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SYMPOSIUM

Predicted Blood Glucose from Insulin Administration Based on Values from Miscoded Glucose Meters

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Abstract

Objectives:

The proper use of many types of self-monitored blood glucose (SMBG) meters requires calibration to match strip code. Studies have demonstrated the occurrence and impact on insulin dose of coding errors with SMBG meters. This paper reflects additional analyses performed with data from Raine *et al.* (JDST, 2:205-210, 2007). It attempts to relate potential insulin dose errors to possible adverse blood glucose outcomes when glucose meters are miscoded.

Methods:

Five sets of glucose meters were used. Two sets of meters were autocoded and therefore could not be miscoded, and three sets required manual coding. Two of each set of manually coded meters were deliberately miscoded, and one from each set was properly coded. Subjects (n = 116) had finger stick blood glucose obtained at fasting, as well as at 1 and 2 hours after a fixed meal (Boost®; Novartis Medical Nutrition U.S., Basel, Switzerland). Deviations of meter blood glucose results from the reference method (YSI) were used to predict insulin dose errors and resultant blood glucose outcomes based on these deviations.

Results:

Using insulin sensitivity data, it was determined that, given an actual blood glucose of 150–400 mg/dl, an error greater than +40 mg/dl would be required to calculate an insulin dose sufficient to produce a blood glucose of less than 70 mg/dl. Conversely, an error less than or equal to -70 mg/dl would be required to derive an insulin dose insufficient to correct an elevated blood glucose to less than 180 mg/dl.

For miscoded meters, the estimated probability to produce a blood glucose reduction to less than or equal to 70 mg/dl was 10.40%. The corresponding probabilities for autocoded and correctly coded manual meters were 2.52% ($p < 0.0001$) and 1.46% ($p < 0.0001$), respectively.

Furthermore, the errors from miscoded meters were large enough to produce a calculated blood glucose outcome less than or equal to 50 mg/dl in 42 of 833 instances. Autocoded meters produced zero (0) outcomes less than or equal to 50 mg/dl out of 279 instances, and correctly coded manual meters produced 1 of 416.

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Abbreviations: (A1c) glycosylated hemoglobin, (BG) blood glucose, (CGM) continuous glucose monitoring, (DCCT) The Diabetes Control and Complications Trial, (SD) standard deviation, (SMBG) self-monitored blood glucose, (UKPDS) UK Prospective Diabetes Study

Keywords: autocoded meter, blood glucose meter, manually coded meters, miscoded meter, user error

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Abstract *(continued)*

Conclusions:
Improperly coded blood glucose meters present the potential for insulin dose errors and resultant clinically significant hypoglycemia or hyperglycemia. Patients should be instructed and periodically reinstructed in the proper use of blood glucose meters, particularly for meters that require coding.

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Introduction

The Diabetes Control and Complications Trial (DCCT) demonstrated a reduction in microvascular events with intensive glycemic control in the type 1 diabetes patient. This reduction seemed to occur at the expense of a significant increase in hypoglycemic events in the intensive versus the conventional group. After 21 months of followup of the first 817 DCCT entrants, 216 subjects reported 714 episodes of severe hypoglycemia; 549 (77%) of those episodes occurred in intensively treated subjects.[1] While the DCCT demonstrated reduced complications in type 1 diabetes, other studies including the UK Prospective Diabetes Study (UKPDS) and Kumamoto demonstrated improved outcomes in the type 2 population. UKPDS (but not Kumamoto) demonstrated an increase in severe hypoglycemia in the intensively treated groups.[2,3] In the DCCT, predictors of severe hypoglycemia included history of severe hypoglycemia, longer duration of diabetes, higher baseline glycosylated hemoglobin (A1c) levels, and a lower recent A1c. Multivariate analyses failed to yield predictive models with high sensitivity. There are no indicators from DCCT investigators of glucose meter errors being related to hypoglycemic events.

