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Glitazone in Diabetes

Relationship to patient dual public/private sector use

In its evidence-based guidelines for type 2 diabetes (1), the Veterans Health Administration (VHA) recommends a second-generation sulfonylurea or metformin as first-line drug therapy. Metformin or sulfonylurea is added to the first agent if HbA_{1c} (A1C) control is not satisfactory. Because of their modest effect on A1C, unknown long-term safety, and high cost, the VHA recommends reserving thiazolidinediones (glitazones) for selected patients. We compared community versus Veterans Affairs (VA) primary care providers regarding initiation of glitazone therapy and presence of contraindications in veterans, who frequently obtain care both within and outside the VHA.

Glitazone prescription at the Birmingham VA Medical Center (BVAMC) required endocrinology consultation in fiscal year 2002. Using the VHA's electronic medical record, we identified all consultations to the BVAMC endocrinology service in fiscal year 2002 and performed structured chart review. We assessed adherence to then-current guidelines for glitazone use, including *1*) failure of combination metformin-sulfonylurea therapy and patient refusal of insulin or 2) insulin dose >75 units/day and A1C >1% above target.

We noted whether glitazone therapy was started by private physicians (110 patients) or by a request originating from within the VHA (65 patients). These two patient groups did not differ significantly in age, sex, or duration of diabetes. Insulin was tried before glitazone was initiated in 28% of patients treated within the VHA and 19% of those treated outside the VHA ($P = 0.178$). VHA physicians were more likely than community practitioners to have tried a metformin-sulfonylurea combination before rosiglitazone (74.4 vs. 44.4%, $P = 0.0005$). Of patients started on rosiglitazone within the VHA, 48.9% had A1C improvements of <0.5% (information unavailable for community physicians). However, VHA physicians used maximum rosiglitazone doses in only 17% of patients compared with 29% outside VHA. Heart failure was present in 12% of patients when rosiglitazone was requested, with no difference between community and VHA physicians in failing to recognize this contraindication ($P = 0.813$). From clinic notes, medication costs were the reason for seeking VHA care in 52% of patients whose glitazone had been initiated outside the VHA.

The differences between VHA and community physicians in initiating thiazolidinedione therapy may reflect differences in prescribing patterns across different systems. However, individuals treated in the community who found glitazones prohibitively expensive might have sought out the VHA. As we did, but in a more general population, Lederle and Parenti (2) documented that over half of veterans transferring to the VHA from community health care did so because of drug costs. Patients on less costly hypoglycemic regimens might be less likely to seek dual care. Therefore, we cannot easily extrapolate our findings to the entire private sector. Of note, medication costs contribute to poorer glycemic control in individuals with chronic illnesses (3). Piette et al. (4) found more medication underuse in patients with limited or no medication insurance than in VHA users.

In summary, we found that requests for initiating rosiglitazone were more guideline concordant when originating from within the VHA than from community physicians but that contraindications were not always recognized by either source. These expensive medications, the long-term safety of which is still unknown, may be significantly overused.

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Observations on Online Services for Diabetes Management

Kwon et al. (1) demonstrated that an Internet-based blood glucose monitoring system, which provided frequent and responsive interactions between patients and their physicians online, can be as effective as face-to-face diabetes follow-ups. Routine medical services typically include face-to-face patient education, in which each patient receives his/her education materials (such as goals to achieve and the knowledge and skills for self-management). To extend patient education for a lasting effect, we have developed a patient-oriented education management (POEM) system (available at www.dmc.idv.tw) (2).

In the system, we reorganize each patient's education materials, medication data, and laboratory test results at every visit and then present the information on the Web. The system also provides reminders for the next follow-up with e-mails and short messages via cell phone. This way, the patient or his/her family can easily access the materials after leaving the hospital and constantly review medical care data and education materials for improvement of his/her diabetes condition.

To evaluate the system, we conducted an 8-month follow-up study. A total of 274 patients with type 2 diabetes were randomly recruited from the hospital: 134 (57% men and 43% women) in the experimental group (using the POEM system) and 140 (46% men and 54% women) in the control group. Subjects were aged 66.0 ± 8.5 and 61.2 ± 12 years in the experimental and control groups, respectively. Diabetes duration was 5.28 ± 4.70 and 7.01 ± 5.44 years in the experimental and control groups, respectively. Improvements in diabetes condition were evaluated by laboratory test results, including fasting blood glucose, HbA_{1c} (A1C), total cholesterol level, triglycerides, and HDL.

