Glucose Meters with Built-In Automated Bolus Calculator: Gadget or Real Value for Insulin-Treated Diabetic Patients?

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ABSTRACT

Self-monitoring of blood glucose is now widely recognized as efficacious to enhance and facilitate diabetes management. More than just a means of recording and storing data, some blood glucose meters (BGMs) are now designed with an embedded automated bolus calculator (ABC) with the goal to propose patients recommendations about insulin dosage. The growing literature in this field tends to claim that these new smart BGMs make patient’s life easier and decision making safer. The main purpose of this review is to verify whether BGMs with a built-in ABC indeed improve the willingness and the ability of insulin-treated patients to make adequate therapeutic decisions and positively impact the metabolic control and the quality of life of ABC users. It appears that, as long as the education provided by caregivers remains a top priority, BGMs with a built-in ABC (more than just electronic gadgets) can be regarded as bringing real value to insulin-treated patients with diabetes.

Keywords: Blood glucose meters; Bolus calculator; Diabetes; Hypoglycemia; Self-monitoring; Quality of life

INTRODUCTION

Evidence accumulated over past decades convincingly demonstrates that adequate and sustainable metabolic control in people with diabetes results in better micro- and macrovascular outcomes [1–6]. In addition, when this control occurs early on, it may confer a so-called metabolic memory [6]. However, it must be admitted that such achievement remains elusive in a significant proportion of patients, as more than 60% of them are not reaching the advised glycated hemoglobin (HbA1c) goal of <7% [7].

In addition to marked improvements in the medical treatment of diabetes, increasing
evidence indicates that regular assessment of blood glucose (BG) levels may help insulin-treated patients to achieve better glycemic control. Self-monitoring of BG (SMBG) contributes to better adjustment of therapies, and helps to reach treat-to-target goals. More importantly, SMBG can act as an educational tool to support patients to better adhere to their treatment [8–16]. SMBG may provide fruitful feedback about how nutrition therapy, physical activity, and medications influence BG levels and alerts about hypo- and hyperglycemia [15]. However, some patients are reluctant to use SMBG due to the pain associated with finger sticks and the cost associated with SMBG supplies. Additionally, some patients are unable to interpret SMBG data and translate it into appropriate therapeutic decisions [15].

One way to improve SMBG acceptance is to provide therapy algorithms to support patients [especially those treated by multiple daily injection (MDI) or continuous subcutaneous insulin infusion (CSII)] when interpreting their values, and to react accordingly. Such tools are already on the market.

METHODS

The question raised in this review is whether BG meters (BGMs) with a built-in automated bolus calculator (ABC) represent an added value in patient performance and ability to make the right therapeutic decisions, which may impact both metabolic control and quality of life. A literature search was carried out using Medline and PubMed to select papers where an ABC was used in addition to SMBG. The papers quoted in this review were selected to bring insights into specific questions concerning improved capability of patients to make therapeutic decisions, treatment satisfaction, improved metabolic control and decreased glycemic variability, and reduced fear and rate of hypoglycemia.

Premeal Short-Acting Insulin Dose Calculations

For SMBG to be considered useful, it should be used regularly and correctly at the very least. This goal is achieved when patients and healthcare providers (HCPs) know how to translate the data into appropriate insulin dose adjustments [16]. To help patients make the right decision, software has been developed to calculate doses of short-acting insulin before meals. This type of software has been available in insulin pumps for over 10 years, but was only recently integrated into BGMs and mobile device applications [17]. MDI- and CSII-treated patients are challenged with complex mathematics before deciding on a premeal short-acting insulin dose, at least three-times daily. Patients are supposed to calculate their insulin dose based on the following formula:

\[
\text{Insulin dosage} \ (U) = \frac{\text{glucose load} \ (g)}{\text{IGR}} + \frac{(aBGL) - (tBGL)}{\text{CF}} - \text{[IOB]}
\]

