Case Study: The Benefits of Making a Dietitian Referral for Pre-diabetes

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Presentation

Initial consultation. D.G., a 54-year-old white man, was referred to a registered dietitian (RD) for pre-diabetes. He had been identified as having pre-diabetes 8 months earlier and was trying to lose weight on his own.

The initial assessment indicated that his height was 67" and current weight was 185 lb (BMI 29 kg/m^2). His waist measurement was 35", and a 3-year weight history indicated weight fluctuations between 173 and 191 lb.

Recent laboratory tests showed a fasting blood glucose (FBG) of 123 mg/dl, total cholesterol of 249 mg/dl, triglyceride level of 297 mg/dl, HDL cholesterol of 42 mg/dl, and LDL cholesterol of 148 mg/dl. D.G. reported taking atenolol for hypertension and daily aspirin. The referring health care provider stated that D.G. was at increased health risk because of "probable metabolic syndrome."

The RD reviewed with D.G. his diabetes risk factors: age, personal medical history of hypertension, dyslipidemia, pre-diabetes, and BMI > 25 kg/m^2. He reported engaging in aerobic exercise five times each week for 35–60 minutes per session, but said he had been unsuccessful at eating less fat to lower his cholesterol.

After obtaining information on his usual food intake, the RD recommended that D.G. limit his food intake to 1,800 cal/day, his total fat intake to 25–30% of calories (50–60 g), and his saturated fat intake to 7–10% of calories (14–20 g). They discussed ways to lower calories by eating smaller portions, making lower-fat food choices, and limiting foods high in sugar, such as regular soda. The RD encouraged him to maintain his aerobic exercise routine.

D.G. was assessed to be at the "action" stage of the readiness-to-change behavior change model for physical activity and at the "preparation" stage for managing weight and choosing low-fat foods. He was very motivated to live a healthy lifestyle and reduce his risk of developing diabetes and heart disease. He had strong support from his wife.

D.G. enrolled in a phone-based lifestyle counseling program and received nutrition and disease-prevention information. He agreed to track his food intake using an online food log and nutritional analysis program and to participate in regular follow-up with the RD for several months.

RD follow-up at 6 months. D.G. reported that his weight was 165 lb. He had lost 20 lb and reduced his BMI to 25.8 kg/m^2. He was keeping a food log and meeting his fat and calorie goals. Laboratory results at the 6-month follow-up showed an FBG of 109 mg/dl (down 14 mg/dl), a total cholesterol of 226 mg/dl (down 23 mg/dl), a triglyceride level of 154 (down 143 mg/dl), an HDL cholesterol level of 46 (up 4 mg/dl), and an LDL cholesterol level of 149 (up 1 mg/dl). D.G. reported that he wanted to lose an additional 10 lb for a goal weight of 155 lb. He reported being more confident in his ability to make healthy food choices and to maintain his aerobic exercise program. He felt positive about his support system.

The RD congratulated D.G. for the progress he had made and assessed him to be at the "action" stage of change for making food choices that were low in fat and saturated fat and at the "maintenance" stage for continuing with his aerobic exercise. The RD noted that reducing saturated fat further (to 7%) could lower LDL cholesterol but that sometimes a cholesterol-lowering medication may also be necessary.

D.G. decided that he had the tools he needed to continue on his own. He planned to maintain his aerobic exercise program and work at further reducing total fat and saturated fat intake, portion sizes, and foods high in sugar, while increasing his fruit and vegetable intake. He agreed to follow up with his health care provider to have his blood glucose and cholesterol level checked on a regular basis.

Clinic visit 9 months after initial RD consultation. D.G.'s care provider started him on atorvastatin because, even with dietary changes, his blood lipids remained outside of goal: total cholesterol of 241 mg/dl, triglyceride level of 185 mg/dl, HDL cholesterol level of 52 mg/dl, and LDL cholesterol level of 152 mg/d. His FBG was 112 mg/dl, and his weight was 171 lb (up 6 lb).

Clinic visit 1 year after initial RD consultation. With sustained weight loss, a low-fat diet, and cholesterol-lowering medication, D.G.'s metabolic outcomes were at goal: total cholesterol of 123 mg/dl (down 118 mg/dl), triglyceride level of 117 mg/dl (down 68 mg/dl), HDL cholesterol level of 49 mg/dl (down 3 mg/dl), and LDL cholesterol level of 51 (down 101 mg/dl). His FBG was 99 mg/dl (down 13 mg/dl), and his weight was 166 lb (down 5 lb).

