate 54, UCL 54.74, 1200 Brussels, Belgium. E-mail: orsalia.alexopoulou@diab.ucl.ac.be.

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Mild, Reversible Pancytopenia Induced by Rosiglitazone

Rosiglitazone, a member of the thiazolidinediones, is a well-established oral antidiabetic agent. It reduces plasma glucose levels and glucose production, increases glucose clearance, and significantly improves insulin sensitivity, pancreatic β -cell function, and cardiovascular risk factors (1). In addition to the potential risk of liver toxicity, thiazolidinediones can cause fluid retention, which can exacerbate congestive heart failure (2). Hematologic effects reported in clinical trials include only small decreases in Hb and hematocrit. A recent report described rosiglitazone-induced protection against myelotoxicity produced by 5-fluorouracil (3). We report a case of mild, reversible pancytopenia during treatment with rosiglitazone for type 2 diabetes.

A 56-year-old physician with a previous history of ischemic heart disease and hypertension developed symptoms of hyperglycemia and glycosuria and was diagnosed with type 2 diabetes. Treatment with 4 mg rosiglitazone per day was

added to previous daily treatment with 100 mg acetylsalicylic acid, 80 mg slow-release propranolol, 5 mg amlodipine besylate, 10 mg phenoxybenzamine, and 10 mg simvastatin. The patient was symptom free. At that time, hematologic indexes were Hb 14.4 g/dl, hematocrit 40.5%, white blood cell count 6,700/ μ l, and platelets 238,000/ μ l. HbA_{1c} was 10.9%.

During treatment, all hematologic indexes decreased following a dose-dependent pattern with rosiglitazone dose. On 8 mg rosiglitazone per day, Hb decreased to 13 g/dl, hematocrit to 37.8%, white blood cell count to 4,300/ μ l, and platelets to 169,000/ μ l. On 12 mg rosiglitazone per day (a dose exceeding the recommended maximal dose), Hb decreased to 12.3 g/dl, hematocrit to 34.9%, white blood cell count to 3,600/ μ l, and platelets to 138,000/ μ l. When rosiglitazone was decreased to 4 mg daily, Hb increased to 12.7 g/dl, hematocrit to 35.8%, and white blood cell count to 4,200/ μ l. Two months after rosiglitazone was stopped and replaced with 1.5 mg repaglinide daily, Hb returned to 13.9 g/dl, hematocrit to 42.2%, white blood cell count to 6,100/ μ l, and platelets to 157,000/ μ l.

No other medication was added or changed during this time. No edema or other signs of fluid overload developed during treatment. Currently, the patient is treated with 1.5 mg repaglinide per day, and his diabetes is well controlled.

To date, the only known adverse hematologic effect of rosiglitazone is mild anemia presumed to be secondary to increased plasma volume. Furthermore, a recent report describes a hematologic advantage of rosiglitazone through the proliferation of granulocyte-macrophage colony-forming units associated with its treatment, an effect attributable to its insulin-sensitizing actions (3). The case presented here demonstrates the development of mild, reversible, and dose-related pancytopenia associated with rosiglitazone treatment. This adverse event seems to be a dose-related rather than an idiosyncratic one. The Hb/hematocrit changes are consistent with many other reports and are ascribed to an increased plasma volume, but the white blood cell count and platelet decreases indicate an effect on the bone marrow. Clinicians should be made aware of the possibility of hematologic toxicities occurring with rosiglitazone therapy. Pa-

tients should have their erythrocytes, leukocytes, and platelets monitored while on this drug.

YORAM MAARAVI, MD
JOCHANAN STESSMAN, MD

From the Department of Rehabilitation and Geriatric Medicine, Hadassah-Hebrew University Medical Center, Mount Scopus, Jerusalem.

Address correspondence to Yoram Maaravi, MD, Department of Rehabilitation and Geriatric Medicine, Hadassah University Hospital, Mount Scopus, P.O. Box 24035, Jerusalem 91240, Israel. E-mail: maaravi@md2.huji.ac.il.

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COMMENTS AND RESPONSES

SF-36 and Diabetes Outcome Measures

In a recent issue of *Diabetes Care*, Hill-Briggs et al. (1) found that the Medical Outcomes Study 36-item short form (SF-36) did not improve in a population whose outcome measures (HbA_{1c}, triglycerides, and diastolic blood pressure) showed modest improvement. We found a similar lack of change in the standard SF-36 in a group of patients whose HbA_{1c} levels, measured in a boronate affinity assay in which the upper limit of normal was 6.8%, fell >3.0% from an initial median of 11.9% (2). Hill-Briggs et al. suggested that diabetes-specific questions be either added to the SF-36 or used alone to

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Initiation of Insulin in Patients With Type 2 Diabetes Failing Oral Therapy

Response to Raskin et al. and Mikhail and Cope

Our previous publication regarding the initiation of insulin therapy in patients with type 2 diabetes failing oral therapy (1) and the recent study by Raskin et al. (2) has raised interesting discussion (3,4). Raskin et al. reported that glycemic control was better in patients treated with BIAsp 70/30 plus oral antidiabetic agents (OADs) than in those receiving insulin glargine plus OADs (mean end point HbA_{1c} 6.91 vs. 7.41%). In contrast, we demonstrated that glycemic control was better in patients treated with insulin glargine plus OADs compared with 70/30 insulin alone (mean end point HbA_{1c} 7.15 vs. 7.49%). Major discrepancies between the Raskin et al. study and our study exist, including considerably poorer metabolic control at study base-

line in the Raskin et al. study (HbA_{1c} 9.8 vs. 8.8%), the use of different OADs, a markedly higher insulin dose at study end (78.5 IU BIAsp 70/30 vs. 28.2 IU in our insulin glargine plus OAD study group), and a dramatic weight gain in the BIAsp 70/30 group (5.4 kg vs. only 1.4 kg in our insulin glargine plus OAD group).

On the surface, it might appear that according to Raskin et al., premix insulin plus OADs were more effective than insulin glargine plus OADs. However, this does not take into account other factors that influence treatment management, including insulin dose, number of daily injections, complexity when monitoring blood glucose, incidence of hypoglycemia, weight gain, and quality of life. Indeed, in both studies, insulin dose and the incidence of hypoglycemia were significantly greater with premix insulin versus insulin glargine. Further analysis has indicated that although the method for identifying hypoglycemia was very different between the two studies, the nearly fivefold higher incidence of hypoglycemia observed in the premixed arm is of major clinical relevance. Aside from the debilitating effect of hypoglycemia on the patient and carers, hypoglycemia has important health economic implications. Additionally, whereas insulin glargine is injected only once daily, premix insulin requires twice-daily administration and blood glucose monitoring two to four times daily, a likely barrier to achieving treatment success, particularly in clinical practice with insulin-naïve patients being initiated to insulin therapy. Furthermore, one might question whether the results obtained by Raskin et al. reflect the true potential of insulin glargine; given the low

risk of hypoglycemia observed with insulin glargine, more aggressive titration of this insulin in their study may have achieved a greater decrease in HbA_{1c}.

We believe that one injection of insulin glargine in combination with two OADs is a simple, safe, and effective treatment option for patients with type 2 diabetes with moderately unstable blood glucose control.

HANS U. JANKA, MD

From Klinikum Bremen-Nord, Bremen, Germany.

Address correspondence to Prof. Hans U. Janka, Klinikum Bremen-Nord, 2nd Medizinische Abteilung, Hammersbecker Str. 228, 28755 Bremen, Germany. E-mail: hans.janka@klinikum-bremen-nord.de.

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