BRIEF REPORT

'White Coat' Hyperglycemia

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A visit to a physician's office may provoke an increase in blood pressure. Stress is also a well-known glycemic aggravation, and managing diabetes with ongoing stress is often difficult. Two patients with diabetes mellitus in whom anxiety and stress contributed to transient hyperglycemia that impacted adversely on their diabetes management are presented. "White coat" hyperglycemia should be suspected when the clinical glucose levels are higher than the glucose levels measured by the patient at home and the clinical glycohemoglobin levels. The recognition of white coat hyperglycemia is especially important with the recent findings that intensive therapy effectively delays the onset and slows the progression of diabetic complications in patients with insulin-dependent diabetes mellitus. Failure to appreciate white coat hyperglycemia will increase the risk of hypoglycemic episodes, some of which may be severe and life threatening. *(Arch Fam Med. 1994;3:461-464)*

It is well known that a visit to a physician's office may provoke an increase of blood pressure.[1] What causes the "white coat" blood pressure response remains unclear, but one explanation for this phenomenon may be anxiety. The concern that one's blood pressure is high may cause an increased level of sympathetic arousal followed by a rise in plasma catecholamine levels, so that the blood pressure remains high.

In their offices, physicians use the patient's clinical glucose levels and the home-monitored log book of glucose levels to assess recent glycemic control. It is not uncommon to find the clincal glucose levels to be higher than the self-monitored levels. Patients often ascribe this difference to the stresses of attending the clinic, analogous to the phenomenon of white coat hypertension. It is well known that stress aggravates glycemic control, and the treatment of diabetic patients with ongoing stress is often difficult.[2] The frequency of white coat hyperglycemia is unclear. However, Campbell et al[3] found that in 19 of 34 patients with at least two consecutive clinical blood glucose levels that were more than 5 mmol/L (90 mg/dL) higher than the mean self-reported level, the difference was due to transient hyperglycemia related to office attendance rather than errors in the self-monitoring technique. Their measurement of glycated proteins helped to assess the causes of discrepancies between the clinical and the self-recorded blood glucose levels in their study.

Two patients with diabetes mellitus, in whom anxiety and stress were contributing factors to transient hyperglycemia that impacted negatively on their diabetes management, are discussed herein. White coat hyperglycemia should be suspected when the clinical glucose levels do not correspond with the self-monitored glucose levels and the glycohemoglobin levels.

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REPORT OF CASES

CASE 1

A 54-year-old white woman had a 15-year history of non–insulin-dependent diabetes mellitus; she has required insulin therapy for the last 7 years. Her insulin dose was 35 U of NPH insulin (Humulin N) and 5 U of regular human insulin (Humulin R) once daily, before breakfast. She had mild diabetic retinopathy and peripheral neuropathy but no diabetic nephropathy. Despite the use of insulin, she denied ever experiencing any hypoglycemic reactions. Her only other medical condition was hypertension, well controlled with indapamide (Lozol) and lisinopril (Zestril). She was receiving amitriptyline hydrochloride (Elavil) for her peripheral neuropathy and sleep difficulties. During repeated office visits, her random blood glucose levels, whether fasting, preprandial, or postprandial, were consistently higher than 14.0 mmol/L (250 mg/dL). Clinical and self-reported glucose levels were obtained with the LIFESCAN One Touch I and II blood glucose monitoring systems (Lifescan Inc, Milpitas, Calif). Glucose levels were measured in the laboratory by the glucose oxidase method with a Beckman glucose analyzer (Beckman, Palo Alto, Calif). She candidly admitted that she became very anxious during visits to the physician's office. Her home-monitored glucose levels were consistently lower, ranging from 5.0 to 11.1 mmol/L (90 to 200 mg/dL). Assessment of her monitoring techniques was done at regular intervals (at least yearly). The repeated and large discrepancies in glucose levels could not be explained by errors in her monitoring technique. Furthermore, the variable in the glucose levels could not be explained by the timing of the insulin administration or the interval between the intake of food and the measurement of glucose levels. Her self-monitored data were consistent with the clinical glycohemoglobin levels, ranging between 7.0% to 8.0% (normal range, 3.4% to 6.2%), suggesting clinic-related transient hyperglycemia. Her glucose and glycohemoglobin levels are outlined in the **Table**. Despite the concordance of home-monitored glucose levels and glycohemoglobin levels, she started therapy consisting of 5 U of NPH insulin before dinner because of the persistent elevation of clinical glucose levels in October 1990. She reported that her home-monitored glucose levels were lower, ranging from 4.0 to 9.7 mmol/L (72 to 175 mg/dL), and she began reporting spells that sounded like hypoglycemia. A clinical glucose level was 12.3 mmol/L (223 mg/dL) 1 month after starting the additional insulin therapy, her best ever clinical level. In early February 1991, she presented to the office complaining of nervousness and decreased mentation and was very diaphoretic. The clinical glucose level read "LLL," (low, low, low) with a laboratory glucose level of 2.3 mmol/L (41 mg/dL). The glycohemoglobin level had decreased to 6.7%. She responded to oral glucose supplementation, and her evening insulin therapy was discontinued. Her long-term glycemic control continues to be about the same, despite the persistent hyperglycemic episodes during office visits (Table).

