THE EFFECTS OF ALTERNATIVE-SITE BLOOD GLUCOSE MONITORING ON TESTING FREQUENCY, PAIN RATING, AND GLYCOXYLATED HEMOGLOBIN

by

Nancy Bennion

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ABSTRACT

The Effects of Alternative-site Blood Glucose Monitoring on Testing Frequency, Pain Rating, and Glycosylated Hemoglobin

by

Nancy Bennion, Master of Science

Utah State University, 2004

Major Professor: Dr. Nedra Christensen
Department: Food and Nutrition Science

A crossover design study was conducted to determine if reducing pain, by using alternative sites off the finger tip, would increase testing frequency and improve clinical outcome as measured by glycosylated hemoglobin. Subjects with type 1 and type 2 diabetes tested with the FreeStyle alternative-site meter (group 1) or tested with their original meter (group 2). After 3 months the subjects used the alternate meter. Testing frequency and blood glucose concentrations were recorded for the month before the study began and monthly thereafter. Glycosylated hemoglobin was tested initially, at the crossover point, and at study conclusion. Insulin users increased testing frequency from 2.4 to 3.0 tests per day. Testing frequency for non–insulin users remained the same at 1.5 tests per day. Testing frequency was essentially the same with the FreeStyle and the original meters. The average hemoglobin A1c was 7.4% (standard deviation 1.5%) initially, 7.3% (standard deviation 1.5%) at the crossover point, and 6.9% (standard deviation 1.1%) after 6 months. There was no significant difference in hemoglobin A1c
measurements between meter types after 6 months. Thirteen months later a final hemoglobin A1c, testing frequency, and a questionnaire regarding meter preference and pain rating were obtained. Seventy-four percent of participants preferred the alternative-site meter, which was rated as significantly ($p < .05$) less painful. Testing frequency significantly improved ($p = .001$) while free strips were being provided. Testing frequency 13 months later was not significantly different from the baseline ($p = .101$). Hemoglobin A1c was significantly lower 6 months after the study began ($p = .000$) and 13 months later ($p = .008$) at baseline.
I would like to thank TheraSense, Inc. for providing financial assistance enabling me to conduct this research. I would especially like to thank my major professor, Dr. Nedra Christensen, and my committee members, Drs. Deloy Hendricks and Richard Cutler, for their support and assistance throughout the entire process.

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Nancy Bennion
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CHAPTER I
GENERAL INTRODUCTION

Definition of Diabetes Mellitus

Diabetes mellitus is a syndrome resulting in hyperglycemia secondary to lack of insulin or impaired effectiveness of insulin. Insulin is the major hormone responsible for promoting the uptake of glucose from the bloodstream into the many organ and tissue cells of the body. As the effectiveness of insulin is diminished, blood glucose rises above normal, physiologic levels. Distinct symptoms of diabetes include polydypsia, polyphagia and polyuria.

Diabetes mellitus can be classified as insulin-dependent diabetes mellitus (type 1 DM) or non-insulin-dependent diabetes mellitus (type 2 DM). While both types of diabetes mellitus have unique features and characteristics, treatment revolves around achieving and maintaining blood glucose levels within normal limits. The overall goal for both types is essentially normoglycemia.

Although hyperglycemia is the hallmark abnormality seen in people with diabetes mellitus, other complications develop as the disease progresses. Complications include diabetic ketoacidosis, neuropathy, retinopathy, and vascular disease. If complications develop, physical and financial burdens increase.

Diabetes mellitus has been described as an epidemic. Diabetes mellitus is expected to increase in incidence in the U.S. Boyle et al. projected that by 2050 nearly 29 million Americans will be diagnosed with the disease. An increase in 18 million
cases in a span of less than 50 years will likely result in a sharp rise in national morbidity and mortality. Because diabetes is ever-increasing in the U.S., treatment of the disease will have an ever-increasing impact on all Americans. As the number of people with diabetes mellitus increases, the economic burden of the disease will become more severe.

The Diabetes Control and Complications Trial (DCCT) proved that achieving blood glucose levels within a normal range reduced the complications associated with diabetes.² It can be deduced that improved blood glucose control also results in less economic burden of the disease. Therefore, treatment modalities that improve glucose control and ultimately reduce the severity of the complications of diabetes mellitus have become even more important.

Self Monitoring of Blood Glucose

Since the DCCT trial, guidelines for treatment and care have been developed by the American Diabetes Association.³ These guidelines include self-monitoring of blood glucose (SMBG) four times daily if insulin therapy is used to treat the disease, or (SMBG) two times daily if insulin therapy is not a treatment modality.³

Previous research has demonstrated that SMBG is essential for achieving clinically acceptable hemoglobin A¹c levels.⁴,⁵ The DCCT proved that low hemoglobin A¹c scores directly correlated with a decrease in the complications of diabetes mellitus.² In essence, SMBG is believed to have a direct and positive effect on blood glucose that translates into reduced morbidity and mortality for those with the disease.
Despite recommendations for SMBG from the American Diabetes Association and the DCCT trial, most people diagnosed with diabetes are not monitoring blood glucoses as frequently as recommended. Because SMBG is recognized as an effective and important treatment, causes for decreased SMBG in people with diabetes have been studied.