Insulin dosage is expressed in units (U). The first part of the equation corresponds to a division between the glucose load and the insulin to glucose (or carbohydrate) ratio (IGR). The glucose load, expressed in grams (g), represents the amount of glucose intended to be consumed, whereas IGR represents how many grams of ingested glucose 1 U of insulin covers. According to Walsh et al., IGR is calculated as: \(5.7 \times \text{weight (kg)} / \text{total daily dose (TDD)}\) [18]. The correction dose, the second part of the equation, is calculated by subtracting the actual blood glucose level (aBGL) from the target blood glucose level (tBGL), divided by
the correction factor (CF), also referred to as the insulin sensitivity factor (ISF) in other studies [19–22]. CF represents how much 1 unit of insulin lowers BG and is calculated as: 1,960 mg/dL/TDD, according to Walsh et al. [18]. Insulin on board (IOB), the third part of the equation, corresponds to how much insulin remains theoretically active in the body from the last dose. The IOB amount should be taken into account and subtracted from the correction dose. Of note, King recently proposed rounded formulas for IGR (300/TDD), CF (1,500/TDD), and total basal insulin dosage [TBD = 0.2 x weight (kg)], which gives a slightly higher estimate for bolus insulin and a lower estimate for TBD [23]. The factors, IGR, CF, tBGL, and IOB, should be continuously tailored by the HCP for each patient.

One may easily understand that even well-educated and motivated patients will inevitably consider these calculations time consuming with, on a long-term basis, the risk of mistakes when dealing with so many variables clustered in this equation. In reality, a significant proportion of people with diabetes deal with low literacy and low numeracy skills, which often results in misinterpretation of the recorded information, wrong therapeutic decisions, and low therapeutic compliance, thereby precluding correct metabolic control [24–27]. Thus, one way diabetes device manufacturers sought to facilitate the process of therapeutic decisions was to incorporate an ABC into insulin pumps and BGMs. BGMs with built-in ABCs are mainly designed for MDI-treated patients, as insulin pump users already have calculators integrated into their pump. These “smart” BGMs are also conceived to provide an electronic log book and to store information regarding insulin intake, food consumption, physical activity, and health information. They are sometimes engineered to transmit data to web databases where they are interpreted by specialized software systems [28].

Do BGMs with Built-In ABCs Help Insulin-Treated Patients to Make Appropriate Therapeutic Decisions, While Improving Treatment Satisfaction?

A recently published study reported performances achieved by 205 insulin-treated patients (47.6% with type 1 diabetes and 52.4% with type 2 diabetes) who were asked, based on scenarios of high or normal glucose test results provided by control solutions, to manually calculate mealtime doses of short-acting insulin, followed by the same calculation using a glucose meter with a built-in ABC [29]. Two cohorts of patients, either carbohydrate counters (n = 101) who were using a sophisticated formula, or noncarbohydrate counters (n = 104) who were using a simplified formula, were considered for the study. The results showed that 63% of doses calculated manually by the participants were erroneous, whereas only 6% of incorrect responses were recorded when calculations were performed with an ABC. Eighty-three percent of subjects felt confident about using the ABC and 87% preferred the automated method to the manual calculation. The study was not designed to evaluate the direct impact of ABCs on metabolic control, as the testing was based on control solution values, not on actual blood tests [29].

These results are in line with several previous studies that showed only a small proportion of people with diabetes able to adequately calculate insulin doses, while taking into account glucose load and BG levels. This may explain the low level of treatment compliance and therapeutic inertia over the long duration
of diabetes [24, 30, 31]. These data are also reminiscent of those from a 2008 study that demonstrated a benefit of using an ABC in a pediatric population of CSII-treated patients, both in terms of personal satisfaction and improved preprandial and 2-h postprandial BG levels [32]. In one older study [31], an improvement in treatment satisfaction, adherence, and quality of life was shown in 83 adolescents using MDI or CSII. Another study with 49 CSII-treated patients [33] reported better postprandial BG excursions and good confidence in the doses advised by the device (Table 1 [29, 31–33]).

Do BGMs with Built-In ABCs Help to Improve Metabolic Control in Insulin-Treated Patients?

