Self-Monitoring of Diabetes Mellitus
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Introduction

What is Self-Monitoring of Diabetes Mellitus (SMDM)?

Blood glucose self-monitoring (BGSM) is a term introduced during the middle 1980's. It designates the performance of chemical tests for blood glucose by the diabetic patient himself. Previously, we also used the terms patient monitoring or home monitoring (including also testing for urine glucose).

Today it would be better to use the more comprehensive term, self-monitoring of diabetes (SMDM). This could then include not only the chemical testing but also the patient's self-evaluation of diet, knowledge about the disease etc. However, the overwhelming documentation in the literature concerns blood and urine testing.

Commercially produced test strip (dipstick) testing for urine glucose and ketones was introduced in the middle 1940's, and until the 1960's these tests were almost exclusively used by medical personnel. At that time, some diabetologists started to teach their patients to perform the tests themselves and the doctors then used the results for adjusting the treatment, especially the dose of Insulin.

Blood glucose tests were introduced in the early 1970's and within a short time, patients were instructed to try the new techniques at home. During the last ten years, interest has almost exclusively centered on blood glucose analysis, especially after the introduction of more user-friendly analytical instruments ("reflectance meters"). Thus, blood glucose self-monitoring (BGSM) is the current MESH term (Medical Subject Headings) used for a computerized literature search, e.g. through Medline or through Index Medicus.

Self-monitoring comprises not only the chemical testing itself, but includes a number of different steps:

- blood/urine sampling,
- knowledge on how to use the test strip or instrument reader,
- keeping a protocol,
- using the results to evaluate the patient's metabolic state,
- and most important of all
- making use of the results to adjust the therapy in order to achieve as near-normal metabolism as possible.
The perfect situation is difficult to reach in all fields of life, and so it is for BGSM. The new techniques are no doubt attractive. However, they also demand motivation and enthusiasm from the patient as well as from his doctor.

Thus, SMDM entails willingness to learn, discipline to perform the tests and to keep to the protocol, and, not least, an understanding of the importance of rigorously following the instructions of the technical procedure. In many countries sampling of blood, and even more of urine, is looked upon as dirty and socially unacceptable. Up to 25 per cent of diabetics have manifested depression, and some feel stigmatized by their affliction with a chronic disease.\(^1\)\(^2\) Therefore the last thing they would want to do would be to show up with instruments and test strip containers which they may consider as signs of their subjectively inferior state.

Testing is also costly -- and prohibitively so -- in many developing countries. On the other hand, some countries supply the equipment and consumables at no cost to the patient.

This review will focus on blood glucose monitoring but will also briefly consider urine testing and other modalities of SMDM.

What are the goals of SMDM?

The primary aim of SMDM is to allow a (near-) normalization of the diabetic state, i.e. a more strict control of the abnormal metabolism. This in turn implies the potential of preventing, or at least delaying the development of multisystem complications associated with diabetes and which may affect the eyes, kidneys, heart, blood vessels, and nervous system (see below).

There are also secondary goals:

1. Identification of the metabolic emergency situation

A. Objectively, i.e. the chemical verification of hypoglycemia, hyperglycemia and ketosis.

With the introduction of intensive insulin therapy BGSM has become essential for the prevention of high-risk hypoglycemia.

B. Subjectively, BGSM may teach the patient to recognize the symptoms of hypoglycemia, as well as hyperglycemia.

2. Improvement of the diabetic patient's understanding of his disease. This will not only help to correct the metabolic imbalance, but it may raise the mood of the patient, as he will find that he can influence his life in a better and more controlled way.

3. Promotion of better communication between doctor and patient. The physician becomes more interested and devotes more time to the individual patient.
4. Replacement of hospital admission and lengthy stay with metabolic control at home. This is now the present policy for diabetic women during pregnancy.

