Effects and Correlates of Blood Glucose Awareness Training Among Patients With IDDM

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Whereas self-monitoring of blood glucose (SMBG) is the recommended source of information on which to make self-care decisions, patients frequently use estimates of their own blood glucose (BG). This study evaluated whether patients with insulin-dependent diabetes mellitus (IDDM) could learn to improve accuracy of BG estimations and whether this would lead to improved metabolic control. Subjects in BG awareness training improved both their BG-estimation accuracy and glycosylated hemoglobin (HbA_1) compared with the control group. Initial BG-estimation accuracy was marginally associated with pretreatment HbA_1 and months of previous SMBG experience. Posttreatment improvement was associated with pretreatment BG-estimation accuracy and the ability to counterregulate to insulin-induced hypoglycemia. *Diabetes Care* 12:313–18, 1989

Awareness of blood glucose (BG) fluctuations is a keystone in the self-management of insulin-dependent diabetes mellitus (IDDM). Self-monitoring of blood glucose (SMBG) has been shown capable of providing accurate and immediate BG information (1). However, it has the shortcomings of expense, inconvenience, and mild aversiveness and has failed to be associated with consistent improvement in metabolic control (2). Alternatively, patients frequently rely on their own estimates of BG levels to make significant clinical decisions (3,4). There are five sources of information for BG estimates: adrenergic physical symptoms (5,6); neuroglycopenic cognitive dysfunctions (7,8); physical symptoms of hyperglycemia (5,6); mood states (9,10); and external cues such as timing, amount and type of insulin, food, and exercise. Cox et al. (11) demonstrated that IDDM patients, with SMBG experience, were accurate at estimating their BG levels 46% of the time when given access to internal adrenergic, affective, and neuroglycopenic cues and accurate 60% when based on both internal and external sources of information in their home environment.

Can accuracy of BG estimation be improved with discrimination training? Discrimination training involves an individual making a BG estimate on the basis of perceived BG-relevant information, then receiving feedback as to the accuracy of this estimate through SMBG, and subsequently refining future use of this information. Early efforts at training patients to use such information to improve accuracy of BG estimation met with failure (6,9,11). However, recent research has demonstrated that patients can use internal cues (13), external cues (14), or both (13) to improve accuracy of BG estimation. The successful nature of the latter studies included structured discrimination training and alternative means of quantifying estimation accuracy. Cox et al. (13) used a training manual focusing on how BG affects physical, affective, and neuroglycopenic symptoms and had patients record such experienced symptoms (estimated BG and actual SMBG results) at home. Whereas estimation accuracy did improve, the effects on glycosylated hemoglobin (HbA_1) were not tested. Roales-Nieto (14) had patients record external cues (insulin, food, and exercise) to improve accuracy of BG estimation. This study reported a 64% reduction in estimation error and a 33% reduction in daily average BG, but HbA_1 was not tested.

Glucose 1 mM = 18 mg/dl

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Quantification of BG accuracy has traditionally used correlation analysis, percent deviation, or regression models. These all have significant clinical and statistical shortcomings (1,11,13,15–18). A correlational coefficient is a measure of the formal interdependence of the two variables but is not a measure of numerical agreement of the two variables. Percent deviation of estimate from actual BG is inappropriately inflated by overestimates relative to underestimates, i.e., underestimates can never reach 100%, whereas overestimates are not so constrained. Linear regression determines accuracy by two coefficients of regression (a intercept, b slope) instead of by one value, and also is not a measure of numerical agreement. In addition, these approaches only quantify statistically how estimates relate to SMBG, and do not consider the degree of danger certain inaccurate estimates represent, e.g., a patient thinking she/he is hyperglycemic and treating this presumed BG when in fact she/he is hypoglycemic. A more sensitive approach is the use of the error grid that quantifies the nature of both accurate and inaccurate BG estimates (1,11,15–18; Fig. 1). This involves defining estimates as accurate (A zones) if they are within 20% of the SMBG result or if they represent hypoglycemic readings (<70 mg/dl) when the SMBG reading is also hypoglycemic (17). Inaccurate estimates can lead to either benign (B zones) clinical decisions or potentially dangerous immediate clinical decisions such as overcorrecting (C zones) already acceptable BG levels or failure to detect (D zones) and therefore treat extreme BG levels (<70 or >180 mg/dl), or erroneous (E zones) treatment decisions where hypoglycemia is confused for hyperglycemia or vice versa.* Estimates above the diagonal represent overestimates, whereas those below the diagonal represent underestimates.