Deterrents to SMBG have been hypothesized to include the pain associated with SMBG and the financial burden associated with SMBG. However, the extent each barrier plays has yet to be outlined.

The financial burden of purchasing blood glucose monitoring strips can be immense. Not all people with diabetes have an insurance provider that covers the entire cost of strips. Therefore, it is likely that the economic drain plays a major role in decreasing testing frequency.

Advances in technology have resulted in blood glucose monitors that require approximately one-tenth the amount of blood that traditional finger-stick blood glucose monitoring systems require. These new monitoring devices allow for decreased depth in lancing devices to draw blood. In addition, blood may be obtained from sites other than finger-tips. Forearm testing, possible with the new, alternative-site meters, permit testing in locations with fewer nerve-endings per square centimeter. In summary, new, alternative-site meters potentially allow for decreased pain and possibly increased SMBG.

We aimed to outline some factors that may significantly affect frequency of SMBG. The purpose of this research was four-fold:
1) To determine if pain associated with SMBG was decreased using an alternative-site meter as opposed to a traditional finger-stick meter.

2) To determine if patients with diabetes had increased SMBG using an alternative-site meter as opposed to a traditional finger-stick meter.

3) To determine if providing free SMBG strips increased testing frequency.

4) To determine the effects of an alternative-site meter on hemoglobin A1c measurements.

References


CHAPTER II

ALTERNATIVE-SITE GLUCOSE TESTING: A Crossover Design ¹

Abstract

A crossover design study was conducted to determine if reducing pain, by using alternative sites off the finger tip, would increase testing frequency and improve clinical outcome as measured by hemoglobin A1c (HbA1c). Subjects with type 1 and type 2 diabetes tested with the FreeStyle meter (group 1) or tested with their original meter (group 2). After three months the subjects used the alternate meter. Testing frequency and blood glucose concentrations were recorded for the month before the study began and monthly thereafter. HbA1c was tested initially, at the crossover point, and at study conclusion. Insulin users increased testing frequency from 2.4 to 3.0 tests/day. Testing frequency for non–insulin users remained the same at 1.5 tests/day. Testing frequency was the same with the FreeStyle and the original meters. The average HbA1c was 7.4% (SD 1.5%) initially, 7.3% (SD 1.5%) at the crossover point, and 6.9% (SD 1.1%) at study conclusion. There was no significant difference in HbA1c measurements between meter types. Preference rankings were 76% for FreeStyle, 20% for their original meter, and 4% preferred both meters equally. This population tended to be in good glycemic control with 70% having HbA1c at 8.0 at study initiation. Subjects preferred testing with the FreeStyle meter (76%), but did not increase testing frequency. Study participants tended to be in good testing compliance and glycemic control with little room for improvement.

Introduction

The American Diabetes Association reported in an October 1998 statistical report that diabetes mellitus affects 15.7 million people in the United States, comprising almost 6% of the population (8.2% of the total population over age 20, and 18.4% over age 65, with a distribution of 7.5 million men and 8.1 million women). This disease is characterized by insulin insufficiency, lack of insulin production and/or resistance to insulin. Lack of control leads to hyperglycemia and is associated with a variety of serious complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease.

The cost associated with diabetes in the United States was $98 billion in 1997. This includes $44.1 billion in direct costs and an additional $54 billion in indirect costs due to disability and mortality. Improvement in diabetes control, which can be measured in hemoglobin A1c (HbA1c) levels, decreases the complications of diabetes. Gilmer and O’Conner report a 1% improvement in HbA1c level from 10% to 9% was associated with a $4,116 ± 1,178 difference in cost over 3 years, and a HbA1c improvement from 9% to 8% had a reduction of cost by $3,090 ± 960. Increasing the frequency of self-monitoring of blood glucose values resulted in an improvement (lowering) of HbA1c levels. A linear relationship between the number of strips used and a decrease in the HbA1c level in type 1 patients had been reported. Evans reported that the total number of reagent strips dispensed reduced HbA1c levels by 0.7% for every extra 180 test strips in a 6-month period. In a 6-month period, 180 strips would be one blood glucose reading per day.
The importance of normoglycemia for the prevention of diabetic complications is recognized. Self-monitoring of blood glucose (SMBG) has been recommended as a technique for control of blood glucose and should be an integral part of the treatment plan. Despite the clear benefit of glucose monitoring in the successful treatment of diabetes, patients are reluctant to comply with testing regimens. In a study conducted in Scotland to determine the number of glucose monitoring strips that were dispensed from the pharmacy compared to the records for prescriptions, only 20% redeemed enough reagent strips to test daily. There were 16% (128) of the 807 type 1 patients who did not obtain any reagent strips and only 1% (8) who obtained enough strips to test four times per day. For the 258 patients with type 1 diabetes that had a recorded HbA1c, only 152 (59%) had obtained at least one packet of reagent strips. Similarly 170 of the 290 (59%) of type 2 patients with a recorded HbA1c obtained one packet of reagent strips. This corresponds to data obtained from the National Health Interview Study conducted in the United States on the frequency of blood glucose testing by Harris. The results showed only 40% of type 1 and 26% of type 2 taking insulin tested their blood glucose at least once daily. There were 21% of type 1 and 47% of type 2 patients who did not test their own blood glucose. Only 5% of type 2 (not on insulin) tested their blood glucose daily.