A recent study showed a significant improvement in HbA1c values after a 6-month follow-up in 40 consecutive MDI-treated type 1 diabetes patients using an ABC, compared to standard methods (−0.85% vs. −0.007%; \( P < 0.05 \)) [34]. This ABC-associated improvement in metabolic control was further confirmed in a recent Danish study that reported, after 16 weeks, improved metabolic control (HbA1c −0.7%) and treatment satisfaction in a study group of MDI-treated patients (called the CarbCountABC arm) that received a 3-h educational program, flexible intensive insulin therapy (FIIT) and an ABC as compared to a group that only received FIIT education (HbA1c −0.1%) [35]. The patients in the CarbCountABC arm also experienced less glycemic variability than those in the control group and spent more time in the normal BG range. They also needed less insulin due to more appropriate dosing and less correction of hyperglycemia. The results are in line with those reported in a study of insulin guidance software loaded into a personal data assistant. In this group of 123 MDI-treated adult subjects with type 1 diabetes, there was an improvement in glycemic control, but no change in insulin dose and no weight gain over a 12-month period [36]. In addition, a higher proportion of ABC users reached HbA1c values <7.5%, while remaining within target limit BG levels (70–150 mg/dL). Quite recently, a prospective study performed over a period of 1 year where 30 type 1 diabetic patients were asked to use an ABC, showed a significant decrease in diurnal glucose variability (\( P < 0.005 \)), and improved HbA1c (\( P = 0.007 \)) and postprandial BG (\( P < 0.05 \)) values. The frequency of hypoglycemia was not increased [37].

In a small study (\( n = 18 \)) published in 2008 comparing ABC users to nonusers, improved metabolic control did not occur [34]. Although mean postprandial BG levels in the ABC users were significantly lowered compared to nonusers, HbA1c values were not significantly improved [38]. Noteworthy, this was an observational study, not a randomized study. Furthermore, the decision whether to use the ABC or not was left to the patient’s discretion. Two other quite recent studies in CSII-treated young type 1 diabetic patients reached the same conclusion. There was an improvement in 2-h postprandial BG levels and glucose variability, but no significant improvement of HbA1c values [39, 40]. The discrepancies between these studies can be understood considering differences in study design and duration (Table 2 [34–40]).

Are There Other Advantages to Using BGMs with Built-In ABCs?

Another relevant advantage of using an ABC, besides easier bolus calculation and the likely improvement in metabolic control, or at least in
Table 1 Impact of an ABC on patient satisfaction and quality of life

| References       | Study design                                                                 | Objectives                                                                 | Results                                                                 |
|------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------|
| Sussman et al. [29] | Multicenter study comparing manual versus ABC-assisted calculations of insulin doses | Evaluation of error frequency when insulin dosages calculated either manually or with an ABC | Significant reduction of errors when doses calculated with an ABC ($P < 0.001$)                      |
|                  | 205 MDI-treated patients                                                   |                                                                           | Improved confidence and preference of using an ABC ($P < 0.00001$)   |
|                  | 47.6% type 1 diabetes; 52.4% type 2 diabetes; 104 non-CC; 101 CC           |                                                                           | Increased adherence may optimize the use of meal-time insulin          |
| Glaser et al. [31] | 12-month randomized control trial comparing an IDC device to conventional methods for insulin doses | Impact of an ABC on metabolic control                                      | Higher rate of calculation errors with conventional methods            |
|                  | 83 MDI- or CSII-treated type 1 diabetes adolescents                         |                                                                           |                                                                       |
|                  | Impact of an ABC on treatment satisfaction, regimen adherence, and quality of life |                                                                           | Improvement in treatment satisfaction, adherence, and quality of life |
|                  | No change in HbA$_1c$ among ABC users                                       |                                                                           |                                                                       |
| Shashaj et al. [32] | 2-week crossover study comparing an ABC (Bolus Wizard) to conventional methods for insulin doses | Improvement of pre- and postprandial glycemic control                      | Significant reduction in pre- and 2-h postprandial BG levels and in the number of correction boluses ($P < 0.05$) |
|                  | 36 CSII-treated type 1 diabetes adolescents                                |                                                                           | Higher satisfaction level among ABC users                             |
| Gross et al. [33] | 7-day crossover study comparing an ABC to conventional methods for insulin doses | Treatment satisfaction                                                    | Less correction boluses to control postprandial hyperglycemia when using the ABC ($P < 0.05$) |
|                  | 49 CSII-treated type 1 diabetes subjects                                   |                                                                           | Less supplemental glucose to raise low BG levels when using the ABC ($P < 0.05$) |
|                  | Improvement of postprandial BG levels                                      |                                                                           | Decreased average deviation of 2-h postprandial BG levels             |
|                  | ABC easy to use and confidence in advised insulin doses                    |                                                                           | ABC easy to use and confidence in advised insulin doses               |