CASE 2

A 40-year-old obese white woman had gestational diabetes mellitus, which developed during her fourth pregnancy at the age of 34 years. Postpartum management consisted of diet control, which was unsuccessful. She ultimately started insulin therapy after mild elevations of hepatic enzyme levels developed while taking glipizide (Glucotrol), an oral sulfonylurea. Therapy for the management of glucose levels consisted of 40 U of NPH insulin and 40 U of regular human insulin 30 minutes before breakfast and dinner. She had no known diabetic complications. Her self-monitored glucose levels ranged from 5.5 to 13.3 mmol/L (100 to 240 mg/dL). Six months ago, her glycohemoglobin level was 7.6%, which was in accordance with her home-monitored glucose levels. She also was very anxious during office visits, as demonstrated by random clinical glucose levels of 15.5 mmol/L (280 mg/dL) and 17.6 mmol/L (317 mg/dL) during visits to her family physician. Dysfunctional uterine bleeding that required dilation and curettage developed. Since she was very obese, her gynecologist recommended that the procedure be performed under general anesthesia in the outpatient surgical suite. Not unexpectedly she was very anxious, and because of an isolated preoperative glucose level of 20.9 mmol/L (376 mg/dL), her surgery was canceled. She was admitted to the hospital for management of her poorly controlled diabetes mellitus. A repeated determination of the glucose level 4 hours after admission, when she was more relaxed, was 12.3 mmol/L (221 mg/dL). Her glycohemoglobin level was 7.9%. She was discharged from the hospital after consultation with an endocrinologist.

COMMENT

These two patients illustrate the problems encountered when managing diabetes based on isolated clincial determination of glucose levels. Health care providers managing diabetes face a therapeutic dilemma when the patient's clinical glucose levels are repeatedly higher than those recorded at home. Like hypertension, transient rises in glucose levels can occur during an office visit and may not be a true reflection of long-term glycemic control. This dilemma was nicely demonstrated in the study by Campbell et al.[3] Approximately half of the glycemic discrepancies in their patients were due to transient hyperglycemia related to office visits. Another important finding in their study was the large number of errors in the self-monitoring techniques of the patients. Self-

Determination of Glucose and Glycohemoglobin Levels in Patient 1*

Date of Evaluations†	Glucose Levels, mmol/L (mg/dL)‡ Clinical	Laboratory	Glycohemoglobin Level, %§	Comments
1/19/89	19.6 (353)	22.6 (407)	7.4	NPH insulin, 35 U, and regular human insulin, 5 U, every morning
2/16/89	15.3 (275)	...	...	...
4/20/89	17.1 (307)	...	...	...
5/93/89	...	14.8 (267), F	...	...
5/18/89	21.7 (390)	22.8 (411)	7.4	Hematocrit count, 0.42
7/26/89	...	15.3 (275), F	...	...
8/15/89	20.3 (365)	19.3 (348)	...	...
12/12/89	19.2 (346)	...	7.5	...
5/11/90	...	17.1 (307), F	...	...
5/23/90	HHH	22.6 (407)	7.8	...
10/08/90	19.4 (350)	19.7 (354)	8.0	Add 5 U of regular human insulin in evening
11/16/90	12.4 (223)	...	...	...
2/02/91	LLL	2.3 (41)	6.7	Discontinue 5 U of regular human insulin in evening
3/03/91	18.7 (333)	...	...	...
3/07/91	18.6 (335)	...	...	...
4/16/91	14.9 (268)	...	...	...
5/16/91	20.3 (366)	...	6.2	...
9/19/91	16.3 (293), F	17.8 (321), F	7.4	...
1/23/92	19.8 (357)	...	...	...
2/12/92	16.4 (296)	...	...	...
6/16/92	13.7 (246)	...	...	...
9/08/92	14.8 (266)	...	...	...
3/02/93	21.2 (381)	20.6 (370)	9.0	Urinary tract infection
4/13/93	12.3 (222)	...	...	...
5/04/93	17.4 (313)	...	8.2	...
7/06/93	17.7 (319)	...	...	...
7/13/93	19.3 (348)	...	...	...
7/15/93	19.7 (355)	...	...	...
7/27/93	20.4 (368), F	22.6 (407), F	8.1	...
10/05/93	22.1 (380)	...	...	...