This study compared BG awareness training (BGAT) and control subjects (pre- and posttreatment) with the error grid. The primary objective was to evaluate whether BGAT could improve accuracy of BG estimation. Secondary objectives involved assessing BGAT's effect on HbA_1, and identifying those pretreatment variables that influence basal accuracy and treatment effectiveness. Regarding pretreatment variables, it was predicted that improvement in BGAT-estimation accuracy would be positively influenced by more frequent use of SMBG, duration of SMBG, and ability to counterregulate during hypoglycemia and that the less accurate an individual was at pretreatment the more they would improve.

MATERIALS AND METHODS

Subjects. Twenty-two subjects (8 men, 14 women) with IDDM were randomly assigned to BGAT or control groups. Subjects had to have had diabetes for at least 2 yr and taking insulin since diagnosis. The mean ± SD age was 32.4 ± 8.5 yr and mean duration of diabetes was 10.6 ± 7.7 yr. Average SMBG experience ranged from 8 to 48 mo (mean 27.4). All subjects were healthy with no known diabetic complications or taking any antihypertension (e.g., β-blockers) or tricyclic medications that might block adrenergic cues. All subjects were solicited through newspaper advertisements to participate in various behavioral diabetes research projects in exchange for free medical evaluations and $300 for completion of all phases of the study.

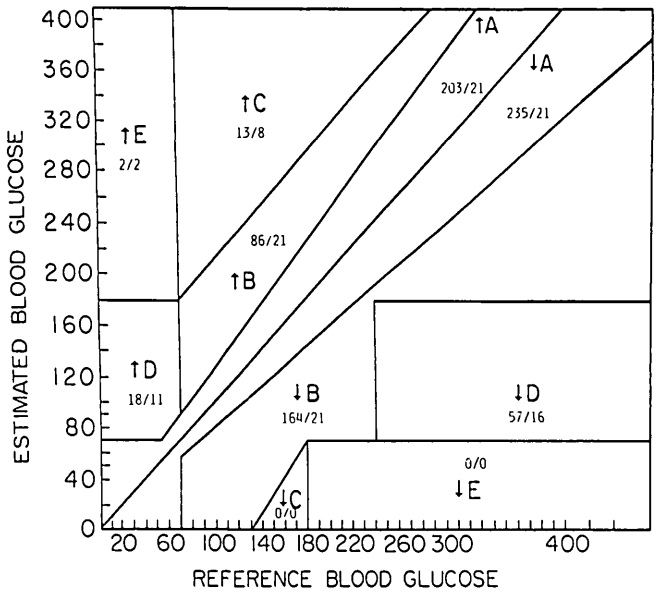

FIG. 1. Error grid with symmetrical upper (overestimates) and lower (underestimates) accurate A zones, benign B zones, overcorrection C zones, failure to detect D zones, and erroneous treatment E zones, with the number of total data points/subjects falling into each zone at pretreatment.

Dependent variables. To evaluate the effects of BGAT on metabolic control, HbA_1 was measured at the initial recruitment session, 2 mo later at pretreatment hospitalization, and at 2 mo posttreatment (Fig. 2). To evaluate the effects of SMBG frequency on accuracy of BG estimation, subjects were given a memory meter (Ames, Elkhart, IN) for 2 wk after recruitment. They were instructed to measure BG at their routine frequency. Gonder-Frederick et al. (20) have demonstrated that use of a memory meter and knowledge of the memory capabilities did not affect patients' routine frequency of SMBG. At recruitment, all subjects were evaluated for accuracy of SMBG results by demonstrating their technique with test solution. To evaluate accuracy of BG estimation, subjects were given beepers that were activated randomly four times daily for 10 days. At the beep they recorded their BG estimate and then collected and recorded an SMBG reading. These home-estimated actual BG readings were used because they yielded equivalent results to data blindly collected in our clinical research unit (13) [SMBG recording errors were as low as 1% (20)], and this was the natural context in which patients

*IBM/PC compatible software for error grid analysis is available from the authors on request.