$ABC$ automated bolus calculator, $BG$ blood glucose, $CC$ carbohydrate counters, CSII continuous subcutaneous insulin infusion, $HbA_1c$ glycated hemoglobin, $IDC$ insulin dosage calculation, $MDI$ multiple daily injection

glucose variability, is the reduction in fear and rate of hypoglycemia. This was shown in a recent study that surveyed 1,412 MDI-treated type 1 diabetes patients, of which 588 responded positively [41]. The vast majority of them (76.7%) claimed to use the ABC quite often or
always. In 52% of respondents, the fear of hypoglycemia was reduced and most of them (78.8%) reported a high confidence in the insulin dose calculation. In addition, 89.3% reported that bolus calculation was made easy or very easy when the bolus advisor was used. Although
reduced fear of hypoglycemia is not a parameter systematically reported in the literature, most of the studies point out patient satisfaction and the improved confidence in insulin dosage when using an ABC. One may therefore presume that the number of patients who skip insulin dosages or commit calculation errors is likely to be lower among those using an ABC compared to those without. It is also more likely that ABC users are more prone to follow insulin titration instructions, which are key in maintaining adequate metabolic control over time.

Even though data are contradictory about hypoglycemic events, with at least one study reporting more severe hypoglycemia among ABC users [36], a recent study by Bergenstal et al. [42], where an insulin support decision algorithm was tested both in subjects with type 1 and type 2 diabetes, rather supports the idea that the frequency of hypoglycemia is lower among patients using an ABC. Thus, less hypoglycemic episodes occurred in the groups using the algorithm despite the higher rate of insulin adjustment. Another important piece of information brought forward by this paper is related to the fact that besides subjects with type 1 diabetes, two groups of subjects with type 2 diabetes (treated either with basal–bolus therapy or twice-daily biphasic insulin) also appeared to show benefit from the computer decision system. This indicates that smart BGMs should not be reserved only for subjects with type 1 diabetes, but rather offered to all MDI-treated patients, regardless of the type of diabetes (Table 3 [41, 42]).

DISCUSSION

Although a consensus is emerging that SMBG increases awareness of diabetes, as well as patient’s empowerment and reassurance, there are also papers reporting worsened quality of life among patients using the SMBG method. Of note, these studies were performed with type 2 diabetes patients who reported increased anxiety and depression, and even obsessive behaviour [43–47]. These feelings were often associated with HCPs lack of interest to actively check and use SMBG results that were otherwise carefully collected by patients. This highlights the pivotal educational role of HCPs about the importance they bring to the interpretation of SMBG results. From this viewpoint, there is little doubt that improved quality of life and patient empowerment resulting from an increased capability to use structured SMBG data and translate it into appropriate therapeutic decisions are two hallmarks of BGMs with built-in ABCs. HCPs in combination with an ABC can educate patients to interpret SMBG values and make appropriate therapeutic decisions to meet metabolic targets. Patients must deal with an overload of variables such as BG levels, ICR, glucose intake, target values, IOB, and physical activity before making insulin dose decisions. When correctly implemented and tailored to each patient, the main advantage of an ABC is to provide appropriate means to quickly make daily decisions, which may contribute to a reduction in hypoglycemic events and metabolic instability. The literature reveals that BGMs with built-in ABCs are used more often and with increased confidence by patients, which could be viewed as a real advantage, especially for those who are confronted to low numeracy and/or low literacy issues. One may reasonably suppose that, because of improved metabolic performances and quality of life, the increasing use of BGMs with built-in ABCs may result in reduced risks of long term micro- and macrovascular complications. This medical improvement may of course have positive economic consequences because of long-term
improved HbA1c and a reduced rate of diabetes complications [13].