**Clinical glucose levels were determined with the LIFESCAN One Touch I and II blood glucose monitoring systems (Lifescan Inc, Milpitas, Calif). High- and low-control solutions were used to check the operation of the meters. Laboratory glucose levels were measured by the glucose oxidase method with a Beckman glucose analyzer (Beckman, Palo Alto, Calif). Normal range for glucose levels is 3.8 to 6.1 mmol/L (70 to 110 mg/dL).*

†Clinical and laboratory glucose levels obtained on the same date were from blood samples drawn at the same time but from different aliquots and were obtained in two diferent places.

‡HHH indicates high, high, high; LLL, low, low, low; and F, fasting.

§The normal range of glycohemoglobin levels is from 3.4% to 6.2%.

monitoring techniques must be retested at regular intervals as a routine, with retraining or transfer of the task when necessary.[3]

The treatment of isolated elevations in glucose levels must be done cautiously, particularly for those elevated levels obtained during office visits. Furthermore, an isolated, elevated glucose level may not indicate a need to postpone necessary surgical procedures. The availability of a preoperative glycohemoglobin level would assist the anesthesiologist in the management of the diabetes and determine if the preoperative glucose level truly reflects the patient's long-term glycemic control. While patient 1 nicely demonstrates the differences between clincial and home-monitored glucose levels and the risk of not appreciating white coat hyperglycemia, the case of patient 2 is less clear. Her transient rise in glucose levels preoperatively may reflect changes in food intake, medication instructions, and/or insulin administration and may not be purely related to stress and anxiety.

Retesting of the self-monitoring technique and the measurement of glycohemoglobin levels will help the clinician to distinguish white coat office hyperglycemia from hyperglycemia due to poor glycemic control. The measurement of glycohemoglobin levels will provide an objective index of overall glycemic control. For example, a glycohemoglobin level in the range of 6% to 8%, based on an upper limit of the normal level of 6.2%, indicates acceptable glycemic control with mean daily glucose levels ranging from 6.4 to 8.3 mmol/L (115 to 150 mg/dL) over the past 60 to 90 days. If the glycohemoglobin level

is consistent with self-monitoring data, eg, glycosylated hemoglobin of 7% with a mean self-monitored glucose level of 7.2 mmol/L (130 mg/dL), this would imply clinic-related transient white coat hyperglycemia. A level consistent with the raised clinical blood glucose levels, eg, a glycohemoglobin level of 11% with a clincal glucose level of 12.5 mmol/L (225 mg/dL), would suggest poor glycemic control and the need for retesting the self-monitoring technique.

The awareness of white coat hyperglycemia becomes increasingly more important with the recent report of the Diabetes Control and Complications Trial Research Group.[4] Intensifying insulin therapy increases the risk for hypoglycemia. It is therefore critical that health care providers identify those individuals with clinical glucose levels that are discordantly higher than those obtained at home. Failure to appreciate white coat hyperglycemia will increase the incidence of hypoglycemic events, some of which may be life threatening.

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Conversions From Système International (SI) Units to Conventional Units (Modified From *The SI Manual in Health Care*)

System*	Component	SI Reference Interval†	SI Unit‡	Conversion Factor (Divide by)	Conventional Reference Interval†	Conventional Unit
B	Hematocrit					
	Female	0.33-0.43	1	0.01	33-43	%

**B represents blood.*
†These reference values are not intended to be definitive since each laboratory determines its own values. They are provided for illustration only.
‡An arabic one in this column indicates that this item, formerly expressed in percent, should be expressed as a decimal (or the appropriate part of 1).

Practice Commentary

Anxiety and stress are ubiquitous and mostly indefinable in everyday terms. However, all practitioners have experienced the power of these forces on the clinical aspects of numerous medical problems, including control of glucose levels in diabetics. Undoubtedly, these phenomena are complex, and perhaps 100 years from now we will know the underlying science of stress and anxiety. Currently, clinicians can use the biomedical model to collect observational data, such as the measurement of glycohemoglobin levels, to sort out errors in monitoring and reporting.

This is also an opportunity to apply the biopsychosocial model to better understand the science of the relational process, ie, the other science of thoughts, feelings, and language, which can affect our clinical responses and outcomes of care. Engel[1] would remind us that the observational and relational processes are complementary, supplementary, and interdependent in operation. Understanding both is necessary to become more fully scientific in the care of all aspects of the whole person.

In the meantime, we practitioners need to listen for the meaning that a problem like white coat hypertension or hyperglycemia has to the patient and make sure we are treating the patient rather than the blood pressure or the blood glucose level. These case reports also point out the need to coordinate care among specialists and for comprehensiveness and continuity in the emotional care of these patients.

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