those with IGT, 86.1% among subjects with IFG, 35.7% with "new" IFG, and 12.3% among subjects with normal glucose tolerance. The prevalence of metabolic syndrome increases with age, is higher in men than in women (26.5 vs. 18.3%, respectively, $P = 0.001$), and is higher in rural than in urban areas (26.0 vs. 20.6%, respectively, $P = 0.037$).

The average daily energy intake was 2,509 kcal, to which carbohydrates contributed 53.3%, fats contributed 31.8%, and proteins contributed 14.9%. Comparing the OGTT(−) group with the three groups of various degrees of glucose intolerance, after age and sex adjustment, no differences were found regarding energy intake (range 2,551–2,231 kcal) or the qualitative composition of the diet (carbohydrates 53.1–54.9%, proteins 14.4–15.4%, and fats 30.7–32.1%). Moreover, the above parameters did not differ between subjects with or without metabolic syndrome.

In conclusion, the study revealed a very high prevalence of diabetes and IGT in Cyprus, among the highest in Europe, compared with five centers of the DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) study (1) and higher than in the U.S. (2), while the prevalence of metabolic syndrome is comparable with that of other Western countries (3). Dietary habits, evaluated by cross-sectional analysis, do not seem to contribute to the development of glucose intolerance. Interventions aimed at IGT and the components of metabolic syndrome are urgently needed in order to reduce the incidence of diabetes.

THEODOROS LOIZOU, MD[1]
STAVROS POULOUKAS, PHD[2]
CHARALAMBOS TOUNTAS, MD[3]
ANASTASIA THANOPOULOU, MD[3]
VASILIOS KARAMANOS, MD[3]

From the [1]Nicosia Diabetes Centre, Nicosia, Cyprus; the [2]Department of Computer Science, Intercollege, Nicosia, Cyprus; and the [3]Diabetes Centre, Department of Internal Medicine, National University of Athens, Athens, Greece.

Address correspondence to Theodoros Loizou, MD, Griva Digeni 48, Nicosia 1080, Cyprus. E-mail: dorosloizou@yahoo.com.

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The Metabolic Syndrome and Glucose Tolerance Status Deterioration Over 23-Year Follow-Up

Individuals with impaired glucose tolerance or impaired fasting glucose are at high risk of developing type 2 diabetes and cardiovascular diseases (1). Identifying those individuals whose glucose tolerance status (GTS) will deteriorate over the years would be of public health importance, due to its preventive implications.

We assessed the metabolic syndrome and lifestyle habits as predictors of 23-year GTS deterioration among survivors of a nationwide longitudinal study (the Israeli Glucose Intolerance, Obesity and Hypertension Study) subsample (2). The study was approved by the institutional review board, and all subjects gave written informed consent. Among the 562 nondiabetic subjects at baseline to whom either oral glucose tolerance test or fasting glucose were available at follow-up (298 male and 264 female subjects, mean age 70.4 ± 6.8 years), 54.6% deteriorated (i.e., they were normoglycemic at baseline and became impaired or diabetic at follow-up or were impaired and became diabetic). Male subjects experienced higher deterioration rates (59.4%) than female subjects (49.2%) ($P = 0.02$). Among the ethnic groups, North African–born subjects had the highest rates of deterioration and European/American-born subjects the lowest (67.4 and 47.1%, respectively; $P = 0.01$). Those who have ever smoked cigarettes and sedentary individuals exhibited higher deterioration rates than those who have never smoked and those currently physically active (58.6 vs. 50.9%, $P = 0.06$ for smoking and 59.7 vs. 50.6%, $P = 0.03$ for physical activity, respectively). All metabolic syndrome components other than HDL cholesterol were found to be significantly associated to deterioration. In multiple logistic regression analysis, subjects with the metabolic syndrome had a sex-, age-, ethnic origin–, smoking-, and physical activity–adjusted 3.09 increased risk for GTS deterioration (95% CI 1.67–5.72; C index = 0.65).

In the study, an increasing number of metabolic syndrome components were significantly associated with increasing rates of deterioration in GTS from 43.2% among those who had none of the components to almost 90% in those who had four or five components ($P < 0.001$).

Presence of the metabolic syndrome at baseline was found to predict both the deterioration in GTS, a smoldering process on the axis of time, and diabetes incidence. When evaluating its predictive value in detecting type 2 diabetes or GTS deterioration, one must relate to the paradigm of fasting blood glucose being a component of both the outcome and the metabolic syndrome. Our study exhibited similar results, with metabolic syndrome not including fasting blood glucose (odds ratio for deterioration of those positive for metabolic syndrome 2.22 [95% CI 1.19–4.11]). Assuming that those who did not survive were subjects with the less-favorable health status, these results are most likely underestimated. Modifiable lifestyle characteristics were found to predict 23-year GTS deterioration in order to facilitate the prevention or delay of type 2 diabetes.

RACHEL S. DANKNER, MD, MPH[1,2]
ANGELA CHETRIT, MA[1]
URI GOLDBOURT, PHD[2,3]

From the [1]Cardiovascular Epidemiology Unit, Gertner Institute for Epidemiology and Health Policy Research, Tel-Hashomer, Israel; the [2]Department of Epidemiology and Preventive Medicine, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; and the [3]Neufeld Cardiac Research Institute, Sheba Medical Center, Tel Hashomer, Israel.

