Long-Term Follow-Up Evaluation of Blood Glucose Awareness Training

DANIEL J. COX, PHD
LINDA GONDER-FREDERICK, PHD
DIANA M. JULIAN, MA
WILLIAM CLARKE, MD

OBJECTIVE— Blood glucose awareness training (BGAT) has been found effective in teaching individuals with insulin-requiring diabetes to improve their ability to better recognize blood glucose (BG) fluctuations. This study investigated whether subjects who underwent BGAT a mean of 4.9 years previously were superior to past control subjects in terms of their ability to recognize BG fluctuations, and whether past BGAT subjects had fewer automobile crashes and lost work days and better glycosylated hemoglobin than control subjects. Additionally, the beneficial effects of providing booster training to past BGAT subjects also was evaluated.

RESEARCH DESIGN AND METHODS— This study followed up 28 past BGAT subjects. Half of these subjects (n = 14) received a simple booster-training program. Twelve previous control subjects also were evaluated. Booster subjects were given a BGAT diary to complete for 2 weeks before evaluation. Evaluation for all subjects included completion of a retrospective questionnaire on work and driving history, blood drawing for a glycosylated hemoglobin analysis, and having subjects estimate and measure their BG levels 50–80 times during a 3- to 4-week period during their daily routine.

RESULTS— At long-term follow-up, BGAT subjects had significantly fewer automobile crashes than control subjects. BGAT subjects receiving booster training were significantly more accurate at estimating their BG levels and were more aware of hypoglycemia. Post hoc analyses indicated that the ability to accurately estimate BG fluctuations correlated positively with follow-up glycosylated hemoglobin and the number of hypoglycemic and hyperglycemic symptoms participants demonstrated. Both BGAT and control subjects demonstrated significantly improved glycosylated hemoglobin relative to baseline measures.

CONCLUSIONS— These data suggest that BGAT has long-term benefits, which can be enhanced with booster training. Specifically, BGAT and simple booster training may result in reduction of severe hypoglycemic episodes and automobile crashes in the long term.

From the University of Virginia Health Sciences Center, Charlottesville, Virginia.

Address correspondence and reprint requests to Daniel J. Cox, PhD, Drawer F, Box BRH, University of Virginia Health Sciences Center, Charlottesville, VA 22901.

Received for publication 5 April 1993 and accepted in revised form 2 September 1993.

BGAT, blood glucose awareness training; BG, blood glucose; ANOVA, analysis of variance.

Blood glucose awareness training (BGAT) is a patient education procedure designed to teach insulin-requiring diabetic patients to more accurately estimate their general blood glucose (BG) levels and specifically detect hypoglycemia. BGAT involves teaching patients how to identify symptoms sensitive and specific to their hypoglycemia and hyperglycemia. Additionally, it teaches patients how to accurately interpret information concerning types, amounts, and timing of insulin, food, and exercise to better anticipate extreme BG levels. BGAT typically requires seven weekly classes, reading the training manual, and daily homework exercises designed to apply and personalize the material presented in a particular chapter of the manual. Numerous studies have now demonstrated, in the short term, that BGAT is effective in improving patients' ability to estimate their BG levels and glycosylated hemoglobin (1–10). Maintenance of such gains is critical in evaluating the cost-effectiveness of BGAT. No studies to date have evaluated the long-term benefits of BGAT. With the growing concern about the increased incidence of hypoglycemia with attempts to normalize BG (11–14), it is especially important to know whether BGAT leads to greater awareness of hypoglycemia and fewer severe hypoglycemic episodes in the long term.

This study followed-up subjects who had participated in BGAT and control subjects from our previous studies (1,3). At follow-up, half (n = 14) of the BGAT subjects received a brief booster-training program intended to review BGAT procedures. The general question addressed was: Are BGAT participants better off at long-term follow-up compared with baseline or control subjects? The specific hypotheses tested were *1*) at long-term follow-up, BGAT subjects in general would be more accurate at estimating their BG levels and more aware of their hypoglycemia in particular; 2) BGAT subjects would have fewer nega-

Table 1—*Subject characteristics for the three groups*

	Control group	BGAT group	BGAT plus booster
Final *n*	13	14	14
Age (years)	41.1 ± 3.1	40.3 ± 3.2	47.2 ± 4.3
Duration of disease (years)	17.6 ± 4.0	14.2 ± 1.8	17.1 ± 2.8
Follow-up (months)	47.0 ± 5.3	51.2 ± 3.6	55.5 ± 4.0

Data are means ± SD.

tive consequences caused by severe hypoglycemic episodes, as defined by lost work days and fewer automobile crashes; 3) BGAT subjects would maintain their improved glycosylated hemoglobin; and 4) a brief booster-training program would enhance overall accuracy of BG estimation and, specifically, sensitivity to hypoglycemia.