The evaluation of glucose control in most patients depends on A1c and self-monitoring of blood glucose (SMBG). SMBG is currently the only convenient, patient-available tool providing immediate blood glucose results. The exception to this statement is continuous glucose monitoring (CGM). Even CGM, at the current state of the technology, requires calibration by SMBG.

In this article, we quantify the relationship between errors in (self-monitored) blood glucose estimation and resultant incorrect insulin doses. Incorrect insulin doses due to miscoded meters can result in otherwise unexplained glucose excursions. Of further concern are the additional risks from erroneous trending of glucose variation caused by faulty SMBG results in light of the increasing use of SMBG-calibrated CGM.

To our knowledge, there are no published data indicating that erroneous SMBG data contribute to unexplained hypoglycemia or hyperglycemia. A study to approximate the number and risk for emergency department visits for adverse events involving medications indicated an estimated 177,504 emergency department visits for adverse drug events among U.S. patients 65 years of age or older (2004–2005). Warfarin (17.3%), insulin (13.0%), and digoxin (3.2%) accounted for 33.3% of such visits.[4] There is no indication or inference that glucose meter errors accounted for insulin-related emergency department visits.

Patients and health care professionals regularly use SMBG data for diabetic therapeutic adjustment, and increasingly for CGM calibration. What if the data are erroneous? Several studies demonstrated that improper use of glucose meters is not uncommon; errors in meter coding are reported in studies at around 16%.[5,6,7]

In our published study, blood glucose (BG) data obtained from deliberately miscoded glucose meters were used to demonstrate potential errors in insulin dose based on erroneous blood glucose results caused by miscoding.[8] In the current paper we relate these calculated potential insulin dose errors to possible adverse blood glucose outcomes.

Materials and Methods

Some blood glucose meters need to be calibrated to assure that the code in the meter matches the code of the test strip being used. The purpose of the code number

is to correct for differences in reactivity between test strip lots. With meters that require manual coding, this is accomplished by the end user inserting a code chip or code strip, or manually changing the code number in the meter. In contrast, autocoded meters automatically set the correct code number any time a test strip or test disc is inserted into the meter, thereby relieving the end user of this task.

Five sets of glucose meters were used in the study. Two sets of meters were autocoded (labeled "A" and "B") and therefore could not be miscoded. Three sets of meters required manual coding (C, D, and E). Two of each set of manually coded meters were deliberately miscoded (labeled "Miscode 1," "Miscode 2"), and one from each set (labeled "Correct Code") was properly coded. Subjects from three clinical sites (n = 116) had finger stick blood glucose obtained at fasting, as well as at 1 and 2 hours after a fixed meal (Boost®; Novartis Medical Nutrition U.S., Basel, Switzerland). Blood glucose values were obtained from autocoded meters, correctly coded manually coded meters, miscoded meters, and from YSI analyzers (YSI Life Sciences, Yellow Springs, OH); 2223 blood glucose results were evaluated (1528 meters and 695 YSI analyzers). Deviations of meter blood glucose results from the reference method (YSI) were used to predict insulin dose errors and resultant blood glucose outcomes based on these deviations. Glucose meter deviations from YSI values were evaluated. A Monte Carlo computer simulation model used the frequency distribution of deviations to determine potential insulin dose errors.

The current paper describes the resultant adverse blood glucose effects projected from the calculated insulin dose errors using an insulin sensitivity formula.

Results

There were 1528 meter values taken from 116 subjects in the fasting state **(Table 1)**. Data were collected at fasting and at 1 and 2 hours after a fixed meal. Fasting data were chosen for this analysis, because fasting values are more likely to be corrected with insulin than post-meal values.

Table 1.
Numbers of Glucose Measures from All Meters

Number of Meter BG Measures	
Auto Coded	279
Manual Correct Code	416
Manual Miscoded	833
YSI	695
Total	2223

The maximal high deviation from YSI values was +146 mg/dl for miscoded meters, +61 mg/dl for autocoded meters, and +89 mg/dl for correctly coded manual meters **(Figure 1)**. Differences in high deviations between miscoded and either autocoded or correctly coded manual meters were statistically significant ($p < 0.0001$), but the difference between autocoded and correctly coded manual meters was not ($p = 0.9343$).