5. Better metabolic control may mean that the patient feels better (admittedly this applies only to a few patients).

*Do we need near-normalization of glucose metabolism?*

Of course, the ultimate question is:

Does better metabolic control really delay or prevent the development of diabetic complications? If this cannot be documented, the primary goal of SMDM will lose its importance.\(^3\,^5\)

The question above is not possible to answer with our present knowledge. However, personally I have been impressed by a number of studies indicating that after intensive treatment and achievement of metabolic regulation:

1. There appears to be an overall correlation between the prevalence of diabetic complications and the degree of diabetes control (evaluated as long-term blood glucose or hemoglobin A1c levels) in a number of retrospective population studies.\(^6\)

2. Microalbuminuria, an early sign of diabetic nephropathy, may be reversed.\(^7\)

3. Plasma lipoprotein abnormalities seen in diabetic patients are normalized.\(^8\)

4. The increased cardiovascular morbidity and mortality seen in patients with impaired glucose tolerance, are decreased to control levels by diet control and tolbutamide.\(^9\)

5. Maternal and fetal morbidity and mortality seen in pregnancy complicated by diabetes, are markedly reduced.

6. Nerve conduction velocity, which is often low in diabetic patients, may improve.\(^10\)

7. Dogs with streptozotocin-induced diabetes develop retinal microaneurysms within 1-2 years, but hardly any if insulin treatment is given.\(^11\)

**Analytical Methodology**

In the hospital-based clinical chemistry laboratory, almost all glucose analyses are done with wet chemistry, i.e. with reagents in liquid form. The reading instrument evaluates transmittance /absorbance of light passing through the liquid phase in a spectrophotometer. A wide range of enzymatic techniques is available, e.g. glucose oxidase, hexokinase, or glucose dehydrogenase.
In contrast, for home monitoring dry chemistry must be used, i.e. with lyophilised reagents impregnated into a porous matrix. The latter is usually a filter paper test pad with a porous film above to exclude infiltration of red cells into the matrix. It is even possible to incorporate reagents which destroy interfering reducing substances.

The colour change of the test pad correlates with the glucose level in the sample and is measured in a reflectometer. This instrument registers the amount of light that is reflected from the surface of the test strip. A parallel circuit measures and corrects for the aging and decay of the photodiode and light diodes used.

At least one instrument uses an electrosensor to monitor the redox potential of the reaction mixture. In another device blood is sucked by capillary action into a disposable plastic cuvette with a thin slit. In the latter instrument the blood reacts with dried chemicals, allowing conventional transmittance spectrophotometric reading in a small automated instrument.

Commonly a two-step enzymatic technique is utilized for colour development. In the first step, hydrogen peroxide is produced by the action of glucose oxidase on glucose. In the second step, the hydrogen peroxide formed changes the colour of an indicator substance through the action of peroxidase. Previously, much attention has been devoted to the interference of reducing substances in the second step, but that problem has now been solved.¹²

It is important for the physician to understand that the glucose level in capillary whole blood may differ from that in plasma from venous blood (approximately, 14% lower in whole blood; lower in venous than in capillary blood postprandially).

A positive spin-off effect was the introduction of the same technique in the hospital setting, especially for stat blood glucose measurements, as well as avoiding the need for repeated phlebotomy, often several times a day. However, these methods are designed to evaluate diabetic control, but not to diagnose diabetes.

_Update on technical improvements_

The following are the main technical improvements achieved during the last decade.

**BLOOD GLUCOSE ANALYSIS:**

1. Near-painless blood sampling by using springloaded lancets with very sharp points. Sampling, "finger prick", is performed from the more blood-rich lateral sides of the fingertips (not the thumb), or by using a fine insulin needle towards the paronychial region.

2. More and better defined colour changes of the test pad (and the printed "colour blocks" on the comparison chart) for different concentration levels. Under optimal
conditions the visual evaluation of the test strip is almost as reliable as the instrument reading. However, for psychological and practical reasons almost all patients prefer the meter.

3. Smaller and more sophisticated reading instruments. The size of the instruments has now been reduced to that of a pen or a credit card. The instrument can by itself register the time points for blood sample application and for reading the reaction. The result is shown on a digital display or as a verbal readout from a talking monitor. If necessary, it can also give error messages, e.g. if the drop of blood is too small.

4. New test strips, needing less participation by the patient. The first step was to try to avoid the previously necessary washing or wiping away of the drop of blood applied to the test strip surface, so that the instrument could see and read the colour of the testpad. Today, it is possible to apply the drop of blood on the top surface of the test strip, allow the red cells to be retained and while the plasma filters through to an underlying reaction layer, evaluate the colour change from the undersurface. In this way, it has become possible to avoid reliance on the operator, except for the application of blood.

5. Quality control systems produced by the manufacturer of the instrument.

6. Memory chips, enabling all results (with times and dates) to be documented together. With manual logbooks some patients tend to cheat the system by recording lower, i.e. "better" results than the real measurement.

