

An Innovative Approach for Predicting Severe Hypoglycemia

Reviewed by Linda M. Siminerio, RN, PhD, CDE

STUDY

Cox DJ, Gonder-Frederick L, Ritterband L, Clarke W, Kovatchev BP: Prediction of severe hypoglycemia. *Diabetes Care* 30:1370–1373, 2007

SUMMARY

Objective. Research demonstrates the importance of achieving near-normal glycemia in the prevention of diabetes-related complications.¹ However, in an effort to attain euglycemia, one runs the risk for hypoglycemia.² Severe hypoglycemia (SH), a low blood glucose resulting in stupor, seizure, or unconsciousness, prohibits self-treatment. To prevent SH, one must be able to anticipate when an event may occur to initiate treatment steps or identify warning signs and take action to stop further progression. The objective of this study was to test methods for predicting SH by using blood glucose meter readings.

Design and methods. One hundred adults with type 1 diabetes and 79 insulin-using adults with type 2 diabetes participated in this study. Their self-monitoring of blood glucose (SMBG) readings were stored on memory meters, and the patients were asked biweekly about the occurrence of SH.

Results. Relative risk (RR) for SH, quantified by the ratio of an individual's low blood glucose index (LBGI) based on the previous 150 SMBG readings to the LBGI based on recent SMBG readings, increased significantly in the 24-hour period

before SH episodes in individuals with either type 1 or type 2 diabetes. An algorithm detected 58% of impending SH episodes when three SMBG readings were available in the 24 hours before an event. Detection increased if five SMBG readings were available in the 24 hours before an episode.

Conclusion. The investigators concluded that SH often follows a specific blood glucose pattern that is identifiable with SMBG. Thus, partial prediction of impending SH is possible, offering an opportunity for self-management in the prevention of significant hypoglycemia episodes.

COMMENTARY

The investigators in this trial have a long history in the study of hypoglycemia and in identifying methods for early detection and treatment.³ They previously demonstrated that the LBGI, a measure of the frequency and extent of low SMBG readings, accounts for as much as 40–55% of future SH episodes.⁴ Here, they nicely drew on their work with the LBGI and used it as a methodology in this study of SH.

Because SH can result in a number of debilitating outcomes such as cognitive dysfunction,⁵ accidents, seizures, coma, and death,⁶ it has been associated with patient fear and is identified as a barrier to glycemic control in diabetes.⁷ Strategies that offer patients an opportunity for early detection and immediate treatment

have the potential to alleviate fears and this significant barrier to meeting treatment goals.

Determining ways to alleviate the risk of hypoglycemia is crucially important because the risk for hypoglycemia has been posed as one reason for clinical inertia (the failure to intensify diabetes management in a timely manner).⁸ The complexity of diabetes management requires health professionals to be able to support their patients with the appropriate amount of time, education, and long-term support strategies necessary for effective self-management. This is particularly true in areas related to treatment intensification and to identification and treatment of hypoglycemia.

The majority of patients with diabetes are seen in a primary care setting,⁹ which presents interesting challenges for the facilitation of intensified therapies. Team-based care has been shown to be the best predictor of improved glycemia.¹⁰ However, primary care practices are often ill-equipped to manage intensive regimens because they may not have the necessary access to team and support services.¹¹

The decision to delay therapy in many cases may be related to fears about inadequate educational resources and added workload. One can appreciate the reluctance of busy practitioners who avoid the potential for hypoglycemia in their patients, particularly in those who are vulnerable to SH.

Diabetes is a complex disease that requires patients to be knowledgeable and able to make daily decisions that affect their own health.¹² Thus, the onus is on patients to be responsible for hypoglycemia management. The authors of this study present an evidence-based, practical hypoglycemia-prevention tool for clinicians and educators to use with their patients who are at high risk for SH.

The benefits of SMBG have been shown to be of limited value if patients are not taught how to respond appropriately to the results they get through testing.¹³ This study demonstrated that patients can use their SMBG results to identify patterns and prevent SH, the most feared outcome of insulin therapy.

When more SMBG readings were done, the accuracy of SH prediction appeared to increase. This finding offers a unique opportunity for clinicians and educators to help patients, particularly those experiencing SH events, avoid future events by recommending and supporting increased SMBG and pattern observation. Offering this life-saving strategy has the potential to alleviate fears and reluctance to aggressively achieve glycemic control for both patients and providers.

Interestingly, the investigators found that the accuracy of prediction was somewhat higher in type 2 diabetic subjects. This is of particular importance because delayed intensification (i.e., clinical inertia) is most often associated with the treatment of patients with type 2 diabetes.