Diabetes, unlike many other diseases, is a self-management disease. Because nearly 95% of the required care falls upon the patient, satisfaction and comfort of the blood glucose monitoring method are pertinent issues in diabetes treatments. Low adherence to diabetes regimens is likely due to multifactorial causes. Rodin summarizes that one cause of low adherence rates occurs because the treatment for diabetes is
complex, intrusive, and inconvenient. Therefore, much focus in diabetes care has turned towards less painful and intrusive means of testing blood glucose.

Loveland\textsuperscript{8} reported a significant increase in satisfaction score from study participants who compared the traditional finger-stick method with the less painful thumb stick method. Carley\textsuperscript{9} also found a small decrease in pain felt by study participants who compared the thumb stick method of testing blood glucoses with a method using the ear lobe to test. While testing on the ear lobe may be less painful, for many patients this method is inconvenient and not practical.\textsuperscript{10} Fortunately, advances in technology have shown forearm glucose testing is an accurate and realistic alternative to finger-stick or even thumb-stick sites for glucose testing.\textsuperscript{11,12}

The FreeStyle\textsuperscript{TM} monitoring system requires a very small drop of blood, 0.3 mL, which allows testing from areas with much lower blood perfusion than the fingertips. Forearm, upper arm, hand, thigh, and calf are approved alternate sites for testing with the FreeStyle meter, and the paucity of pain receptors at these alternate sites allows glucose testing with reduced pain. Our study comparing the FreeStyle monitor to subjects’ current finger-stick monitor was designed to show that patients using alternative site meters may benefit from an increase in frequency of testing and improved HbA1c scores. We also aimed to show that, given a choice, most diabetic patients would prefer to use an alternative site meter as opposed to a traditional finger-stick meter.
Materials and Methods

Participants were recruited from the Utah Valley Diabetes Management Clinic where general guidelines for patient care include instructing patients to check blood glucose with a meter four times each day if insulin therapy is used and two times each day if insulin therapy is not used. Approximately 900 notification letters concerning the study were mailed out to patients who had at one time been a patient at the Utah Valley Diabetes Management Clinic. Requirements to be a study participant included a diagnosis of type 1 or type 2 diabetes mellitus, having a meter with a programmable memory, and being 18 years or older. All study participants used a finger-stick meter when not using the FreeStyle meter.

A cross-over study design was selected. Study participants were matched by (a) gender; (b) age; (c) duration of diabetes; and (d) use of insulin therapy or lack of and separated into two groups. Groups 1 and 2 of matched participants had initial HbA1c averages of 7.3 and 7.6, respectively. Those in group one were given the FreeStyle meter to use for three months; the second group was instructed to use their own personal meter. After 3 months of study, participants in group 1 placed their FreeStyle meter in a holding box at the clinic and were instructed to use their own personal meter. The second group was given the FreeStyle meter to use. The duration of the study totaled 6 months.

Participants in the study attended monthly classes at the clinic during which four different topics pertaining to nutrition and diabetes were discussed. The class sizes consisted of 2-15 study participants. During the class, participants’ meters were downloaded for the previous month’s readings, and participants received test strips to use
during the upcoming month. Those in the study on insulin therapy received 125 strips monthly; those in the study not using insulin therapy received 75 strips monthly. Participants were given the same number of strips throughout the study and were not rewarded or penalized for testing more or less frequently than the clinic’s recommendations. Meter downloading consisted of recording the number of times each study participant checked his or her blood glucose with the meter they were instructed to use during the previous month. The range of the readings and the monthly average and standard deviation were also recorded from the meter downloads. HbA1c measurements performed on a DCA 2000 Analyzer Model 5031C (Bayer Corporation, Elkhart, IN) were recorded for each study participant at the beginning of the study, after three months (the time when they switched meters), and at the conclusion of the study (after six months). At the conclusion of the study, participants were given a questionnaire to record their meter preference.

Orthogonal regressions were used for all of the correlation analyses conducted in this study. There are two assumptions that guide this choice of analysis. The first is that there is measurement error in both the x and y axes of the correlation. The second is that the magnitude of the error is approximately proportional to the magnitude of the measurement. An orthogonal regression is the proper statistical approach when the first situation exists, and the orthogonal regression can be manipulated to accommodate the second situation.
Results and Discussion

A total of 121 subjects (average initial HbA1c of 7.48%) began the study. By the crossover point, 17 subjects dropped out of the study (average initial HbA1c of 7.72%) leaving 104 subjects (average crossover HbA1c of 7.28%). Another 12 subjects did not participate in the final HbA1c test (average crossover HbA1c of 7.58%) which left 92 subjects (average crossover HbA1c of 7.24%) who completed the study. Of these subjects 62 were insulin users and 30 were non–insulin users; 62 used the arm exclusively as the test site when using FreeStyle; 16 used the arm and the finger, and 14 used the finger exclusively. Many subjects withdrew from the study because they moved away from the study location. The average age of those completing the study was 53.7 years, and the distribution of ages and insulin use is shown in Figure 1. A small subset of the population was younger than 40 years, but the large majority of the population was 40–80 years old.

FIGURE 1. Age distribution of study participants.
Some general trends were observed over the course of the study. Average values for HbA1c, glucose, and testing frequency for the insulin users and non-insulin users are listed in Table 1. The relationship between the HbA1c measurements and the average glucose is shown in Figure 2.