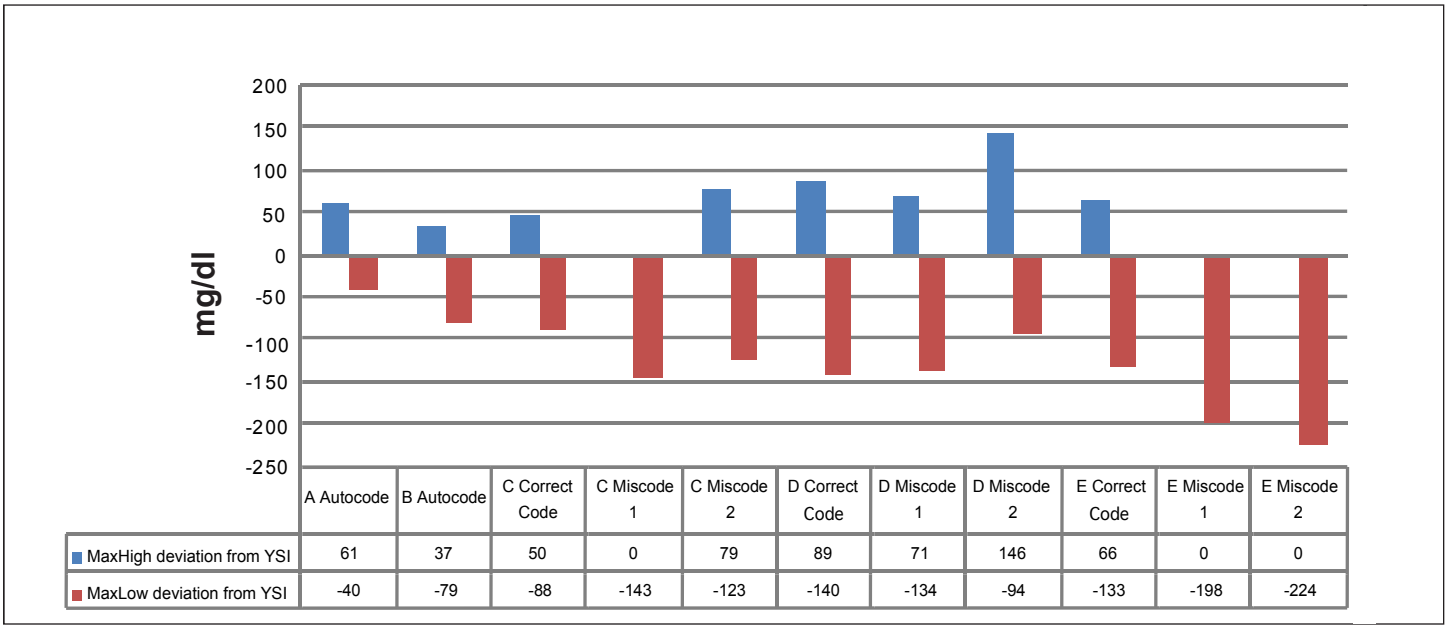

Figure 1. Maximum high and low deviation (mg/dl) from YSI, all meters.

The maximal low deviation from YSI values was -224 mg/dl for miscoded meters, -79 mg/dl for autocoded meters, and -140 mg/dl for correctly coded manual meters **(Figure 1)**. Differences in low deviations between miscoded and either autocoded or correctly coded manual meters were statistically significant ($p < 0.0001$), but the difference between autocoded and correctly coded manual meters was not ($p = 0.1071$).