As the authors suggest, this report on SH sets the groundwork for future study. They report that a major limitation of this study is that patients' reactions to their SMBG readings were not monitored. Future studies could include measurement of patients' diabetes management behaviors that were used in

association with their SMBG results. Subsequent educational strategies for prevention and treatment approaches could be developed from this information.

The patients in this cohort were all adults. Because hypoglycemia, and particularly SH, is a significant challenge in the management of children with diabetes, it would be interesting to test this SMBG algorithm in children and adolescents. Should it perform as well in children, the benefits for anxious pediatric patients, parents, and school staff members would be enormous.

The potential for integrating these strategies into available SMBG technology, such as using online analysis of SMBG data or integration of algorithms into blood glucose meters, could provide early warnings to patients with hypoglycemia alerts and reports. Individuals would be able to take preventive steps to reduce the impending risk of SH by increasing their testing frequency, being more vigilant for warning signs and symptoms, reducing insulin doses, avoiding strenuous exercise, eating extra carbohydrates, delaying driving, and avoiding delays in mealtimes.

This investigative team's continued efforts in finding approaches to mitigate the challenges associated with insulin intensification are crucially important in improving patients' and their practitioners' ability to effectively achieve euglycemia while avoiding the risks of low blood glucose.

REFERENCES

- ¹DCCT Research Group: The effect of intensive treatment of diabetes on the development and progression of long term complications of insulin-dependent diabetes mellitus. *N Engl J Med* 329:978–986, 1993
- ²Cryer PE: Hypoglycaemia: the limiting factor in the glycaemic management of type I

and type II diabetes. *Diabetologia* 45:937–948, 2002

³Kovatchev BP, Cox DJ, Gonder-Frederick LA, Clarke WL: Symmetization of the blood glucose measurement scale and its applications. *Diabetes Care* 20:1655–1658, 1997

⁴Cox DJ, Kovatchev B, Julian D, Gonder-Frederick LA, Polonsky WH, Schlundt DG, Clarke WL: Frequency of severe hypoglycemia in IDDM can be predicted from self-monitoring blood glucose data. *J Clin Endocrinol Metab* 79:1659–1662, 1994

⁵Kovatchev BP, Cox DJ, Gonder-Frederick LA, Young-Hyman D, Schlundt D, Clarke WL: Assessment of risk for severe hypoglycemia among adults with IDDM: validation of the Low Blood Glucose Index. *Diabetes Care* 21:1870–1875, 1998

⁶Reichard P, Phil M: Mortality and treatment side effects during long-term intensified conventional insulin treatment in the Stockholm Diabetes Intervention Study. *Diabetes* 43:313–317, 1994

⁷DCCT Research Group: Hypoglycemia in the Diabetes Control and Complications Trial. *Diabetes* 46:271–286, 1997

⁸Gold AE, Deary IJ, Frier BM: Recurrent severe hypoglycaemia and cognitive function in type I diabetes. *Diabet Med* 10:503–508, 1993

⁹Grant R, Buse J, Meigs J, the University HealthSystem Consortium (UHC) Diabetes Benchmarking Project Team: Quality of diabetes care in U.S. academic medical centers: low rates of medical regimen change. *Diabetes Care* 28:337–342, 2005

¹⁰Shah B, Hux J, Laupacis A, Zinman B, van Walraven C: Clinical inertia in response to inadequate glycemic control: do specialists differ from primary care physicians? *Diabetes Care* 28:600–606, 2005

¹¹Janes G: Ambulatory medical care for diabetes. In *Diabetes in America*. 2nd ed. NIH Publication No. 95–1468. Group NDD, Ed. Bethesda, Md., National Institutes of Health, 1995, p. 541–552.

¹²Shojania K, Ranji S, McDonald K, Grimshaw J, Sundaram V, Rushakoff R, Owens D: Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression analysis. *JAMA* 296:427–440, 2006

¹³Klonoff D, Bergenstal R, Blonde L, Boren S, Church T, Gaffaney J, Jovanovic L, Kendall D, Kollman C, Kovatchev B, Leippert C, Owens D, Polonsky W, Reach G, Renard E, Riddell M, Rubin R, Schnell O, Siminerio L, Vigersky R, Wilson D, Wollitzer A: Consensus report of the Coalition for Clinical Research: self-monitoring of blood glucose. *J Diabetes Sci Technol* 2:1030–1053, 2008

Linda M. Siminerio, RN, PhD, CDE, is director of the University of Pittsburgh Diabetes Institute in Pittsburgh, Pa.