7. Linking the patient's small instrument to a computer, possibly via a telephone modem to the health clinic. In this way the physician may be able to go one step further than just seeing the results, namely letting the computer produce a meaningful pattern to form the basis for a change of insulin therapy.

**URINE GLUCOSE ANALYSIS:**

Although much less talked about, important changes have been introduced:

1. Wider analytical range. The really important requirement is to detect intense glucosuria which indicates an urgent need for a change in treatment. However, as yet some test strips can only differentiate between normal versus slight glucosuria.

2. Prevention of interference from reducing substances in urine, especially ascorbic acid which may function as a competitive inhibitor in the peroxidase step.

*Which test system is the best?*

The best system is the one the patient can use reliably and consistently. The problem is actually not so much to find the single best instrument, but rather to avoid too much diversity within a medical district. At present the market for blood glucose monitoring is
expanding rapidly. One reason is economy, in that several countries supply the equipment and test strips free within the framework of the health insurance organization.

The reflectometer is sold rather inexpensively by the manufacturer, who knows that, by far, the greatest expense will be the disposable reagent material, i.e. the test strips. These are instrument specific, i.e. once the patient or the health organization has decided on an instrument, they are locked in to that manufacturer.

One solution is to form a working group, including laboratory personnel, the diabetologist, the diabetes nurse, and patient representatives. The group evaluates what techniques are available in the market and makes a recommendation for selecting one or two systems in the coming two years. A reevaluation is then made each year.

Due to the technical advances the primary limiting factor for BGSM is no longer technical skills. Even children can be taught to perform BGSM. Motivation is a much more important factor. Without it, patients will often have more difficulties in accepting a dietary restriction order given as a consequence of a very high blood glucose result. In the medical care system someone must take responsibility not only for the initial teaching and training but also for continuous follow-up, quality control and motivation.

Quality Control

In order to achieve the benefits of BGSM, quality control of the test procedure is just as essential as is the continued follow-up from the diabetes team. The need for a quality control system is usually poorly understood by most patients. A discussion about the variability of the test results is often taken as a criticism of the procedure and of the patient's ability to perform the test, i.e. the physician is taken to be ambivalent to BGSM as a whole.

However, by far the major source of error in BGSM is the patient's handling of the procedure. Quality control is the only way to check and improve the results. It should include the use of glucose solutions of known concentration, as well as parallel testing with a reference method. Unfortunately, it also leads to an increase in cost due to consumption of more test strips, expert laboratory time, and record keeping.

When to test?

BLOOD GLUCOSE (BGSM)

Most centers recommend a regular testing schedule for BGSM, either using different times for different days, or repeatedly during one or more days per week, e.g. before and two hours after the three main meals, as well as late at night.
URINE TESTING

Testing for glucosuria is now considered old-fashioned in many centers, maybe unfairly so. It can still be used with advantage for following patients with NIDDM. It being the cheapest and simplest form of testing it is still the mainstay for many countries outside the affluent Western world.

It is important to realize that urine testing can only differentiate between badly and very badly controlled diabetes. For defining good metabolic regulation and especially for diagnosing hypoglycemia blood glucose data are necessary. However, in practice marked hyperglycemia is accompanied by marked glucosuria, and can therefore be used in the continuing care of the patient e.g. during intercurrent infection.

The main medical objection to urine testing is the inter-individual variability in the renal threshold, i.e. that urine glucose concentration is only an indirect reflection of the blood glucose levels, which carry the important information we need to know. However, it is possible to define the individual patient's renal threshold if urine testing is performed -- and recorded -- every time blood glucose is analyzed. Urine testing gives information over the whole time span during which the urine was collected, in contrast to blood glucose estimation, which gives accurate information but only for a specific moment in time. Depending on goals this can be looked upon as either an advantage or a drawback.

Many patients find urine testing "messy and unhygienic", probably based on cultural traditions. Actually, plain urine testing at home can achieve a surprisingly high correlation with HbA1c levels, simply by recording the frequency of glucosuria (i.e. not even considering the possibilities of quantitative grading).  