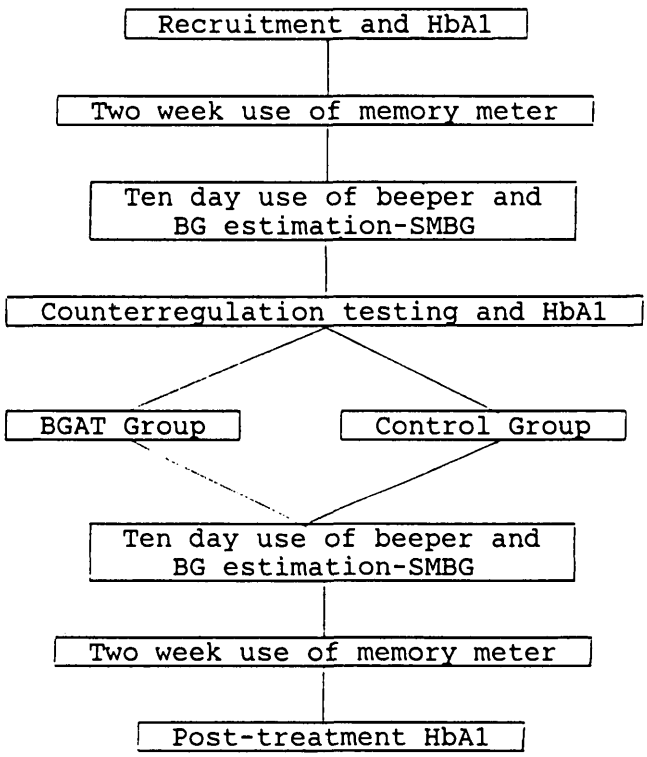

FIG. 2. Flow chart of subjects' timeline through protocol.

estimate their BG. This was repeated pre- and posttreatment. Estimations were compared with SMBG results with the error grid. Beepers were used to avoid subjects estimating their BG at routine times when they would be more familiar with BG fluctuations. To evaluate a subject's ability to counterregulate to hypoglycemia, patients were admitted to the clinical research unit for testing. The night before testing, subjects received overnight intravenous regular insulin to maintain euglycemia. At ~0900 the following morning, subjects received a 2-h constant intravenous infusion of insulin (40 mU · kg^{-1} · h^{-1}). Subjects' BG concentrations were monitored continuously with the Biostator, and insulin infusion was terminated if BG concentration fell to <35 mg/dl or if the subject exhibited signs of neuroglycopenia, e.g., severe lethargy, confusion, disorientation, or inappropriate behavior. Failure to counterregulate was determined when BG did not plateau but continued to drop below 35 mg/dl and/or neuroglycopenic symptoms occurred (21).

Independent variables. Fifteen subjects were randomly assigned to BGAT and seven to control groups. Fewer control subjects were used because previous research has shown that placebo conditions fail to show improvement in BG estimation (10,13) and because of the cost and invasiveness of hospital testing. BGAT used an expanded 105-page training manual during seven consecutive weekly classes.* Each class focused on a different chapter of the training manual and reviewed the previous week's homework. This manual instructed subjects on how to plot their estimated-BG–SMBG results on an error grid and how to interpret them. In addition, the manual instructed subjects on the five sources of BG-relevant information and how to use this in making BG estimations. Homework involved awareness exercises and discrimination training. Awareness exercises consisted of activities that had subjects produce and focus on different internal or external events. For example, subjects performed the Harvard step test to produce and focus on the adrenergic symptom of accelerated heart rate. Discrimination training involved having subjects record time, date, BG-relevant information, estimated BG, and SMBG. In addition, they plotted their estimated-BG–SMBG results on an error grid. At the end of each week, subjects identified those sources of information that led to accurate (A zones) and inaccurate (C–E zones) BG estimations. Control subjects participated in group meetings where they discussed the role of psychological stress on metabolic control and recorded their SMBG, insulin, and food eaten, along with stress levels, in daily diaries (Fig. 2).