RESEARCH DESIGN AND METHODS

— We were able to locate 52 of 64 subjects from two previous studies (1,3), 41 of whom were able and willing to participate. Twenty-eight of these subjects had undergone BGAT and 13 were past control subjects. Table 1 lists subject characteristics. No significant differences existed between groups on any of these variables. Incentives to participate included a free glycosylated hemoglobin determination and a $75 payment at the conclusion of data collection.

At an introductory meeting, subjects signed an informed consent, completed a questionnaire concerning past experiences with hypoglycemia and driving, and had blood drawn for a glycosylated hemoglobin analysis (15). The driving questions were

1. How many years have you been driving? ___ years.
2. Please estimate how many miles you drive a year: ___ miles/year.
3. Have you ever had an automobile accident? Yes _, No _.

If yes, please list the approximate dates of the accidents:

Past BGAT subjects were matched on posttreatment BG estimation accuracy and months of follow-up and then randomly assigned to either BGAT or BGAT plus booster training. Before use of the hand-held computer, BGAT plus booster subjects were given a 2-week diary. This diary was similar to those used in BGAT. Each time booster subjects measured their BG, they recorded in the diary any BG-relevant symptoms and relevant information about insulin, food, and/or exercise; estimated and recorded their BG; measured and logged their actual BG; and plotted their estimated-actual BG readings on an error grid (16,17). Plotting the actual-estimated BG provided booster subjects feedback on the types of estimation errors being made. For example, the error grid provided subjects with information such as whether they were systematically overestimating their low BGs and/or underestimating their high BGs. After 2 weeks of completing diaries, booster subjects were given hand-held computers to collect follow-up data.

All subjects were given a Psion P250 hand-held computer to use immediately before home self-monitoring of BG. They were instructed to use the computer-BG monitoring during routine measurements and whenever they thought their BG was either low or high. Each computer trial required subjects to enter their BG estimates, rate a variety of perceived autonomic and neuroglycopenic symptoms on a 0 = none to 6 = extreme scale, and measure and enter their actual BG results. Subjects were instructed to make a minimum of 50 such entries or continue until they had at least 10 actual BGs <3.9 mM to a maximum of 80 entries. This was accomplished during the subjects' daily routine over a 3- to 4-week interval. We have reported previously how the hand-held computer data identify individual-specific symptoms that correlate with the ability to detect hypoglycemia (18).

The computer tracked date and time of each entry and elapsed time between the computer's prompt to measure BG and the subjects' entry of their actual BG measurement. This allowed a check for compliance by examining whether at least 60 s elapsed between the prompt to measure BG and entry of actual BG. Because it requires at least 1 min to lance the finger, secure a blood sample, and get a BG reading, any BG readings entered in <60 s were considered unreliable and dropped from analysis. Unreliable data represented either fabricated data or BG measurements collected before BG estimates and symptom ratings. Based on this compliance check, we dropped 5 subjects' hand-held computer data from analysis because they consistently entered actual BG values immediately after instructions to measure BG. This resulted in the elimination of hand-held computer data from 2 subjects each in the control and BGAT groups and from 1 subject in the booster group.

Data analysis

The accuracy index is a general index of BG estimation accuracy (2,3,16). The accuracy index is derived by calculating the percentage of accurate estimates (those within 20% of the measured BG or those estimates and actual BG readings, both <3.9 mM) and subtracting the number of dangerously erroneous estimates (failure to recognize either hypoglycemia or hyperglycemia).