Testing for urine ketone bodies (primarily acetoacetate) is still important for any IDDM patient under stress, in conjunction with hyperglycemia or marked glucosuria, as a positive result indicates the need to immediately contact the diabetes team. Testing is usually not recommended for NIDDM patients, as they rarely if ever develop ketoacidosis (however, this seems to occur more frequently in the third world than in Europe or USA). Most teststrips are oversensitive, in that they give positive results after an overnight fast, even in non-diabetics.

Utilization of blood glucose data

It is well known that not all laboratory results lead to diagnostic or therapeutic decisions. This applies to blood glucose measurements as well. A major problem here is "finding too many trees but no forest". The patient or the laboratory provides the physician with a multitude of analytical results, but it may be difficult to find a consistent pattern allowing a therapeutic recommendation for change. For this purpose a computerized interpretation may be the best answer.
Even before that stage, it is imperative that the results are presented in a proper way, preferably as a dated laboratory report. Thus, glucose monitoring without a permanent record is of little use. Another way to waste the benefits of BGSM is if the physician is uninterested in reviewing the data the patient has produced.

SMDM primarily aims at setting up an informative database about the influence of exercise versus dietary pattern in the individual patient, the effect of a change of insulin treatment etc. The insulin dose should normally be adjusted according to blood glucose patterns, and not based on a single blood glucose result. However, this may not be practical for some diabetics having a profession with a highly irregular daily schedule.

*What can be achieved by BGSM?*

Several studies have documented that diligent, frequent use of BGSM can improve HbA1c levels in patients with IDDM, and in some patients achieve near-normoglycemia. BGSM can lead to decreased HbA1c levels unlike other forms of diabetes education which have failed to do so.

The effects are mostly evaluated in the short term but can actually improve over time. There are indicators that metabolic improvement will only be achieved if the patient persists with frequent testing every day, possibly because the patient is then motivated for testing as well as for changing his lifestyle.

BGSM *per se* is not the final answer for metabolic regulation of diabetes. It is of value only as part of a whole concept of cooperation between the patient and the diabetes team, especially the diabetes specialist nurse. Thus, it is clear that little is gained from just ordering the patients to start BGSM without careful instruction in the technique, and without the intense motivation and interest in the follow-up of the patients by the diabetes team.

A literature search reveals many papers on BGSM. However, to a large extent these deal with the laboratory qualifications of the test systems. Many are comparisons with a reference method in the hospital laboratory, i.e. performance in the hands of professional laboratory technicians under optimal conditions, as expressed in terms of accuracy and precision, and correlation coefficients. Thus, they provide little information on how the tests perform during home monitoring by patients themselves.

There is considerably less information on the proficiency level of patients doing BGSM. However, it is clear that so far even the best performing devices have been unable to achieve the analytical goals of consensus documents, i.e. that BGSM measurements should always be within 15% of the reference value. On the other hand, for some patients it may be sufficient to detect deviations from a baseline, i.e. consistency is generally more important than extreme precision and accuracy.
If then the objective documentation of overall metabolic correction activated by BGSM is relatively scarce, what other effects can it achieve? There are actually several other factors to consider:

It is the only objective way for diagnosing hyperglycemia, a prerequisite for introducing intensive insulin therapy.

Many patients clearly express that they had developed a better understanding of the disease. They often state that they felt more in control, and that they no longer dreaded the visits to the diabetes clinic because of reprimands for something they had been unable to understand. -- Nor should one underestimate the learning experience for the diabetologist or diabetes nurse, in their ability to see for the first time the actual day-to-day glucose values. For both patient and medical personnel realistic goals should be set in the form of blood glucose targets at different times of the day.

Communication between patient and the diabetes health team is a crucial factor. BGSM may give an incentive for more frequent contacts. Imagine a patient coming for routine control every three months, i.e. four days a year, and then is suddenly given an opportunity to speak to an interested diabetes nurse every week, i.e. 13 times more often. The participation of the health team may be more important than the blood glucose values themselves. Ibis is also supported by one study in which BGSM could not achieve better control than the personal attention from a diabetes team.23

Consensus recommendations

International recommendations for BGSM are available. Recent consensus documents have been published by the American Diabetes Association and from the European NIDDM Policy Group.24,25 Their general outline and conclusions agree on most issues: BGSM is indispensable for insulin treated patients (IDDM or NIDDM) and may be of value also for other groups with NIDDM.

Which patients should use BGSM?