By losing weight and keeping it off, D.G. has been able to prevent type 2 diabetes for the past 1.5 years, and his FBG has returned to normal. If he does not gain weight and remains physically active, he will likely continue to prevent or delay the development of diabetes.

Questions

1. How is pre-diabetes identified, and what are the current recommendations for its treatment?
2. How can patients with pre-diabetes benefit from being referred to an RD?
3. Is lowering FBG enough when treating patients with pre-diabetes?

Commentary

Pre-diabetes is identified through either the FBG test or the oral glucose tolerance test (OGTT) (Table 1). Either test should be repeated on another day to confirm the presence of the condition.[1]

The Diabetes Prevention Program (DPP) showed that as little as a 5% sustained weight loss (~ 10 lb) and 30 minutes of exercise 5 days a week (150 minutes/week) can reduce type 2 diabetes risk by 58%.[2] DPP researchers found that diet and exercise were more effective than metformin therapy. Participants who were treated with metformin reduced their diabetes risk by only 31%.[2]

Because weight management is the primary treatment recommendation for pre-diabetes, referral to an RD would benefit patients with this condition. An RD can assess a patient's current food intake, activity level, and readiness to change, and then make recommendations for lifestyle change. Nutrition recommendations for pre-diabetes include calorie reduction, reduced intake of total fat (particularly saturated fat), and increased intake of whole grains and dietary fiber.[3] Physical activity recommendations include 2.5 hours of moderate physical activity (such as brisk walking) per week.[2]

Based on an individual's readiness to change and current lifestyle behaviors, the RD can tailor these recommendations to each patient. One way to do this is through use of the Transtheoretical Model.[4] For example, an individual in the "preparation" stage (i.e., planning to make changes within the 30 days) may know what to do (eat healthier), but may not know where to begin changing their food choices. An RD can help this individual develop an eating plan and teach specific how-to skills, such as using nutrition labels choosing lower-fat foods.

Pre-diabetes is associated with the metabolic syndrome—the clustering of obesity, dyslipidemia, and hypertension. An RD can also make nutrition recommendations that will help patients who need to lower their cholesterol and blood pressure. The medical nutrition therapy goals for prevention of diabetes in high-risk individuals include:

- Moderate sustained weight loss of ~ 5%
- Achievement and maintenance of optimal metabolic outcomes, including normal blood lipid, blood pressure, and blood glucose levels
- Modification of nutrient intake for the treatment of comorbidities (i.e., obesity, dyslipidemia, cardiovascular disease, and hypertension)
- Improvement in health through nutritious food choices
- Development of plans to address individual nutritional needs while taking into consideration patients' personal and cultural preferences and lifestyles and respecting their wishes and willingness to change.[3]

Patients with pre-diabetes often have other related medical conditions, so treating pre-diabetes itself is not enough. Metabolic outcomes should be monitored on a regular basis. Changes in lifestyle and, if necessary, the addition or adjustment in medications should be made to maintain optimal blood glucose, blood lipid, and blood pressure levels.[5,6]

Clinical Pearls

- Sustained weight loss of at least 5% is necessary to prevent type 2 diabetes in high-risk patients.
- Patients with pre-diabetes may benefit from a nutrition consultation because an RD can conduct a comprehensive nutrition assessment and provide lifestyle counseling for cholesterol and blood pressure management in addition to management of prediabetic glucose levels.
- The focus of the interventions should not be limited to blood glucose. Because of the association between pre-diabetes and the metabolic syndrome, treating hypertension and dyslipidemia is equally important.
- To reach optimal metabolic outcomes, medications for blood pressure and cholesterol-lowering may be needed in addition to a healthier lifestyle.
- Individuals with pre-diabetes can get valuable benefits from an RD referral including behavior change counseling (i.e., tailored counseling based on an

Table 1. Diagnostic criteria

	Pre-diabetes		
Normal blood glucose	**Impaired fasting glucose**	**Impaired glucose tolerance**	**Diabetes**
Fasting* 70–100 mg/dl Casual** < 140 mg/dl	Fasting 100–125 mgdl	2-hour postprandial 140–199 mg/dl	Fasting ≥ 126 mg/dl *or* 2-hour postprandial ≥ 200 mg/dl

*Fasting—no caloric intake for at least 8 hours
**Casual—any time of the day without regard to time of last meal

individual's motivational readiness to change), individualized nutrition recommendations, and assistance with developing a realistic action plan for diabetes prevention.