A univariate analysis of variance (ANOVA) was performed comparing only the three groups' follow-up accuracy index because of the inequity between pre- and posttreatment data and follow-up data; original (1,3) pre- and

posttreatment accuracy index data were not equivalent to our follow-up data for two reasons: *1*) the current follow-up data were gathered using the hand-held computer, which identified unreliable trials and subjects and did not incorporate these data in the summary accuracy index. In contrast, the original pre- and posttreatment data (1,3) was gathered using diaries, and all data were incorporated in analyses; and 2) our original error grid analysis program, used in the pre- and posttreatment analyses, had a slight but consistent error, classifying overestimates of up to 32%, instead of 20%, as accurate (upper A zones).

Because our booster training occurred for only a 2-week period just before data collection, it did not have an impact on long-term variables, such as automobile crashes, lost work days, or glycosylated hemoglobin. Consequently, booster and nonbooster BGAT subjects were collapsed in comparison with control subjects for such variables. Additionally, although subjects whose hand-held computer data were unreliable were not analyzed for accuracy of BG estimation, these subjects were included when analyzing glycosylated hemoglobin and automobile crashes.

RESULTS

Effects of BGAT and booster training on BG estimation accuracy

A univariate ANOVA on the accuracy indexes for BGAT plus booster, BGAT, and control subjects (39, 30, and 26%, respectively) yielded significant results ($F = 7.02$, $P < 0.001$). Planned contrasts indicated that BGAT plus booster subjects were superior to both BGAT ($t = 2.49$, $P = 0.01$) and control ($t = 3.64$, $P = 0.000$) subjects. BGAT subjects exhibited a trend toward superior estimation of their BG levels compared with control subjects ($t = 1.13$, $P = 0.10$).

Of specific interest was whether BGAT improves subjects' ability to detect hypoglycemia over the long term. The

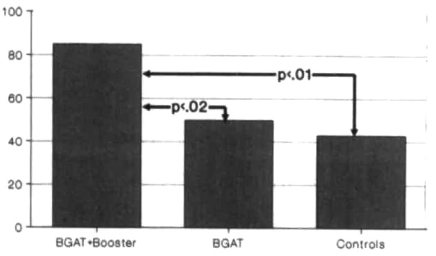

Figure 1—*Percentage detection of hypoglycemia (BG < 2.7 mM) at long-term follow-up for past control subjects and BGAT subjects who did and did not receive booster training.*

percentage of low BGs (<2.8 mM) detected by BGAT plus booster, BGAT, and control subjects was 85, 50, and 43%, respectively. Overall, this was significant ($F = 4.29$, $P < 0.02$), with BGAT plus booster better than either BGAT ($P < 0.02$) or control subjects ($P < 0.01$; Fig. 1). This would suggest that although a trend exists for the original BGAT subjects to be better at estimating their BG levels, subjects who received BGAT with booster training were more accurate in general and specifically more aware of their hypoglycemia.

Ancillary long-term effects of BGAT

Long-term improvement in glycosylated hemoglobin was analyzed with a 2 × 2 (pre-BGAT vs. follow-up; BGAT vs. control, respectively) ANOVA. This revealed no group effect, but a significant time effect ($F = 9.48$, $P < 0.005$), indicating both groups showed improved hemoglobin from baseline (Fig. 2).

Although BGAT did not lead to fewer self-reported lost work days, BGAT was associated with significantly fewer automobile crashes. Respective crash rates per 1,000,000 miles driven were 6.8 vs. 29.8 ($U = 77.5$, $P = 0.01$). Of the control subjects who drove (one subject did not drive), 42% had at least one automobile crash during follow-up. In contrast, only 15% of our BGAT subjects who drove had accidents. One subject in each group had two accidents. The remaining subjects in both groups had only a single accident during follow-up. The mean number of months between the last group treatment session and accidents, for those subjects who had accidents, was 14.0 months for control subjects and 28.3 months for BGAT subjects ($t = 1.02$, $P = 0.13$).

Post hoc analyses

To identify possible relationships with follow-up accuracy index, several exploratory correlations were performed. Follow-up accuracy index was significantly correlated with the number of hypoglycemic symptoms ($r = 0.48$, $P < 0.001$) and hyperglycemic symptoms ($r = 0.60$, $P < 0.001$) as quantified by the hand-held computer (19), posttreatment accuracy index ($r = 0.55$, $P < 0.001$), follow-up glycosylated hemoglobin ($r = 0.30$, $P < 0.01$), and believed ability to estimate BG levels ($r = 0.37$, $P = 0.02$). Follow-up accuracy index was not correlated with the average number of daily self-monitoring of BG determinations or with the percentage of time subjects reported routinely estimating their BG before measuring BG.