The expected relationship was exhibited: the HbA1c was directly proportional to the glucose measurement with a correlation coefficient of 0.68 for insulin users and 0.74 for non-insulin users. The subjects using insulin increased their testing frequency during the study, while the non-insulin using population did not (Table 1).

FIGURE 2. Correlation of HbA1c with mean glucose.
TABLE 1. Overall trends in testing parameters over the course of the study.

<table>
<thead>
<tr>
<th>Study time</th>
<th>HbA1c (%)</th>
<th>p value</th>
<th>Glucose (mg/dL)</th>
<th>Frequency (tests/day)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>7.7</td>
<td>0.108</td>
<td>150</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>7.6</td>
<td>&lt;0.0001</td>
<td>153</td>
<td>3.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>6 months</td>
<td>7.2</td>
<td>&lt;0.0001</td>
<td>154</td>
<td>2.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Noninsulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial</td>
<td>6.8</td>
<td>&lt;0.002</td>
<td>127</td>
<td>1.5</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>3 months</td>
<td>6.6</td>
<td>&lt;0.005</td>
<td>134</td>
<td>1.6</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>6 months</td>
<td>6.3</td>
<td>&lt;0.005</td>
<td>125</td>
<td>1.4</td>
<td>0.07</td>
</tr>
</tbody>
</table>

a We reject the null hypothesis of no significant difference in means, when the p value of the test is less than the significance level of $\alpha = 0.05$.

Of the 92 subjects responding to a questionnaire at the end of the study asking their meter preference, 76% preferred FreeStyle, 20% preferred their original meter, and 4% preferred both meters equally. The testing frequency with FreeStyle is plotted versus the testing frequency with the users' original finger-stick meter (during the study) in Figure 3.

FIGURE 3. The effect of meter type used on testing frequency.
On average, the difference in testing frequency between FreeStyle and the original meter was too small to be clinically relevant: 2.45 test/day with FreeStyle and 2.52 tests/day with the original meter. The meter preference had no influence on testing frequency. Apparently, providing a preferable monitor for glucose testing is not sufficient to increase testing frequency. The influence of using an alternate test site on clinical outcome was assessed by comparing HbA1c results for the 78 subjects who used the arm testing site for FreeStyle, either exclusively or part of the time. The change in HbA1c is shown for FreeStyle and the subjects' original meters in Figures 4 and 5.

![Graph](image)

**FIGURE 4.** Comparison of HbA1c after the FreeStyle meter was used to the HbA1c at the beginning of the study (time 0).
FIGURE 5. Comparison of HbA1c after the original meter was used to the HbA1c at the beginning of the study (time 0).

The average HbA1c was 6.93% when the FreeStyle was used on the arm test site and was 7.08% when the finger-stick meter was used. The difference is not statistically significant (p value = 0.093 versus a significance level of \( \alpha = 0.05 \)). In general, the choice of test site did not have an influence on the clinical outcome as measured by HbA1c. There were four cases where there was a substantial change in HbA1c over the course of the study as indicated by the numerals 1–4 on Figures 4 and 5. The study data for these subjects are listed in Table 2.
TABLE 2. Subjects who experienced a substantial change in HbA1c over the course of the study.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Study period (month)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HbA1c (%)</td>
<td>8.4</td>
<td>7.4</td>
<td>5.8</td>
<td>6.9</td>
<td>13.4</td>
<td>120</td>
<td>137</td>
</tr>
<tr>
<td></td>
<td>Average glucose (mg/dL)</td>
<td>No data</td>
<td>172</td>
<td>119</td>
<td>169</td>
<td>134</td>
<td>120</td>
<td>137</td>
</tr>
<tr>
<td></td>
<td>Frequency (tests/day)</td>
<td>No data</td>
<td>1.6</td>
<td>0.6</td>
<td>1.0</td>
<td>1.3</td>
<td>1.4</td>
<td>1.8</td>
</tr>
<tr>
<td>2</td>
<td>HbA1c (%)</td>
<td>11.2</td>
<td>10.0</td>
<td>6.6</td>
<td>10.9</td>
<td>12.6</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Average glucose (mg/dL)</td>
<td>No data</td>
<td>275</td>
<td>291</td>
<td>158</td>
<td>183</td>
<td>126</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>Frequency (tests/day)</td>
<td>No data</td>
<td>2.5</td>
<td>2.7</td>
<td>3.3</td>
<td>2.6</td>
<td>2.6</td>
<td>2.7</td>
</tr>
<tr>
<td>3</td>
<td>HbA1c (%)</td>
<td>12.2</td>
<td>11.8</td>
<td>9.2</td>
<td>16.1</td>
<td>208</td>
<td>208</td>
<td>161</td>
</tr>
<tr>
<td></td>
<td>Average glucose (mg/dL)</td>
<td>No data</td>
<td>269</td>
<td>312</td>
<td>no data</td>
<td>232</td>
<td>208</td>
<td>161</td>
</tr>
<tr>
<td></td>
<td>Frequency (tests/day)</td>
<td>No data</td>
<td>0.9</td>
<td>0.6</td>
<td>no data</td>
<td>0.1</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>4</td>
<td>HbA1c (%)</td>
<td>5.2</td>
<td>6</td>
<td>9.2</td>
<td>254</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Average glucose (mg/dL)</td>
<td>108</td>
<td>129</td>
<td>135</td>
<td>139</td>
<td>184</td>
<td>209</td>
<td>254</td>
</tr>
<tr>
<td></td>
<td>Frequency (tests/day)</td>
<td>1.9</td>
<td>0.5</td>
<td>2.1</td>
<td>2.2</td>
<td>1.9</td>
<td>1.9</td>
<td>1.8</td>
</tr>
</tbody>
</table>

The entries in bold type indicate results obtained with the FreeStyle system.