REFERENCES

[1]American Diabetes Association: Diagnosis and classification of diabetes mellitus (Position Statement). *Diabetes Care* 28 (Suppl. 1):S37–S42, 2005

[2]American Diabetes Association: Prevention or delay of type 2 diabetes (Position Statement). *Diabetes Care* 27 (Suppl. 1):S47–S54, 2004

[3]American Diabetes Association: Nutrition principles and recommendations in diabetes (Position Statement). *Diabetes Care* 27 (Suppl. 1):S36–S46, 2004

[4]Prochaska JO, Velicer WF: Transtheoretical model of health behavior change. *Am J Health Promotion* 12:38–48, 1997

[5]National Institutes of Health: *Third report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults*. (NIH publ. no. 02-5215) Bethesda, Md., National Institutes of Health, 2001

[6]National Institutes of Health: *The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure*. (NIH publ. no. 04-5230). Bethesda, Md., National Institutes of Health, 2004

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Case Study: Diagnosis of Insulinoma Using Continuous Glucose Monitoring System in a Patient With Diabetes

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Presentation

K.D., a 20-year-old white female college student was brought by her parents for evaluation of hypoglycemia. She had experienced multiple episodes of palpitations, blurred vision, and left facial paresthesias for a year, progressively worsening and occurring more frequently in the 2 months just before her appointment.

Usually the episodes occurred between 3:00 and 7:30 P.M. The symptoms occurred without regard to meals and were relieved with food or juice. Her most severe witnessed episode, which occurred while she was at college, happened a few days before the consultation, while K.D. was working, 2 hours postprandially. Observers reported that she appeared confused, agitated, and diaphoretic. Her glucose via fingerstick by paramedics was 35 mg/dl. She received intravenous dextrose, and subsequently her glucose rose to 217 mg/dl with resolution of her symptoms. She had several episodes with neuroglycopenic symptoms and glucose levels of 35–45 mg/dl.

There was no history indicating diabetic medications in her home. She also complained of a 25-lb weight gain during the past year.

A year before her visit, K.D. was diagnosed with diabetes by oral glucose tolerance test (OGTT). The results were:

Fasting blood glucose:	86 mg/dl
30 minutes:	229 mg/dl
60 minutes:	232 mg/dl
120 minutes:	235 mg/dl
180 minutes:	165 mg/dl

At that time, she had a normal hemoglobin A_{1c}, and she was instructed in diet and exercise. No antidiabetic medications had been prescribed.

K.D. had a psychiatric evaluation, was diagnosed with depression, and was started on sertraline. In the month before the consultation, she also had a neurological work-up with negative computed tomography scans of the head and normal electroencephalogram.

Her family history was significant only for diabetes of a maternal aunt. She denied allergies or use of cigarettes, alcohol, or illicit drugs. She was taking sertraline, 50 mg daily for the past year; ethinyl estradiol/norgestimate, one daily for the past 2 years; and oxcarbazepine, 175 mg twice daily for the past week.

Physical examination did not reveal any orthostasis and was essentially normal. On the day of her office visit, concomitant with a random glucose of 62 mg/dl, K.D.'s insulin level was 37 μ/ml (normal: 2–15 μ/ml), and her C-peptide level was 7.7 ng/ml (normal: 1.1–4.6 ng/ml).

Her cortisol level was 18 μ/dl (normal: 3–17 μg/dl). Thyroid-stimulating hormone, liver function tests, creatinine, and electrolytes were normal. There were no measurable blood levels of sulfonylurea. She was given a glucometer and was advised to check her fasting blood glucose and also blood glucose levels whenever her symptoms suggested hypoglycemia.

K.D. returned to clinic 2 weeks later complaining of persistent hypoglycemic episodes. At that time, a continuous glucose monitoring system (CGMS) was applied (Figures 1 and 2). The patient had multiple and frequent episodes of

