LETTERS TO THE EDITOR

Maximal Dose Glyburide Therapy in Markedly Symptomatic Patients with Type II Diabetes: A New Use for an Old Friend*

To the editor:

An article in July 1996 issue of JCEM entitled “Extensive Personal Experience: Maximal Dose Glyburide Therapy in Markedly Symptomatic Patients with Type II Diabetes: A New Use for an Old Friend” by Dr. Peters and Dr. Davidson raises some interesting points regarding the therapy of newly onset diabetes mellitus. However, I was concerned regarding the fact that several patients had large amounts of urinary ketones at the time the diagnosis was made. Twelve patients had moderate to large amounts of ketones in their urine raising some uncertainty in my mind about how the authors diagnosed Type II diabetes mellitus. No information regarding individual patients’ serum bicarbonate levels or serum pH were included, except in an aggregate manner. It is unclear whether some of the patients actually had Type I diabetes mellitus.

Unfortunately, clinicians may be inadvertently swayed to using the authors’ approach in patients who should be started on insulin therapy. I think it essential that the authors clearly define what they mean by “Type II diabetes” and to clarify the acid base status of each individual patient, so treated in their paper, to help us further refine their approach. I am afraid without such information, widespread use of their algorithm may produce some harm.

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Maximal Dose Glyburide Therapy in Markedly Symptomatic Patients with Type II Diabetes: A New Use for an Old Friend—Author’s Response†

To the editor:

Differentiating between new onset type I and type II diabetes can sometimes be difficult, especially as some patients who initially present with diabetic ketoacidosis (DKA) may actually have type 2 diabetes that can ultimately be treated with oral medications or diet alone (1). However, we feel that our clinical criteria for entering patients into these protocols and the close follow-up provided ensured safe management. The ability to maintain adequate oral hydration was required in all patients, excluding those with dehydration (a common feature of DKA). Lean patients were quickly started on insulin if sulfonylurea agent therapy failed (e.g., if FPG concentration > 300 mg/dL 1 week after starting oral medication). Of the 17 patients with urine ketones of at least 1+ and 11 had serum ketones measured that were positive in only 5. Four months after starting maximal doses of a sulfonylurea agent in these 17 patients, 3 were on diet alone, 10 were still taking a sulfonylurea agent (most were on a submaximal dose), and 2 were on insulin. Six patients with urine ketones of at least 1+ had serum bicarbonate levels below the normal value of 22 mEq/L (range 17–21 mEq/L). Four months later, 2 of these patients were on diet alone, and 4 were still taking a sulfonylurea agent. Therefore, we feel that this approach is safe and effective for most patients with new onset diabetes who do not have clinical features of the DKA syndrome. Because of the close follow-up provided, even patients with slowly evolving type I diabetes can be followed in this manner, as they are started on insulin as soon as persistent hyperglycemia occurs.

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References


Vitamin D Receptor Gene Polymorphisms Are Associated with Osteoporosis in Japanese Women³

To the editor:

In a recent article of JCEM (December 1995), Lim et al reported lack of association between vitamin D receptor (VDR) genotypes and osteoporosis in Koreans (1). We analyzed the VDR alleles in 68 Japanese female patients with osteoporosis and 66 age-matched volunteers women. Our data suggest that BB homozygosity of the VDR gene is a strong genetic risk factor for osteoporosis in Japanese women.

From among patients who consulted orthopedists with complaints of lumbago and/or osteoporotic fractures from September 1994 to August 1995, we selected 87 female patients with BMD of less than –2 SD from the mean peak bone mass of healthy Japanese women. BMD was measured in the lumbar spine (L2–L4) by dual energy X-ray absorptiometry (DXA), using DCS-3000 (Aloka Co., Tokyo, Japan). Values of BMD in L2–L4, 2 SD, and 2.5 SD below the mean peak bone mass of healthy Japanese women were 0.86 g/cm² and 0.81 g/cm², respectively. All patients fulfilled the diagnostic criteria of osteoporosis proposed by the Ministry of Health and Welfare of Japan in 1993 (4 points or more). In patients with vertebral fractures or deformities in L2–L4, BMD values in the distal radius and the whole bone were used for diagnosis. No patients had endocrine disorders. Ten patients were not available for further study. Another nine patients over 80 yr of age were excluded from the case-control study because we could not obtain age-matched controls. The remaining 68 patients were used for the present genetic analysis (mean age 65.0; SD 8.8). Sixty-six age-matched apparently healthy female volunteers who lived in the same districts and had never been diagnosed as having osteoporosis before were analyzed as a control (mean age 64.9; SD 6.3). BMD in L2–L4 of controls was also measured by DAX as described above. None of the control subjects had vertebral fractures, none fulfilled the diagnostic criteria of osteoporosis described above, and none had taken calcium supplements. None of the patients or controls had undergone estrogen replacement therapy. DNA was extracted from peripheral leukocytes by the standard phenol-chloroform procedure, and VDR-gene allelic polymorphisms were assessed by BsmI endonuclease restriction after specific PCR amplification (2). Genotypic polymorphism was defined as BB (absence of restriction site on both alleles), bb (presence of restriction site on both alleles), and Bb (heterozygous).

The results are shown in Table 1. Mean levels of BMD (SD) in L2–L4 of patients and controls were 0.76 (0.15) and 0.92 (0.15), respectively, and the difference was significant (P < 0.001). Sixteen out of 68 patients had the BB genotype, while only 2 out of 66 controls had the BB genotype. This difference was significant (P < 0.001). Odds ratios (95% CI) for osteoporosis of BB and Bb genotypes were 12.0 (5.2–2.6) and 3.0 (8.1–1.1), respectively. In addition, 25 patients had vertebral fractures, and odds ratios (95% CI) for vertebral fractures of BB and Bb genotypes were 14.3 (7.9–2.6) and 4.8 (16.1–1.4), respectively. The World Health Organization (WHO) proposed new diagnostic categories for osteoporosis in 1994, and established osteoporosis (severe osteoporosis) was defined as BMD value of more than 2.5 SD below the young adult mean in the presence of one or more fragility fractures (3). Using these categories, 23 patients were diagnosed with established osteoporosis, and odds ratios (95 % CI) for established osteoporosis of BB and Bb genotypes were 13.0 (49.7–1.6) and 5.2 (177.7–1.5), respectively.

We also analyzed 102 healthy Japanese elementary school children

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