CONCLUSIONS— Although BGAT was not originally designed to produce long-term effects, these data indicate that BGAT led to sustained improvement in glycosylated hemoglobin and fewer automobile accidents. BGAT plus a low effort booster training led to greater gen-

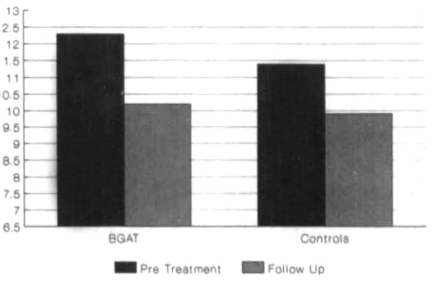

Figure 2—*Glycosylated hemoglobin from original pretreatment data and current follow-up data for previous control and BGAT subjects.*

eral accuracy in estimating BG and detecting hypoglycemia in particular. Although improved metabolic control is important, it was not unique to BGAT. Our control subjects, who participated in general diabetes education classes, also showed a sustained metabolic improvement. This would suggest that both group programs were effective in sustaining improved self-care behaviors. However, because we did not have a no-treatment control group, we cannot rule out the possibility that the simple passage of time was responsible for this improvement.

One of the more interesting findings of this study is that BGAT may lead to fewer automobile accidents. Our recent experimental study (19) demonstrates that moderate hypoglycemia (2.8 mM) was associated with multiple significant disruptions in driving performance. In that study, we reported that only 50% of the subjects who were made moderately hypoglycemic were aware that they should not drive. Our current data suggest that the effect of BGAT is to increase awareness of when not to drive. The potential of such an effect might be made more robust if periodic booster training were provided.

Findings from the Diabetes Control and Complications Trial (20) indicate that normalization of BG is associated with significant reduction in risk of long-term diabetic complications, but it is also associated with an increased risk of severe hypoglycemia. The fact that a relatively simple and inexpensive booster training increased detection of BGs <2.8 mM may have significant implications for those individuals pursuing normalization of metabolic control. Because the occurrence of severe hypoglycemia has been demonstrated to impair driving performance (19) and repeated episodes of severe hypoglycemia has been associated with brain damage (21–23), a simple procedure such as BGAT and periodic booster training may be beneficial in reducing risks associated with normalization of BG control.

This study also demonstrates the need to collect field data using a procedure, such as the hand-held computer, capable of identifying unreliable data. Five subjects (12%) in our sample were dropped from analysis because they apparently provided unreliable data. After identifying unreliable data, we contacted these subjects to confirm that they had either measured their BG before entering their estimates or entered fabricated BG readings. In all cases, suspicions raised by the computer were confirmed by the interview.

Because BGAT has been repeatedly demonstrated to improve detection of BG levels, and our current study has indicated that it has a significant long-term benefit, future research should focus on training that specifically incorporates periodic practice and therefore enduring benefits. This study suggests that such training may be accomplished by incorporating the simple procedure of periodic booster-training diaries. Exploratory correlations suggest that such training would be most effective with those patients who have the largest number of BG-relevant symptoms and those with the highest posttraining accuracy.

Acknowledgments— This study was supported in part by National Institutes of Health Grants RO1-DK-28288 and RR-00847.