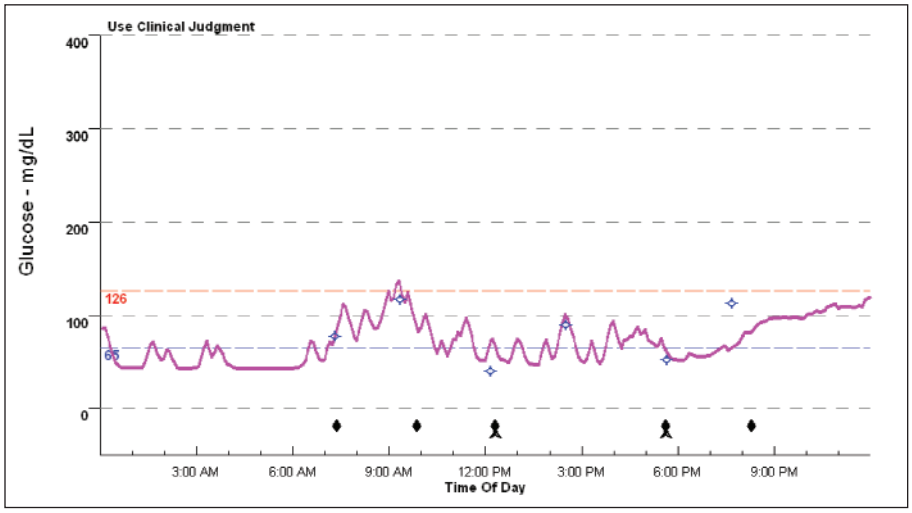

Figure 1. The continuous line represents the sensor glucose values. The blue asterisk respresents the meter blood glucose readings that were entered into the monitor. If there are no interruptions in glucose monitoring, then the number of paired sensor glucose values/meter blood glucose readings should match the number of meter blood glucose readings. In this graph, the flat line represents sensor blood glucose readings < 40 mg/dl. The CGMS cannot sense < 40 mg/dl.

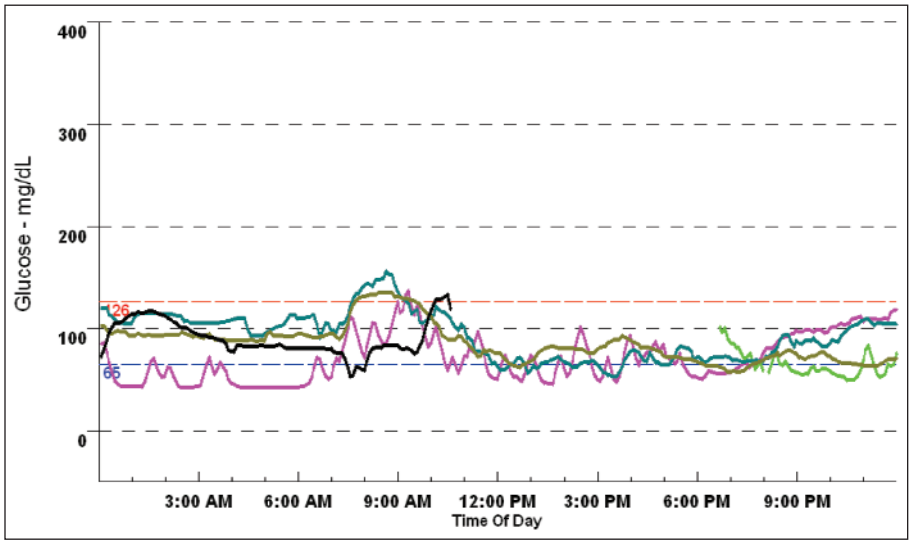

Figure 2. This graph presents all of the CGMS data superimposed over a 24-hour period, with each day presented as a separate plot line.

blood glucose levels < 55 mg/dl independent of the time of the day. It is worth noticing that she had blood glucose < 40 mg/dl for more than 2 hours continuously during sleep.

The patient was hospitalized for a 72-hour fast test. Within 20 minutes of the start of the fast, her blood glucose fell to 16 mg/dl. At the same time, her insulin was 18 μ/ml; proinsulin was 534.5 pmol/l (normal: 2.1–26.8 pmol/l); C-peptide level was 7.6 ng/ml (normal: 1.1–4.6 ng/ml); and β-hydroxybutyrate was 0.2 mmol/l (normal: 0.0–0.3 mmol/l). Drug screens for sulfonyluea and repaglinide were negative.

A magnetic resonance imaging scan with contrast of her abdomen showed a 1.2-cm lesion in the tail of the pancreas. The patient underwent successful enucleation of the tumor, which revealed insulinoma. The postoperative course was uncomplicated.

Materials and methods. The CGMS (MiniMed, Sylmar, Calif.) was placed on the patient, and glucose levels were monitored for 87 hours. The patient was instructed and trained on the use of CGMS before its placement. The patient's capillary blood glucose levels were checked and recorded at least four times a day and whenever she experience neuroglycopenic symptoms. She was also asked to record in a diary her meals and physical activity.

CGMS is designed to continuously and automatically monitor glucose values in subcutaneous tissue fluid within a range of 40–400 mg/dl. The CGMS records sensor signals every 5 minutes, providing 288 glucose readings per day. When the glucose readings are < 40 mg/dl, the graph appears as a flat line.