The average glucose for subject 1 decreased in the second half of the study while the subject used FreeStyle with an increased testing frequency. Subject 2 had a steady decrease in glucose average over the course of the study; the testing frequency with both meters remained constant. Subject 3 experienced a decrease in average glucose in the second half of the study, but the testing frequency during this period decreased substantially when the subject crossed over from using FreeStyle to using their original meter. Subject 4 experienced a substantial increase in glucose average in the second half of the study using their original meter with no significant change in the testing frequency. There is no consistent pattern of testing frequency or meter used that would explain the HbA1c changes for these four subjects.

In recent literature there has been discussions as to whether or not differences in glucose readings for off-finger tests would have a detrimental effect on glucose control.\textsuperscript{13,14} There was an average improvement in glucose control for subjects who used FreeStyle on the arm testing site as measured by the modest improvement in the HbA1c over the course of the study (7.29% to 6.93%). The meter used did not have an influence
on this result. The only case of a substantial increase in HbA1c occurred when the original finger test meter was in use (subject 4). There were no significant adverse events reported in the study when either arm testing or finger testing was used.

It was originally thought that less painful glucose testing would encourage an increase in testing frequency. Although 76% of the subjects preferred the FreeStyle system to the finger stick device they were accustomed to using, this did not translate into more frequent testing. The population of this study, however, might not have been ideal for testing this hypothesis. The degree of glycemic control for this population was quite good with 42% of the prestudy HbA1c tests of 7.0% or below, and 29% between 7.1 and 8.0%. This left only 30% of the population for which a change in therapy was necessary. Perhaps a more realistic approach to testing the hypothesis is to determine whether patients would be willing to undergo more aggressive treatment, which would require more frequent testing, if a less painful testing alternative were available.

Conclusion

A large majority of the subjects (76%) preferred the FreeStyle meter over the finger-stick meter they were using when the study began; 20% preferred their original finger-stick meter, and 4% preferred both meters equally. The preference for the FreeStyle meter did not lead to an increase in testing frequency with this meter. There was an average increase in testing frequency among insulin users for all meters, and there was also an average improvement in HbA1c tests among all participants. The change from a finger to an off-finger glucose test had no net effect on glycemic control as measured by HbA1c.


CHAPTER III

ALTERNATIVE-SITE BLOOD GLUCOSE MONITORS AND COST OF STRIPS:
THE EFFECTS ON METER PREFERENCE AND PAIN RATING, TESTING
FREQUENCY AND GLYCOXYLATED HEMOGLOBIN.

Abstract

A 6-month study providing free testing strips was used to compare testing
frequency and glycosylated hemoglobin of participants given an alternative-site meter.
Thirteen months later a final glycosylated hemoglobin measurement, testing frequency,
and a questionnaire regarding meter preference and pain rating were obtained. Seventy-
six percent of participants preferred the alternative-site meter, which was rated as
significantly (p < .05) less painful. Testing frequency significantly improved (p = .001)
while free strips were being provided. Testing frequency thirteen months later was not
significantly different from the baseline testing frequency (p = .101). Hemoglobin A1c
was significantly lower 6 months after the study began (p = .000) and 13 months later (p
= .008) than the baseline hemoglobin A1c. We conclude that: 1) patients in our study
preferred the alternative-site meter; 2) patients in our study experienced a positive effect
in hemoglobin A1c measurements; and 3) cost of strips does play a role in testing
frequency.
Introduction

Diabetes Mellitus, a disease with many long-term debilitating effects, is expected to increase in incidence in the United States. Because diabetes is a growing epidemic, treatment of the disease will have an ever-increasing impact on Americans.

The Diabetes Control and Complications Trial proved a direct relationship between glycosylated hemoglobin measurements (HbA1c) in diabetic patients and the development of diabetic complications. Reduction in HbA1c, and thus the complications of diabetes, is dependent on the management of medical nutritional therapy, routine exercise and medications.

The goal of diabetes management is to achieve normoglycemia. Self-monitoring of blood glucose (SMBG) is considered to be an essential step in maintaining normoglycemia. Karter reaffirmed the importance of SMBG. Using a cohort study design, Karter showed that SMBG in type 1 diabetics at a frequency greater than or equal to 3 times per day and daily for type 2 diabetics was significantly associated with lower HbA1c levels. These findings support the clinical recommendations suggested by the American Diabetes Association. The majority of diabetics, both type 1 and type 2, do not test blood glucose daily. A follow-up study, associating the frequency of SMBG with HbA1c, conducted by Anderson found that increasing the frequency of self-monitoring of blood glucose was followed by a decrease in HbA1c levels. Identifying factors that motivate or increase SMBG are, consequently, important steps reducing the morbidity and mortality related to diabetes.
There are many impeding factors responsible for the insufficient frequency of blood glucose monitoring. These inhibitors include emotional, physical, social, and environmental. Jones\textsuperscript{6} concluded that people with diabetes who listed the fewest barriers to self-monitoring of blood glucose are more likely to check blood glucoses. However, determining the extent each barrier plays is yet to be outlined. Psychological and social factors relating to SMBG have been studied.\textsuperscript{7} Other factors that may have influence on testing frequency and HbA1c include the monitoring device and pain associated with monitoring as well as the expense of blood glucose monitoring.