To be efficacious, smart BGMs that are expected to increase patient adherence to BG monitoring, should be used by patients who form a cohesive team with caregivers. It is of course important that all patients understand the relevance of SMBG and how to use it. Noteworthy, this should be done while always questioning the suggestions delivered by the machine. For instance, a BGM cannot exempt the patient to always predict changes in the physical activity or diet habits in the hours that follow the injection of insulin. Other parameters, such as concurrent illnesses and special medications (e.g., corticoids), must also be taken into account. For all of these reasons, ABC devices should be proposed to insulin-treated patients who already have strong skills to calculate bolus manually. This is the price to pay for them to really understand and critically review dosage recommendations proposed by the software. According to the principle that nothing is definitively fixed in the life of patients and that everything may change overtime, the customization of the device must be continuously proposed and supervised by HCPs who should keep explaining to patients what to do with recorded data. Thus, the key aspect for a successful use of a smart BGM is education. Regular assessments must be foreseen to make sure that recommendations provided by the system are done in a safe way and always in close connection with the patient needs. As long as the principle of ongoing education is

| References       | Study design                                                                 | Objectives                                                                 | Results                                                                                     |
|------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Barnard et al. [41] | Survey of 588 MDI-treated type 1 diabetic patients using an ABC              | Reduced fear of hypoglycemia, Prognosis of patients to achieve improved glycemic control | Mild or significant reduction in fear of hypoglycemia in 52% of respondents, Improvement or significant improvement in the confidence in the insulin dose calculation in 78.8% of respondents, Bolus calculation made easy or very easy by the ABC in 89.3% of respondents |
| Bergenstal et al. [42] | 12-week intervention period (testing the Diabetes Insulin Guidance system following a 4-week baseline run-in period, 20 MDI-treated CC type 1 diabetes patients, 20 MDI-treated non-CC type 2 diabetes patients, and six twice-daily biphasic-treated type 2 diabetes patients | Primary: fraction of software dosage adjustment approved by the study team, Secondary: improved glycemic control | Improvement in average BG levels ($P < 0.03$), Improvement in mean HbA1c ($P < 0.03$), Reduction by 25.2% of hypoglycemic events ($P = 0.02$) |

ABC automated bolus calculator, CC carbohydrate counters, BG blood glucose, HbA1c glycated hemoglobin, MDI multiple daily injection
kept in mind, one may expect that using an automated decision support algorithm will bring a great relief to patients, especially to those who are carbohydrate counters, because they must deal with more difficult math than those treated with fixed doses of insulin eventually corrected by CF.

The reduced risk of hypoglycemia is certainly another relevant advantage of BGMs with built-in ABCs. The fear of hypoglycemia, just as a low level of education, often precludes the ability of patients to make changes and is a source of therapeutic inertia. Hypoglycemia is one of the main causes of alteration of the patient’s quality of life. The ongoing technical improvements and, for instance, the recent progresses in telemedicine should make us more confident in the ability of support decision software to alert patients in real time about hypoglycemia [48]. This is of course crucial as, most of the time, actual systems do not warn enough patients about hypoglycemia and about the importance of managing it before injecting the next dose of insulin. In addition, they should also encourage patients to inject insulin as soon as BG levels are getting back to normal, a requirement that is often neglected by patients when recovering from hypoglycemia.

Decision softwares were initially designed to help patients dealing with doses of short- or rapid-acting insulin. Unfortunately, fasting values, that are also known to influence HbA1c values [49], are not yet included enough in the calculation process. It should be easy for manufacturers to propose ABC devices able to counsel doses of long-acting insulin based on few days of fasting BG levels. Positive or negative trends in relation with chosen target values would then be recorded and translated into suggestions to increase or decrease the dosages of basal insulin.

CONCLUSION

BGMs with an embarked ABC are effective motivational tools that should be considered more than just gadgets. They do bring a real value in patient empowerment that is now considered essential in diabetes management. But this statement remains pertinent as long as the principle of ongoing education and the tight cohesion with the HCPs team are preserved.

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