C-peptide was determined by a chemiluminescent immunoassay (Associated Regional and University Pathologists, Salt Lake City, Utah). Insulin levels were quantitated by paramagnetic-particle chemiluminescent immunoassay (Beckman Coulter Access analyzer and insulin reagent pack; Chaska, Minn.) The two-site enzyme immunoassay measured the proinsulin level. The sulfonylurea panel was performed by the high performance liquid chromatography method. Finally, for the repaglinide level, the liquid chromatography–tandem mass spectrometry method was used.

Questions

1. What is the differential diagnosis of high insulin?
2. What are the indications for CGMS use?
3. At what point should the CGMS be used for the differential diagnosis of hypoglycemia?

Commentary

Insulinoma, a rare islet tumor of the pancreas, is characterized by symptomatic hypoglycemia, inappropriately increased plasma insulin, proinsulin, and

C-peptide levels during an episode of spontaneous hypoglycemia.[1]

The coexistence of insulinoma and diabetes is rare and has been reported in diabetic patients whose hypoglycemic symptoms were explained by the presence of insulinoma.[2–9]

The CGMS is a sensor system for measuring the glucose concentrations continuously in subcutaneous tissue. It has been mostly useful for detecting unrecognized hypoglycemia in patients with type 1 or type 2 diabetes.[10,11]

We have described here a young female patient with a diabetic OGTT and persistent symptomatic hypoglycemia for whom continuous glucose monitoring played a major role in diagnosing insulinoma. This case appears to be the first report of a patient with insulinoma and concomitant diabetes in which continuous glucose monitoring was used as an important diagnostic tool.

At the age of 20, K.D. presented with hypoglycemia associated with neuroglycopenic symptoms. Because she had had a diabetic OGTT a year before, it was initially suspected that she might have reactive hypoglycemia. What made this patient's presentation more intriguing was that her symptoms of spontaneous hypoglycemia were progressively intensifying in severity and frequency. The persistence of hypoglycemia during the day, but not reported by the patient during the night, led to the consideration of using the CGMS as a diagnostic tool to document the hypoglycemic episodes.

The insulinoma was considered as a possible diagnosis only after review of the striking CGMS results. The episodes of hypoglycemia during the night were frequent, and recovery was spontaneous. The CGMS showed low blood glucose of < 40 mg/dl throughout a 24-hour period, most strikingly nocturnally (Figures 1 and 2), despite the fact that the patient denied any hypoglycemic symptoms during the night. This was the major contribution of CGMS in suggesting the diagnosis of insulinoma.

The absence of neuroglycopenic symptoms during the night with blood glucose levels < 40 mg/dl can probably be explained by the fact that young healthy women may have plasma glucose values in the range of 40 mg/dl without any symptoms.[12] Another interesting point of this case was that during the CGMS use, there was nocturnal hypoglycemia during only 1 of the 3 full days of monitoring (Figure 1). This is not commonly seen with the classical presentation of insulinomas, in which hypoglycemia is frequently seen during the longest caloric restriction, which usually occurs during the night.

The CGMS has been shown to provide a good correlation between blood and interstitial glucose levels.[13,14] It has also been used in the detection of unrecognized hypoglycemia in patients with type 1 or type 2 diabetes.[10,11] Here, it was used to detect possible unusual causes of hypoglycemia, such as insulinoma.

In this case, the CGMS was in place over a period of 87 hours, even though 72 hours is the norm. This difference is simply related to the patient's delay in returning the CGMS. A striking issue of this case is that the CGMS correlated perfectly with the fingerstick glucose of the patient, despite the longer use period. This is an indication that the technique of the CGMS has significantly improved, and its reliability has been increased.

The CGMS has limitations because it measures interstitial fluid glucose rather than serum levels. However, Monsod et al.[15] have shown that the CGMS can accurately predict plasma glucose concentrations during hypoglycemia and hyperinsulinemia. This accuracy diminishes, though, toward the 40 mg/dl glucose level, and inaccurate readings can be obtained.[16]

It is likely that K.D. had two independent conditions (i.e., insulinoma and type 2 diabetes). Earlier reports in the literature have described the coexistence of diabetes and insulinoma.[2–9] The diagnosis of these two coexistent diseases is very challenging. This patient is the youngest one ever reported in the literature with these two diagnoses; the age range in previous reports was 45–78 years.[2–9] The time that lapsed from the onset of her symptoms until the final diagnosis was approximately 12 months, which is short when compared to the previously reported cases, where the time range was 13–24 months.