Data analysis. As reported previously (13), the primary dependent variable for accuracy of BG estimation was a composite score of the error grid. The accuracy index (AI) involves summing the percentage of estimates in the A zones and subtracting the summed percentage of clinically dangerous estimates in zones C–E. B-zone estimates are not calculated in the AI because of their clinical insignificance. AIs have been shown to range from +90% for patient-generated SMBG (compared to a reference laboratory) to −6.75% for diabetic children estimating their own BG level and are unrelated to actual BG distribution (1,22).

A mixed design (group × time) for unequal cell sizes, with time as the repeated measure, was used to evaluate the differential effects of BGAT on both AI and HbA_1. The analysis design differed only for the repeated variable AI, time (including pre- and postdimensions), and HbA_1; because a multiple baseline (recruitment and pretreatment hospitalization) was used, time included three dimensions (recruitment, hospital, and posttreatment). Subsequent *t* tests were used to identify specific effects. Correlation analyses were used to identify factors that covaried with accuracy and improvement.

RESULTS

Figure 1 displays the total frequency of estimates that fell into each zone and the total number of subjects who had such errors at baseline. The pre- and post-AIs for BGAT and control subjects were 41–60 and 51–43%, respectively. Analysis of variance (ANOVA) of AI yielded no group or time effect but produced a significant interaction ($F = 13.60$, $P = .001$). Whereas BGAT showed significant improvement ($t = 4.59$, $P < .001$), control subjects showed nonsignificant decay in accuracy

*The Blood Glucose Awareness Training (BGAT) manual is available on request.

(t = 1.33, P = .23). Subsequent analyses of individual zones indicated that BGAT significantly increased accurate estimates (upper zone A t = 2.00, P = .03; lower zone A t = 2.22, P = .02), whereas becoming more sensitive to hyperglycemia (lower zone D t = 2.52, P = .02) and making fewer benign errors (lower zone B t = 2.28, P = .04) (Fig. 3). Consistent with AI analysis, control subjects demonstrated no significant pre- and postshifts in error grid zones. ANOVA of HbA_1 changes yielded a marginal interaction effect (F = 2.78, P = .07; Fig. 4). Subsequent comparison demonstrated a significant reduction in HbA_1 from recruitment (mean 12.2, t = 2.25, P = .04) and hospital (mean 12.0, t = 2.6, P = .02) to posttreatment (mean 10.8) for BGAT subjects. Correlation analyses were performed to assess the relationship of pretreatment variables on initial accuracy and improvement in BGAT accuracy (Table 1). Initial accuracy (pre-AI) was marginally related to months of SMBG experience and HbA_1. BGAT improvement was marginally negatively related to pre-AI and significantly related to ability to counterregulate. Because of the dichotomous nature of ability to counterregulate, a comparison of improvement was performed. The 12 BGAT subjects who did counterregulate demonstrated significantly more improvement than the 3 who did not (t = 2.88, P = .02). Failure to find a relationship between posttreatment HbA_1 and AI indicates that greater improved accuracy did not directly lead to better metabolic control or vice versa.