The test results (means ± SD) at the first visit for patients' fasting blood glucose, A1C, total cholesterol level, triglycerides, and HDL were 187.54 ± 77.10 and 189.99 ± 73.49 mg/dl, 9.03 ± 2.79 and 8.95 ± 2.23%, 193.29 ± 47.93 and 202.52 ± 58.45 mg/dl, 152.48 ± 70.85 and 157.37 ± 74.88 mg/dl, and 44.97 ± 12.09 and 45.32 ± 12.08 mg/dl in the experimental and control groups, respectively. During 8-month follow-ups, the average results of their fasting blood glucose, A1C, total cholesterol level, triglycerides, and HDL were 114.87 ± 46.98 and 130.29 ± 42.31 mg/dl, 7.38 ± 1.37 and 8.03 ± 1.55%, 169.18 ± 29.46 and 180.50 ± 38.95 mg/dl, 129.06 ± 58.50 and 137.13 ± 64.65 mg/dl, and 45.09 ± 14.02 and 44.27 ± 11.67 mg/dl in the experimental and control groups, respectively.

We performed ANCOVA on the laboratory test results of two groups from the pre- to postintervention periods. The F values of fasting blood glucose, A1C, and total cholesterol level were 7.898 (P = 0.005), 7.345 (P = 0.007), and 4.139 (P = 0.043), respectively. The results showed significant changes between the two groups: patients in the experimental group had better control than those in the control group.

Additionally, we monitored the number of monthly logins by patients during this period. The number of logins started with 9.6 ± 2.9/month per patient, slowly decreased in the following 3 months to 8.5 ± 3.7, and thereafter remained at that level with slight changes. Therefore, the POEM system can motivate patients and enhance the effect of patient education. Consequently, patients can improve the management of their diabetes.

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Serum Vitamin C Levels in Type 2 Diabetic Nephropathy

Serum vitamin C concentrations have been reported to be low in diabetic patients (1). Diabetic nephropathy is known to develop in diabetic individuals, and decreased renal function and hypertension could reportedly accelerate atherosclerosis in patients with type 2 diabetes (2). Observational epidemiologic studies showed an inverse relation between the dietary intake or serum levels of vitamin C and blood pressure (3). Although reduced concentrations of vitamin C were reported in type 2 diabetic retinopathy (4), the concentrations of serum vitamin C in type 2 diabetic patients with diabetic nephropathy have not been previously reported. The aim of the present study is to determine whether the concentrations of serum vitamin C have any relation to type 2 diabetic nephropathy. Since diabetic nephropathy is associated with low-grade inflammation (5), we also examined the inflammatory marker of high-sensitivity C-reactive protein (hs-CRP).

Forty-one type 2 diabetic subjects (age 35–65 years [average 55]) and 15 age- and sex-matched control subjects participated in the study. Any subject who smoked, took vitamins or nonsteroidal anti-inflammatory agents, or was receiving hormone replacement therapy was ineligible for the study. In addition, any patient with a history of macrovascular disease was excluded. Although vitamin C intake did not differ between type 2 diabetic patients and control subjects, serum vitamin C levels were found to be low in type 2 diabetic patients compared with control subjects (4.9 ± 0.3 vs. 6.8 ± 0.4 μg/ml, $P < 0.005$). Serum vitamin C levels significantly correlated with serum creatinine ($r = -0.43$, $P < 0.005$), log hs-CRP ($r = -0.36$, $P < 0.05$), and diastolic blood pressure ($r = -0.33$, $P < 0.05$) in diabetic subjects. No correlation was found between serum vitamin C levels and urinary albumin excretion levels in patients with diabetes. A stepwise multiple regression analysis demonstrated that both creatinine levels ($\beta = -1.232$, F value = 9.09) and log hs-CRP ($\beta = -6.335$, F value = 4.12) were independent determinants of serum vitamin C levels.

In type 2 diabetic patients, low levels of serum vitamin C were closely associated with concomitant renal dysfunction and low-grade inflammation.

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