Traditional finger-stick blood glucose monitoring systems do cause some pain and finger soreness. Recent advances in technology have produced alternative-site blood glucose monitoring systems that use less blood and allow for blood samples to be obtained from sites less painful than finger sticks. Increased satisfaction has been reported with a decrease in pain when a site with fewer nerve endings than the fingertips was used for SMBG.\textsuperscript{8}

The financial barriers that face those with diabetes are large. Medications and blood glucose testing strips add to the expense of the disease, especially to those without insurance coverage. Because blood glucose testing requires the patient to use strips, purchasing strips may influence the patient to test less frequently, avoiding higher economic expenditure on testing strips.

The purpose of this study was to determine: 1) if pain and meter satisfaction play a role in the frequency of SMBG; 2) if providing a less-painful monitoring system would decrease HbA1c; and 3) if the cost of testing strips had an effect on SMBG.
Methods and Statistics

A cross-over study design was chosen for the initial study using patients from Utah Valley Diabetes Management Clinic. Those who participated in the study were recruited via a notification letter sent to all patients of the Utah Valley Diabetes Management Clinic. Study participants were limited to patients 18 years of age or older with a diagnosis of type 1 or type 2 diabetes mellitus and trained to use a program-able blood glucose meter capable of being downloaded in the clinic.

The cross-over design consisted of two matched groups. Study participants were matched by gender, age, duration of diabetes, and use of insulin therapy. Although the two groups were not matched by initial HbA1c levels, the initial HbA1c levels were 7.3% for group one and 7.6% for group two. Group one began the study using the FreeStyle alternative-site meter. Group two began the study using their own finger-stick meter. After three months, study participants in group one placed their FreeStyle meter in a holding box at the clinic and were instructed to use their own personal meter while the second group was given the FreeStyle meter to use. The duration of the study totaled 6 months. Thirteen months after the initial study began and 7 months after the study ended, all subjects that completed the study were asked to participate in a follow-up study visit.

The Therasense FreeStyle meter was used as the alternative-site meter in the study. This meter requires a very small drop of blood (0.3 μl) which allows testing from areas with much lower blood perfusion than the fingertips. Forearm, upper arm, hand, thigh, and calf are FDA approved alternate sites for testing with the FreeStyle meter.
While using the FreeStyle meter, patients were instructed to try using a site other than their fingers, but were not excluded from using their fingers.

Throughout the six-month study, participants met monthly in groups ranging from 2 to 15 participants. Four of the monthly meetings consisted of a 30 minute nutritional education session. Topics included reducing LDL cholesterol through dietary practices, dining at restaurants on a diabetic diet, non-nutritive sweeteners, and estimating portions sizes correctly. The other monthly meetings were dedicated to teaching the use of the alternative-site meter or to collecting the study data (height, weight, downloading meters and providing a copy of the results to the patient). At each monthly meeting, participants were given 75 test strips if they were not using insulin therapy and 125 test strips if insulin therapy was used. Patients were not penalized if they did not use all of the strips given at the previous month’s meeting. Test strips were specific to the meter the patient was using during the upcoming month. The patients incurred no cost for test strips.

During each monthly meeting, participants’ meter readings were downloaded and the number of blood glucose tests for the previous thirty days was recorded. HbA1c measurements were recorded for each study participant at the beginning of the study and at the conclusion of the study (after 6 months).

The third objective of this study (the cost effect of strips for SMBG on testing frequency) was assessed by re-contacting the original study participants for a follow-up HbA1c and to answer a questionnaire regarding meter preference. Participants were asked, through a formal questionnaire, to rate the pain they felt using the alternative-site meter and their original meter on a scale of 1 to 10 (1 being the least pain and 10 being the highest pain). Participants were also asked to list their meter of preference. A paired
A total of 121 participants began the initial study, with 92 participants still enrolled at the 6th month mark. Fifty-nine participants returned for the follow-up questionnaire and HbA1c at the 13th month follow-up. Of those study participants who returned for the follow-up study, 57% were male. Seventy-six percent of those returning after the sixth-month study were using insulin therapy to treat their diabetes mellitus. The participants ranged in age from 21 years to 78 years old. The alternative-site meter was preferred by 74% of the participants who answered the questionnaire. Pain scores were significantly ($p < .05$) less for the alternative-site meter compared to the original finger-stick meter. The standard deviation was 2.5.