Address correspondence to Rachel Dankner, MD, MPH, Cardiovascular Epidemiology Unit, Gertner Institute for Epidemiology and Health Policy Research, Tel-Hashomer, 52621. Israel. E-mail: racheld@gertner.health.gov.il.

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A Rare but Serious Side Effect of Levofloxacin

Hypoglycemia in a geriatric patient

Drugs should always be considered in the differential diagnosis of hypoglycemia. Fluoroquinolones have rarely been associated with hypoglycemia (1,2). Levofloxacine, which belongs to the fluoroquinolone group of antibiotics, has previously been reported to cause hypoglycemia in only one patient who was also receiving oral antidiabetic drugs (2). Herein, we describe an elderly patient with hypoglycemia associated with levofloxacine therapy who did use oral antidiabetic drugs or insulin.

A 64-year-old female with type 2 diabetes treated only by diet was interned for urinary infection and pneumonia. She had no history of malabsorbtion or oral intolerance. The patient's weight was 84 kg, and she was 157 cm tall (corresponding to a BMI of 34.1 kg/m^2). Her current medications included coraspin, omeprazole, and atorvastatin. Cefuroxime 3 × 750 mg/day i.v. was started. During cefuroxime therapy, her blood glucose levels were within normal limits with diet. C-reactive protein level was not decreased. On the 3rd day of treatment, cefuroxime was replaced with levofloxacin (500 mg/day) because of unresponsiveness. During treatment with levofloxacin, the symptoms of diseases diminished significantly, but the patient complained of generalized weakness. On the 2nd day of levofloxacin therapy, the patient became lethargic and disoriented. Blood pressure was 126/72 mmHg, heart rate was 82 bpm and regular, and body temperature was normal. Meningial irritation signs were absent, and pupils were intermediate, symmetric, and reactive. Optic fundi were normal, and no focal neurologic deficit was detected. Other physical findings were unremarkable. Her blood glucose level was measured as 32 mg/dl. The simultaneous blood insulin level was 6.7 IU (normal range 5–25 IU). Other routine hematological and biochemical blood tests were within normal range. Electrocardiography was also normal. A 30% dextrose infusion was started, and the patient thereafter became fully conscious without any neurologic deficit. Although she did not take any insulin during dextrose infusion, her consequent blood glucose levels were measured as 54 and 62 mg/dl in the 1st and following the 4th h. On the 3rd day of levofloxacin treatment, another hypoglycemic episode was observed. During treatment with levofloxacin, she did not change her usual daily diet regimen. Levofloxacin was stopped, and we continued treatment with piperacillin tazobactam. No further episodes of hypoglycemia were observed during follow-up period.

The symptomatic hypoglycemia in our patient developed 1 day after initiating treatment with levofloxacin. Since no other apparent cause for hypoglycemia was found, levofloxacin was the most likely etiology of this dangerous and potentially fatal glucose abnormality. Levofloxacin is an increasingly popular broad-spectrum antibiotic. In general, it has an excellent safety profile and is considered safe in patients with penicillin or cephalosporin allergy (3). Published reports about adverse effects of flouroquinolones are available for ciprofloxacin, gatifloxacin, clinafloxacin, and only one case of levofloxacin (2,4,5).

The previously published reports about fluoroquinolone-associated hypoglycemia consisted of elderly patients with a history of type 2 diabetes, renal dysfunction, and receiving oral sulfonylureas (2,4). Our patient also had only diabetes. Consistent with most published case reports, the hypoglycemia in our patient was documented within 24 h of levofloxacin administration, and intravenous dextrose was required for correction of hypoglycemia. Other factors such as poor oral intake or renal dysfunction that could have contributed to the profound and prolonged hypoglycemia were not present in our patient. The mechanisms by which fluoroquinolones cause hypoglycemia are not fully understood. In one study, increased rat pancreatic islet cell insulin release was claimed to be the mechanism. This process was inhibited by drugs that antagonized adenosine triphosphate-sensitive K^+ channels, suggesting that this channel is involved (6). Use of the Naranjo ADR Probability Scale (7) indicated a probable relationship between the adverse effect of hypoglycemia and levofloxacin therapy in this patient.

This case showed that even one dose of levofloxacin might be associated with significant and even fatal complications in geriatric patients without any previous renal dysfunction or impaired oral intake. To our knowledge, this is the first case of hypoglycemia related to levofloxacin in an elderly diabetic patient not using any oral antidiabetic drugs or insulin. The purpose of this letter is to caution physicians dealing with geriatric patients against the inappropriate use of flouroqunolones in these patients, especially in those with diabetes, since they may have a greater tendency to hypoglycemia. It might be important to monitor blood glucose levels early in the course of therapy.

MEHMET KANBAY, MD[1]
TIMUCIN AYDOGAN, MD[2]
RIFAT BOZALAN, MD[2]
AYSE ISIK, MD[2]
BURAK UZ, MD[2]
ARIF KAYA, MD[2]
ALI AKCAY, MD[1]

From the [1]Department of Nephrology, Fatih University Faculty of Medicine, Ankara, Turkey; and the [2]Department of Internal Medicine, Fatih University Faculty of Medicine, Ankara, Turkey.

Address correspondence to Mehmet Kanbay, MD, 35 sokak 81/5 Oktay Apt., Bahcelievler, Ankara, Turkey. E-mail: drkanbay@yahoo.com.

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