Beside the general recommendation extra emphasis is placed upon special indications such as:

INTENSIVE TREATMENT PROGRAMS

Without BGSM it is difficult and may even be dangerous to run an intensive program (irrespective of the choice between insulin pump or conventional insulin therapy). The decreased levels of glucose and HbA1c are reached at the cost of a threefold increase in frequency of severe hypoglycemia. This risk may be reduced if hypoglycemia is identified earlier.
Furthermore, patients with a previously low blood glucose level commonly lose their subjective sensitivity to the initial symptoms of or defences against neuro-hypoglycemia (so-called hypoglycemia-associated autonomic failure). Many patients are so afraid of hypoglycemia that they deliberately increase their intake of rapidly absorbable carbohydrates. Both situations may be improved through BGSM.

**DIABETIC WOMEN DURING PREGNANCY**

The reduction of morbidity and mortality in children and diabetic mothers through more strict metabolic regulation is one of the most impressive achievements of diabetes treatment. BGSM has had a major impact in this regard and has two major advantages: BGSM is a safe and effective way of managing the pregnant diabetic woman as an outpatient. It motivates the patient and makes her understand the relationship between diet and treatment. Thus, it allows her to stay at home and yet have the same near-optimal metabolic regulation that could have been achieved in the rather artificial environment of a hospital ward. The cost of tests and meters is repaid many times over by the saving in hospital days.

**BRITTLE DIABETES**

Brittleness is regarded by many as inherent to the disease, with unavoidable large swings between hypoglycemia and hyperglycemia. On the other hand there is good evidence that a major factor is noncompliance by the patient and a breakdown of patient-doctor relationship. BGSM may provide a good opportunity to attain better understanding and to initiate an open dialogue. For many patients brittle diabetes can actually be converted into stable diabetes, which may be documented as fewer emergency admissions for hypoglycemia.

**NIDDM** (especially patients with a high renal threshold for glucose)

For NIDDM there are few prospective studies comparing testing for blood versus urine glucose. Testing may lead to better metabolic control in both groups, but without any added advantage in the BGSM group. However, blood testing is several times more expensive than urine testing.

**SMDM in the future**

What can we expect in the future from patient self monitoring and self care? Technically there will certainly be continued development to achieve:

--- User-independent, "foolproof" measurement of blood glucose and glycosylated hemoglobin.
--- Non-invasive or implantable glucose sensors.
-- Memory systems, that not only give date, time and result, but which incorporate:
--- Computer-based algorithms for individual correction of insulin therapy.
This can be done by linkage to a personal computer at home or with the health care center, but preferably through a chip in the glucose meter itself. Decision support systems equipped with a small learning memory chip can give efficient therapeutic guidelines.

It may also be possible to expand the concept of SMDM, i.e. not limiting it to chemical testing (BGSM). One area that could benefit might be diet education, adapted to the need of the individual patient. A French group has introduced a computerized system for dietary education and training. Through the cheap Minitel system monitor connected to the telephone network the diabetic patient has an information database at his disposal 24 hours a day, 365 days a year. Objective measures of metabolic control have improved already after a short time, and the beneficial effect persisted even a year after stopping the study.

Another way could be assertiveness courses to empower the patient to reach personal goals, e.g. a realistic evaluation and encouragement to achieve the maximum of his personal possibilities. Being able to negotiate and reach goals for blood glucose and glycosylated hemoglobin is helpful but may not be enough. Instead of viewing the disease only as a heavy burden, at least some diabetics might be able to see their disease as a challenge to seek more from life.

Conclusion

SMDM is here to stay. It is true that the present documentation of its overall capabilities to improve metabolic control in all patients, as well as of its possibilities to prevent the development of complications is insufficient. However, it seems highly likely that this documentation will become available when there is longer experience with the newer technologies coupled with better training and education of the patients.

One method of evaluation would be to ask the physician or the diabetic patient the following:

What type of follow-up would you recommend for:
-- your son who is diabetic and just starting school?
-- your pregnant sister with diabetes?
-- your diabetic brother with microalbuminuria?
For me it would be an easy choice.

Even if SMDM does not always lead to metabolic improvement, i.e. a change in the treatment, it may contribute in a very positive way to the overall treatment and care of the patient. Patients, diabetologists and nurses agree that SMDM is an excellent tool for improving the understanding of the disorder in the individual patient as well as providing a means for improved communication and motivation. In as much as it encourages the patient to take charge of his diabetes, the overall cost/benefit is positive.
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