Using a repeated measures ANOVA, we compared the SMBG monthly tests for participants at the beginning of the study, 6 months later, and at the 13th month time frame. The frequency of monthly testing significantly ($p = .001$) increased after 6 months. However, there was a decrease in frequency of testing between the 6th month testing frequency and the 13th month testing frequency ($p = .128$) although not significant. The SMBG testing frequency, although lower, was not significantly
different from the SMBG testing frequency at the pre-study stage (p = .101). The 6\textsuperscript{th} month and the 13\textsuperscript{th} month HbA1c scores were both significantly different from the pre-study, initial HbA1c scores (p < .000 and p = .008 respectively). The score for HbA1c from the 6\textsuperscript{th} and the 13\textsuperscript{th} month marks were not significantly different (p = .347). Participants gave the alternative-site meter an average pain rating of 2.5, significantly (p < .05) less than the pain rating of 3.5 for their original meter.

Pre-study checks per month averaged 59.83. After the six-month study, the checks per month averaged 72.17. Thirteen months later testing frequency decreased to an average of 66.5 checks per month. A significant increase occurred for the frequency of testing during the initial six-month study. The testing frequency thirteen months after the study began was not significantly different from the pre-study testing frequency (Table 3).

**TABLE 3. Repeated measures ANOVA for testing frequency.**

<table>
<thead>
<tr>
<th>Comparison of Monthly SMBG</th>
<th>Significance (p)</th>
<th>Mean for Monthly SMBG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Study SMBG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6\textsuperscript{th} Month SMBG</td>
<td>.001</td>
<td>Pre-Study Mean: 59.83 ± 5.48</td>
</tr>
<tr>
<td>13\textsuperscript{th} Month SMBG</td>
<td>.101</td>
<td></td>
</tr>
<tr>
<td>6\textsuperscript{th} Month SMBG</td>
<td>.001</td>
<td>6\textsuperscript{th} Month Mean: 72.17 ± 5.65</td>
</tr>
<tr>
<td>13\textsuperscript{th} Month SMBG</td>
<td>.128</td>
<td></td>
</tr>
</tbody>
</table>

* Degrees of Freedom 2; Mean Square 1793.794; Sum of Squares 3587.589
Initial HbA1c scores averaged 7.5%. After the six-month study HbA1c scores averaged 7.0%. The follow-up study HbA1c scores (one year after the initial study began) averaged 7.1%. Comparing HbA1c scores at the 6th month point with the baseline or beginning HbA1c scores and comparing the final (13th month) HbA1c scores with the baseline HbA1c scores, we found HbA1c scores following the study and one year later were both significantly lower than the initial HbA1c score. There was a slight, but not significant, increase in HbA1c scores from the 6th month mark to the 13th month mark (Table 4).

### TABLE 4. Repeated measures ANOVA for HbA1c.

<table>
<thead>
<tr>
<th>Comparison of HbA1c Scores</th>
<th>Significance (p)</th>
<th>Mean for HbA1c Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Study HbA1c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6th Month HbA1c</td>
<td>.000</td>
<td>Pre-Study Mean: 7.469 ± .171</td>
</tr>
<tr>
<td>13th Month HbA1c</td>
<td>.008</td>
<td></td>
</tr>
<tr>
<td>6th Month HbA1c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-Study HbA1c</td>
<td>.000</td>
<td>6th Month Mean: 6.986 ± .135</td>
</tr>
<tr>
<td>13th Month HbA1c</td>
<td>.347</td>
<td></td>
</tr>
<tr>
<td>13th Month HbA1c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-Study HbA1c</td>
<td>.008</td>
<td>13th Month Mean: 7.085 ± .143</td>
</tr>
<tr>
<td>6th Month HbA1c</td>
<td>.347</td>
<td></td>
</tr>
</tbody>
</table>

* Degrees of Freedom 2; Mean Square 3.845; Sum of Squares 7.690

Of the participants who completed the study, 22 had a HbA1c greater than or equal to 8.0. Fourteen of those preferred the FreeStyle. Using a t-test to compare the HbA1c at the conclusion of the six-month study for those with the higher HbA1c of greater than 8 (those with higher average blood glucose readings), to the final HbA1c 13
months after the study began, there was no significant difference between HbA1c scores ($p = .694$). The standard deviation was 0.78.

Discussion

During the initial six-month study participants were given free testing strips for the meter they were using. The decrease in testing frequency in the follow-up study as compared to the initial study was likely due in part to the absence of free testing strips. The decrease in HbA1c through the initial study was expected secondary to the increase in testing frequency as per study. Likewise the slight, but insignificant increase in HbA1c between the 6th month score and 13 months later was expected with the decrease in testing frequency. The HbA1c scores 13 months after the study remained significantly lower than the baseline HbA1c scores. There was no difference in HbA1c between the 6th month measurement and the 13th month measurement for study subjects who had high HbA1c measurements greater than 8.0% indicating that there was a consistent higher average blood glucose level in these individuals.

A high drop-out rate occurred because the study spanned a total of 13 months. Many participants could not be located for the questionnaire and final HbA1c. Therefore, this data cannot be generalized for all diabetic patients.

Conclusion

Seventy-four percent of the participants who completed our study preferred the alternative-site meter. The alternative-site meter was also rated as significantly less painful. For these study participants, HbA1c and testing frequency both significantly
improved from the baseline measurement to the end of the study. The decrease in
testing frequency 13 months after enrolling in the study may be attributed to the lack of
free strips and monthly contact with health-care providers. Trento has shown the benefit
of improved glucose control for patients with frequent contact with health-care providers.
Even though this decrease in testing frequency was significantly lower than the testing
frequency at the end of the initial study, the change in HbA1c was not significantly
different seven months later in the follow-up study. These results indicate that this study
had positive and lasting effects on HbA1c.