Blood glucose values of less than 70 mg/dl and greater than 180 mg/dl were arbitrarily chosen as clinically significant for an insulin-requiring patient. An insulin sensitivity formula, based on total daily insulin, was used to calculate that a deviation from the standard YSI value of +40 mg/dl would be required to project an insulin dose sufficiently erroneous to result in a blood glucose level less than 70 mg/dl. Conversely, a meter deviation of -70 mg/dl would be required to project an insulin dose that would fail to correct an elevated blood glucose level below 180 mg/dl. Miscoded meters produced values that would result in blood glucose values less than 70 mg/dl in 10.40% of measures. Properly coded manual meters and autocoded meters produced results adequate to produce blood glucose levels less than 70 mg/dl in 1.46% and 2.52% of measures, respectively **(Figure 2)**. The probability for miscoded meters to result in a BG of less than or equal to 70 mg/dl (10.40%) was significantly higher than those of autocoded meters ($p < 0.0001$) and correctly manually coded meters ($p < 0.0001$). The difference between autocoded and correctly manually coded meters was not significant ($p = 0.3937$).

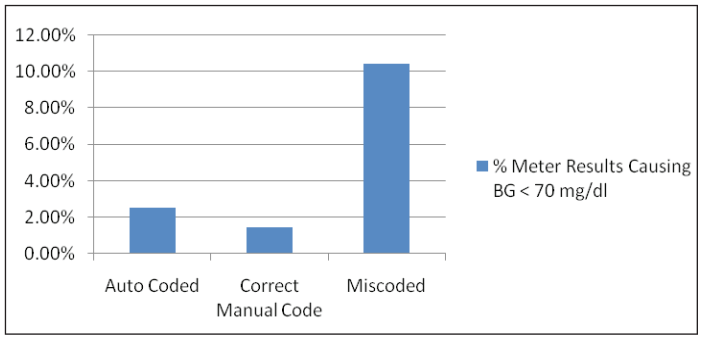

Figure 2. Percentage of meter results causing BG < 70 mg/dl.

In miscoded meter measures ($n = 833$) there were 42 values with errors large enough to result in blood glucose less than 50 mg/dl (data not shown).

Miscoded meters produced results inadequate to correct a blood glucose to less than 180 mg/dl in 17.14% of measures. Properly coded manual meter results were inadequate to produce blood glucose less than 180 mg/dl in 3.15% of measures, as were autocoded meters in 0.36% of measures **(Figure 3)**.

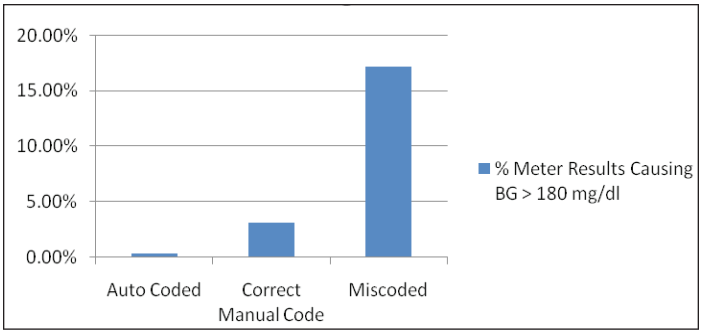

Figure 3. Percentage of meter results causing BG >180 mg/dl.

Discussion

Various schemes (i.e., sliding or correction scales) have been developed using SMBG values to derive corrective insulin doses. One such system was developed by Paul C. Davidson and colleagues. Davidson's formula for determining insulin sensitivity (and thereby a corrective insulin dose) is based on total daily insulin.[9] It is a widely used formula to estimate the dose of rapid-acting insulin needed to correct a single occurrence of hyperglycemia. The current analysis utilizes this scheme to predict possible consequences of inaccurate insulin administration based on improper coding of glucose meters. Davidson's observation showed that dividing the patient's total daily insulin (units) into a constant (generally 1700) gives an estimate of blood glucose (mg/dl) reduction expected from 1 unit of rapid-acting insulin.[10]

We have shown that with deliberately miscoded meters, there was a potential for insulin errors of as much as +5 units when a correction scheme is used to determine an insulin dose, given that a glucose meter is miscoded.[8] In deliberately miscoded meters, errors as great as -36.23% [standard deviation (SD) 6.34] or +26.53% (SD 12.45) relative to the reference YSI glucose were observed.