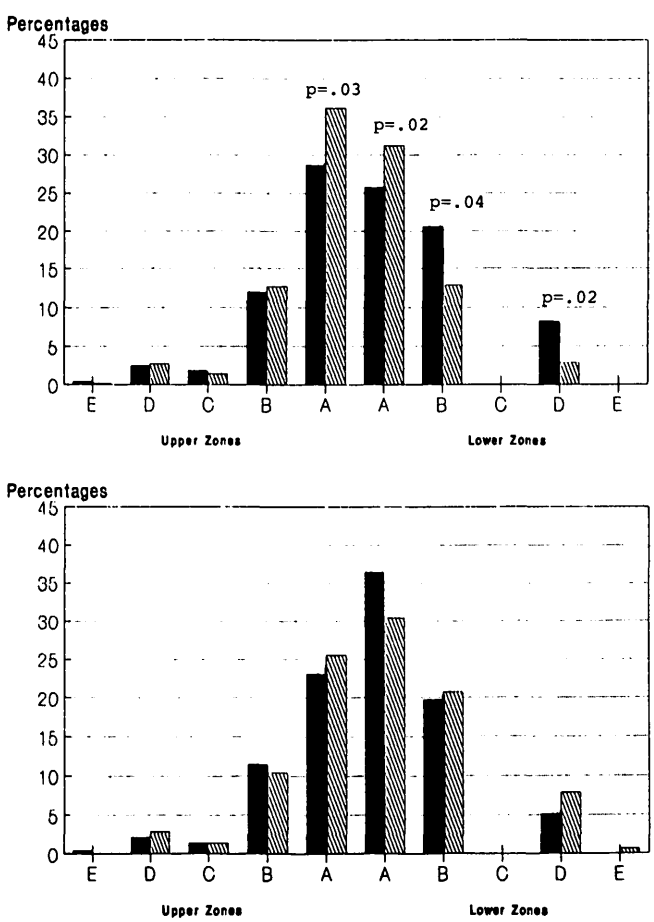

FIG. 3. Pre- (*solid bars*) and post- (*hatched bars*) error-grid analysis zones for blood glucose awareness training (*top*) and control (*bottom*) subjects, where upper E–A zones represent overestimates and lower A–E zones represent underestimates (see Fig. 1).

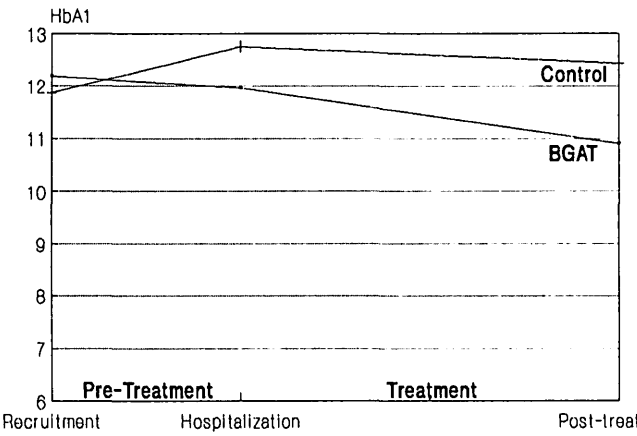

FIG. 4. HbA_1 for blood glucose awareness training (BGAT) and control groups for pretreatment (recruitment and hospitalization) and posttreatment. $P < .04$, BGAT recruitment posttreatment; $P < .02$, hospital vs. posttreatment.

Post hoc analyses. In an effort to further validate AI, frequency of subjects' actual BG (<70, 70–180, >180 mg/dl) was regressed on AI with stepwise and forced-regression models. This showed AI was independent of actual BG distributions, i.e., BG distribution did not produce a significant R^2 in either model.

Whereas distribution of actual BG readings did not relate to pre-AI, pre- and postshifts in these distributions, as indicated by improved HbA_1, were also considered. For example, BGAT subjects may have had more hypo-

TABLE 1
Correlation matrix between pretreatment measures and both initial blood glucose estimation accuracy and improvement in accuracy after blood glucose awareness training

		Blood glucose awareness training
	Preaccuracy index	δ-Accuracy index
Preaccuracy index		−.43†
SMBG frequency in 2 wk	−.20	−.33
Months of SMBG experience	.34†	−.13
Ability to counterregulate	−.18	.61§
HbA_1*	.30‡	−.03

SMBG, self-monitoring of blood glucose.
*Hospital HbA_1 was correlated with the preaccuracy index, whereas posttreatment HbA_1 was correlated with the δ-accuracy index.
†P = .06; ‡P = .08; §P = .013; all other values not significant.

glycemic readings posttreatment and therefore have more undetected hypoglycemic episodes (upper D and E zones). Pre- and postpercentages of undetected hypoglycemic episodes for BGAT and control groups went from 48 to 25 and 50 to 67%, respectively, ($\chi^2 = 17.55$, $P < .001$). Pre- and postpercentages of undetected hyperglycemia (lower D and E zones) were also significantly better ($\chi^2 = 12.5$, $P < .001$) for BGAT than control subjects, going from 18 to 6 and 8 to 13%, respectively.