We conclude that: 1) patients in our study preferred the alternative site meter; 2)
participation in this study had a positive effect on HbA1c; and 3) the cost of SMBG strips
may play a role in frequency of testing.

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CHAPTER IV
GENERAL CONCLUSION

At the conclusion of the 6-month crossover study, 76% of the study participants preferred the alternative-site meter. While both insulin and non-insulin users had increased testing frequency 3 months after the study began, this increase in testing frequency was maintained only by the insulin users after 6 months.

Although the alternative-site meter was definitely the preferred meter, testing frequency was not significantly different between the alternative-site meter and the traditional finger-stick meter over the initial six-month period. HbA1c measurements correlated well (correlation coefficient of 0.68 for insulin users and 0.74 for non-insulin users) with the average blood glucose obtained from the glucose meters. Glycosylated hemoglobin was not significantly different between the two meter types.

At the 13-month follow-up period, a questionnaire was given to the 59 study participants. Similar to the preference rating for the alternative-site meter 6 months after the study began, 74% of the participants rated the alternative-site meter as the meter they favored. Pain scores were rated as significantly lower for the alternative-site meter as opposed to participants' traditional meters.

These 59 participants experienced a significant increase in testing frequency at the 6-month mark over the baseline testing frequency. By the 13-month mark, testing frequency was not significantly different from the baseline testing frequency. HbA1c measurement was significantly lower at the 6-month mark as compared with baseline and remained significantly lower 13 months later from the baseline.
It is apparent that the alternative-site meter is the meter of preference for most people with diabetes. This preference is long-term and likely due to decreased pain associated with the alternative-site meter. Despite being a meter of preference and reduced pain, the alternative-site did not significantly affect testing frequency or HbA1c. In essence, reduced pain and increased meter satisfaction is not enough to increase testing frequency or decrease HbA1c.

For those who completed the 13-month mark of the study, it was noted that providing free blood glucose monitoring strips significantly increased testing frequency. This effect declined when free strips were no longer supplied. The positive effect on HbA1c seen with the increase in testing frequency after 6 months of free strips and education was lasting.

We conclude that providing an alternative-site meter improved patient satisfaction and decreased the pain of self-monitoring blood glucose, but did not affect testing frequency or HbA1c. These results were obtained in a population with relatively good blood glucose control (42 participant HbA1c measurements were less than 7% and 70 participant HbA1c measurements were less than 8%) and may not reflect what would influence those with less well-controlled diabetes mellitus. Providing free blood glucose monitoring strips significantly increased testing frequency only while the strips were provided. Therefore, provision of free blood glucose monitoring strips is a factor in increasing blood glucose monitoring for certain patients.
Appendix A

Questionnaire

Name______________________ Date_________ HbA1c_______

Meter you are currently using__________________________

Meter you used before the study began____________________

If you are not currently using the Therasense FreeStyle meter state the reason for using
the meter you currently use.

Is there a difference between the meter you are using and the Therasense FreeStyle meter
in any of these areas? If so, please circle and explain.

A) Insurance co-pay for strips
B) Convenience or ease in testing
C) Familiarity
D) Accuracy
E) Features of the meter

Please rate the pain level of testing with the Therasense FreeStyle meter.
(1 = no pain, 10 = painful).
1 2 3 4 5 6 7 8 9 10

Please rate the pain level of testing with the meter you are currently using if you are not
using the Therasense FreeStyle meter. (1 = no pain, 10 = painful).
1 2 3 4 5 6 7 8 9 10

While using the FreeStyle meter, did you feel the meter readings were different from
what you expected. If yes, please describe.

If you could change or improve on the Therasense Freestyle meter, what changes
would you recommend. Please list.
Appendix B

Permission Letter from Diabetes Technology and Therapeutics
September 16, 2003

Nancy Bennion
3955 W Old Hwy Rd
Morgan, UT 84050
(801) 588-3436
slhzf@cc.usu.edu

To Permissions Editor:

I am in the process of preparing my thesis in the Food and Nutrition Sciences department at Utah State University. I hope to complete my degree in the Fall of 2003.


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Please indicate your approval of this request by signing in the space provided, and attach any other form necessary to confirm permission. If you have any questions, please call me at the number above.

Thank you for your assistance,

Nancy Bennion

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Signed

Date September 24, 2003

Best wishes for success with your thesis, and continued good luck with all your future endeavors.

Esther
Appendix C

Permission Letter from Coauthor
Dear Geoff McGarraugh:

I am in the process of preparing my thesis in the Food and Nutrition Sciences department at Utah State University. I hope to complete my degree in the Fall of 2003.

I am requesting your permission to include the attached material as shown. I will include acknowledgments and/or appropriate citations to your work as shown and copyright and reprint rights information in a special appendix. The bibliographical citation will appear at the end of the manuscript as shown. Please advise me of any changes you require.

Please indicate your approval of this request by signing in the space provided, attaching any other form or instruction necessary to confirm permission. If you have any questions, please call me at the number above.

I hope you will be able to reply immediately.

Thank you for your cooperation,

Nancy Bennion

I hereby give permission to Nancy Bennion to reprint the following material in her thesis.


Signed: [signature]