As mentioned above, this is the first reported use of a CGMS as a major adjunctive method for detecting hypoglycemia. In this case, the CGMS was well tolerated and very accurate. The CGMS should therefore be considered for the work-up of such patients because it is reliable, safe, and easily performed on an outpatient basis.

Clinical Pearls

- Insulinoma is a rare tumor of the pancreas that should be considered in the differential diagnosis of a young patient with hypoglycemia.
- The coexistence of insulinoma and type 2 diabetes is challenging and often goes unrecognized.
- The CGMS is an adjunctive method for detecting hypoglycemia.
- The CGMS is a safe tool that is easily used on an outpatient basis.

REFERENCES

[1]Service FJ, McMahon MM, O'Brien PC, Ballard DJ: Functioning insulinoma-incidence, recurrence, and long-term survival of patients: a 60-year study. *Mayo Clin Proc* 66:711–719, 1991

[2]Gittler RD, Zucker R, Eisinger R, Stoller N: Amelioration of diabetes mellitus by an insulinoma. *N Engl J Med* 258:932–935, 1958

[3]Knight PO: Insulinoma and generalized islet cell hyperplasia in a patient with diabetes mellitus. *South Med J* 60:119–123, 1967

[4]Kane LA, Grant CS, Nippoldt TB, Service FJ: Insulinoma in a patient with NIDDM. *Diabetes Care* 16:1298–1300, 1993

[5]Svartberg J, Stridsberg M, Wilander E, Andersson DE, Eriksson B: Tumour-induced hypoglycaemia in a patient with insulin-dependent diabetes melittus. *J Intern Med* 239:181–185, 1996

[6]Sakurai A, Aizawa T, Katakura M, Sato Y, Kaneko G, Yoshizawa K, Hashizume K: Insulinoma in a patient with non-insulin-dependent diabetes mellitus. *Endocr J* 44:473–477, 1997

[7]Wildbrett J, Nagel M, Theissig F, Gaertner HJ, Gromeier S, Fischer S, Hanefeld M: [An unusual picture of insulinoma in type-2 diabetes mellitus and morbid obesity]. *Dtsch Med Wschr* 124:248–252, 1999 (article in German)

[8]Arioglu E, Gottlieb NA, Koch CA, Doppman JL, Grey NJ, Gorden P: Natural history of a proinsulin-secreting insulinoma: from symptomatic hypoglycemia to clinical diabetes. *J Clin Endocrinol Metab* 85:3628–3630, 2000

[9]Ravnik-Oblak M, Janez A, Kocijanicic A: Insulinoma induced hypoglycemia in a type 2 diabetic patient. *Wien Klin Wochenschr* 113:339–341, 2001

[10]Chico A, Vidal-Rios P, Subira M, Novials A: The continuous glucose monitoring system is useful for detecting unrecognized hypoglycemias in patients with type 1 and type 2 diabetes but is not better than frequent capillary glucose measurements for improving metabolic control. *Diabetes Care* 26:1153–1157, 2001

[11]Hay LC, Wilmshurst EG, Fulcher G: Unrecognized hypo- and hyperglycemia in well-controlled patients with type 2 diabetes mellitus: the results of continuous glucose monitoring. *Diabetes Technol Therapeut* 5:19–26, 2003

[12]Merimee TJ, Fineberg SE: Homeostasis during fasting. II. Hormone substrate differences between men and women. *J Clin Endocrinol Metab* 37:698–702, 1973

[13]Gross TM, Bode BW, Einhorn D, Kayne DM, Reed JH, White NH and Mastrotoro JJ: Performance evaluation of the MiniMed continuous glucose monitoring system during patient home use. *Diabetes Technol Ther* 2:49–56, 2000

[14]Mastrototaro JJ: The MiniMed continuous glucose monitoring system (CGMS). *J Pediatr Endocrnol Metab* 12:751–758, 1999

[15]Monsod TP, Flanagan DE, Rife F, Saenz R, Caprio S, Sherwin RS, Tamborlane WV: Do sensor glucose levels accurately predict plasma glucose concentrations during hypoglycemia and hyperinsulinemia? *Diabetes Care* 25:889–893, 2002

[16]McGowan K, Thomas W, Moran A: Spurious reporting of nocturnal hypoglycemia by CGMS in patients with tightly controlled type 1 diabetes. *Diabetes Care* 25:1499–1503, 2002

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