In this article, Davidson's formula and data from the "intentional miscoding" study were used to predict glucose levels resulting from miscoded blood glucose meters. Using the Davidson formula, it was determined that a meter error of +40 mg/dl or greater is required to produce an insulin overdose error severe enough to cause a blood glucose less than 70 mg/dl. Conversely, an error of -70 mg/dl or greater was needed to produce an insulin dose under-correction error severe enough to cause a blood glucose of greater than 180 mg/dl. The miscoded meters showed a mean high error of 42.1 mg/dl (maximum 146 mg/dl).

In a patient with a true blood glucose level of 200 mg/dl, an error of this magnitude would produce a

meter reading of 242 mg/dl (200 + 42). If the patient takes a total of 50 units of insulin daily, his or her expected sensitivity is 34 (1700/50). One unit of rapid-acting insulin is expected to reduce blood glucose by 34 mg/dl. If the target glucose is 110 mg/dl, 2.6 (rounded to 3) units of rapid acting insulin are required [(200 – 110)/34)]. The correct 3-unit dose would cause a blood glucose reduction of 102 mg/dl, to an end glucose of 98 mg/dl (200 – 102).

A miscoded meter with an error of 42 mg/dl would indicate the patient has a blood glucose of 242, and would therefore require a 3.8- (rounded to 4) unit insulin dose. Since the true blood glucose is 200 rather than 242, the erroneous insulin dose would reduce blood glucose by 136 mg/dl, to a final glucose level of 64 mg/dl (200 – 136). The maximum miscoded meter error (146 mg/dl) would cause a calculated insulin dose of 7 units with an anticipated glucose reduction of 238 mg/dl (7 x 34), with disastrous results.

Given the intra-patient variability of blood glucose and the need to adjust insulin therapy to that variability, meter-derived information must be accurately related to glucose as well as to the associated time/date stamp. It has been reported that approximately 54% of type 1 patients and 55% of type 2 patients exhibit a dawn phenomenon.[11] Time/date stamp accuracy in adjusting insulin to this and other factors in glucose variability is crucial. An automatic time stamp, included in a glucose meter, would attenuate yet another obstacle to appropriate glucose management, and has been called for in other publications.[12]

Continuous Glucose Monitoring

CGM is likely to have a vital role in the future of glycemic management. The closed-loop system is the ideal. In such a system, CGM is performed by one portion of the system and insulin delivery by another. Safety and efficacy, as with any system, is limited by the accuracy of data collected on one hand, and the precision of the delivery system on the other. Accuracy of the measurement system requires calibration, and calibration requires accurate SMBG data. A paper examining CGM in the twenty-first century indicated: "Currently available CGMs require up to four finger-stick (not alternate site) blood glucose measurements per day for calibration. The ideal time to calibrate is either after fasting or at least 3 hours, postprandially, but not immediately after exercise, or when the blood glucose level is likely to be rising or falling. Without reliable calibration, continuous readings may be inaccurate."[13]

Conclusion

Glucose meters made by major manufacturers in the U.S. are generally accurate. However, when improperly used, erroneous blood glucose values may result. Our previous study demonstrated that miscoded meters have the potential of producing such values.[8]

This paper examines potential glycemic outcomes from insulin doses administered on the basis of improperly coded meters. Insulin dose recommendations based on commonly used correction formulas may result in serious adverse clinical outcomes if glucose data are wrong. CGM calibration may likewise be compromised by data from miscoded meters. It is therefore recommended that patients utilizing manually coded meters have education and structured re-education regarding their proper use. The use of an automatically coded meter eliminates the potential of significant morbidity, particularly in those who have physical or cognitive limits or are challenged to adhere to a program of intensive glucose control.

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