References

1. Cox DJ, Carter WR, Gonder-Frederick LA, Clarke WL, Pohl S: Blood glucose discrimination training in IDDM patients. *Biofeedback Self-Regul* 13:201–16, 1988
2. Cox DJ, Gonder-Frederick LA, Lee JH, Julian DM, Carter WR, Clarke WL: Effects and correlates of blood glucose awareness training among patients with IDDM. *Diabetes Care* 12:313–18, 1989
3. Cox DJ, Gonder-Frederick LA, Julian D, Cryer P, Lee J, Richards F, Clarke W: Intensive vs. standard blood glucose awareness training (BGAT) with insulin-dependent diabetes: mechanisms and ancillary effects. *Psychosom Med* 53:453–62, 1991
4. Frohlich C, Zettler A, Reinecker H, Kulzer B, Imhof P, Cebulla U, Bergis KH: Evaluation eines gruppentrainings zur verbesserung der hypoglykamiewahrnehmung (WT) und angstbewaltigung (AT). *Praxis der Klinischen Verhaltensmedizin und Rehabilitation* 17:30–34, 1992
5. Fritsche A, Reinauer KM, Renn W: *Blood Glucose Awareness During a One-Week Trip to the United States*. German Diabetes Association, 1992
6. Roales-Nieto JG: Blood glucose discrimination in insulin-dependent diabetics. *Behav Mod* 12:116–32, 1988
7. Roales-Nieto JG: Feedback training and external cues in discrimination of blood glucose levels in IDDM. *Anal Mod Conducta* 17:951–65, 1991
8. Luzoro J, Roales-Nieto JG: Discrimination of blood glucose levels in IDDM mediated by external cues and glucose profiles. *Psicothema*. 5:45–65, 1993
9. Nurick M, Bennett-Johnson S: Enhancing blood glucose awareness in adolescents and young adults with IDDM. *Diabetes Care* 14:1–7, 1991
10. Gross AM, Magalnick LJ, Delcher HK: Blood glucose discrimination training and metabolic control in insulin-dependent diabetics. *Behav Res Ther* 23:507–11, 1985
11. Lorenz R, Siebert C, Cleary P, Santiago J, Heyse S, the DCCT Research Group: Epidemiology of severe hypoglycemia in the DCCT (Abstract). *Diabetes* 37 (Suppl. 1):3A, 1988
12. Frank M, Daneman D, Link J, Parker K, Perlman K, Ehrlich R: Frequency of severe hypoglycemia (SH) in children with IDDM (Abstract). *Diabetes* 37 (Suppl. 1): 92A, 1988
13. The DCCT Research Group: Diabetes Control and Complications Trial (DCCT): results of feasibility study. *Diabetes Care* 10:1–19, 1989
14. Bergada I, Suissa S, Dufresne J, Schiffrin A: Severe hypoglycemia in IDDM children. *Diabetes Care* 12:239–44, 1989
15. Herold D, Mifflin J, Boyd J, Savory J, Burns D: Measurement of glycosylated hemoglobin by bornate affinity chroma-

tography. In *Methods in Diabetes Research Volume II: Clinical Methods*. Clarke W, Larner J, Pohl S, Eds. New York, Wiley, 1986, p. 507–18
16. Cox DJ, Richards F, Gonder-Frederick LA, Julian DM, Carter WR, Clarke WL: Error grid analysis: a clarification. *Diabetes Care* 12:235–36, 1989
17. Cox DJ, Clarke W, Pohl S, Gonder-Frederick L, Hoover C, Zimbelman L, Pennebaker JW: Accuracy of perceiving blood glucose in IDDM patients. *Diabetes Care* 8:529–36, 1985
18. Cox DJ, Gonder-Frederick LA, Antoun B, Schroeder DB, Clarke WL: Perceived symptoms in the recognition of hypoglycemia. *Diabetes Care* 16:519–27, 1993
19. Cox DJ, Gonder-Frederick LA, Clarke WL: Driving decrements in type I diabetes during moderate hypoglycemia. *Diabetes* 42:239–43, 1993
20. DCCT Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in IDDM. *N Engl J Med* 329:977–86, 1993
21. Wredling R, Levander S, Adamson U, Lins PE: Permanent neuropsychological impairment after recurrent episodes of severe hypoglycemia in man. *Diabetologia* 33:152–57, 1990
22. Golden MP, Ingersoll GM, Brack CJ, Russell BA, Wright JC, Huberty TJ: Longitudinal relationship of asymptomatic hypoglycemia to cognitive function in IDDM. *Diabetes Care* 12:89–93, 1989
23. Langan SJ, Deary IJ, Hepburn DA, Frier BM: Cumulative cognitive impairment following recurrent severe hypoglycemia in adult patients with insulin-treated diabetes. *Diabetelogia* 34:337–44, 1991