DISCUSSION

This study paralleled two previous studies demonstrating that BGAT is effective in improving accuracy of BG estimation (13). The percentage of pre- and post-AI improvement (49%) and posttreatment AI (60%) are slightly better than previous research with an earlier BGAT manual (23% improvement and 53% posttreatment AI, respectively). As with the previous two studies (13), BGATs primary effect was on increasing accurate (A zones) estimates while decreasing lower D zones, i.e., increasing recognition of hyperglycemia. The clinical significance of reducing lower D zones from 8 to 3% is that, whereas before BGAT, subjects would have and fail to recognize hyperglycemia three times in 10 days, but after BGAT this would occur only once in 10 days. When controlling for shifts in actual BG readings (pre- and posttreatment), BGAT demonstrated increased sensitivity to both hypo- and hyperglycemia. The clinical significance of this is that subjects at pretreatment detected only one of two hypoglycemic episodes, whereas at posttreatment BGAT subjects detected three of four such episodes. In addition, this study demonstrated that BGAT was associated with a reduction in HbA_1 from 12.2 U (recruitment) to 10.8 U (posttreatment). A pretreatment HbA_1 of 12.2 U is typical for IDDM adults in our clinic. It is not clear from the design whether this reduction was a function of subjects focusing on daily BG fluctuations, perceiving termination of unpleasant symptoms (e.g., palpitations and difficulty concentrating), negatively reinforced appropriate self-care behaviors, or having improved information about BG fluctuations. The latter possibility does not seem likely because improvement in AI did not correlate with posttreatment HbA_1. The stability of these improvements in accuracy and metabolic control are not clear from this study.

Baseline accuracy of BG estimation was unrelated to patients' counterregulatory integrity or the frequency of SMBG. Whereas patients who fail to counterregulate may lose adrenergic cues of hypoglycemia, this did not appear to affect their ability to estimate hyperglycemia. Apparent loss of adrenergic symptoms in detection of hypoglycemia may have been compensated for by neuroglycopenic and affective symptoms and external cues. If future research replicates the finding that failure to counterregulate does not compromise ability to detect hypoglycemia, this would suggest that β-blockers and other therapeutic agents thought to produce hypoglycemia unawareness by masking adrenergic symptoms may not put IDDM patients at higher risk. The failure to find a relation between SMBG frequency and initial accuracy suggests that the provision of BG feedback does not enhance BG awareness. This speculation is supported by others investigating the effects of SMBG on accuracy of estimation (10,13).

There is suggestive evidence that the longer an individual has used SMBG, the more accurate the BG estimations are ($P = .06$), and the more accurate the individual is at SMBG, the better the metabolic control ($P = .08$). The latter speculation is confirmed by the experimental finding that BGAT did lead to increased accuracy of BG estimation and reduced HbA_1. Whether this is because greater awareness of BG fluctuations makes possible more relevant and timely self-care interventions or serves as an endogenous reinforcement of compliance is unclear from this investigation.

Consistent with previous research, this study suggests ($P = .06$) that the less accurate an individual is before treatment, the more they will benefit from BGAT (13). This is analogous to saying that the less knowledgeable an individual is about diabetes, the more likely they will benefit from diabetes education. This has two implications. First, it may be more cost-effective to target the least accurate individuals for BGAT. Second, it may suggest that there is a ceiling effect in training BG-estimation accuracy. The posttreatment AIs ranged from 30 to 90%. The mean AI for patient-generated SMBG was 89% in contrast to the post-BGAT mean AI of 60% (18). Both points would indicate that we have not reached a BG-estimation accuracy group ceiling. We are probably more limited by our training procedures than by patients' potential ability. Future research needs to explore alternative and enhanced procedures for training such a skill. BGAT is no substitute for SMBG, and patients with IDDM should be encouraged to rely on SMBG technologies, especially at times when they think their BG is euglycemic (potential D-zone errors).

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