CHAPTER 5

DISCUSSION, SUMMARY AND RECOMMENDATION

5.1 Dicussion

According to the position statement of the American Diabetes Association, self-monitoring of blood glucose (SMBG) is considered an important component of diabetes care and is recommended for all insulin-treated patients. It is also considered desirable in patients treated with sulfonylureas and in all subjects not achieving glycemic goals. Nevertheless, its role and optimal frequency in type 2 diabetes is still matter of debate, and it has been underlined that its indiscriminate use can cause a waste of resources and psychological harm.

The broad issue being addressed is the optimal timing of home glucose monitoring. Should pre-prandial and post-prandial glucose be considered besides the conventional fasting state?

The purpose of glucose testing is to allow patients with diabetes to achieve optimal glycemic control while avoiding hypoglycemia. As many patients with diabetes tend to have relatively high fasting glucose levels in the morning, a phenomenon referred to as the "dawn phenomenon,"[126] restricting glucose measurements to this time decreases the likelihood of detecting low glucose levels, which typically occur in the late afternoon and, more dangerously, during the night. Furthermore, hypoglycemia may occur at different times in different patients. Thus, a strategy of testing glucose at various times during the day is more likely to detect low glucose levels and hence decrease the likelihood of hypoglycemia.

Many glucose-lowering agents, such as metformin, the thiazolidinediones, perhaps the sulfonylurea, and the intermediate- and long-acting insulin given at night, show their greatest effect in the fasting period. Monitoring only fasting glucose levels might lead to the mistaken belief that glycemia is under control, while in actuality there is suboptimal glucose control during the day requiring additional efforts at treatment. Both

nocturnal hypoglycemia and fasting hyperglycemia are commonly found in patients with type 1 diabetes,[27] and have been frequently documented with new continuous interstitial glucose-monitoring devices.[128]

There is no convincing evidence that glycemic control is consistently influenced by self monitoring of blood glucose. Recent studies have suggested that self monitoring of blood glucose may be a waste of time for many patients receiving diabetic pills or insulin.[88] Studies comparing patients with insulin-dependent diabetes who performed home monitoring with those who did not have shown no differences in glycemic control.[26] Even less evidence links monitoring with improved glycemic control in non-insulin-dependent diabetes.

Although the glycemic control was improved by SMBG in most of the subjects, some subjects did not have this benefit. The inappropriate use of self monitoring of glucose is wasteful of national health resources and can cause psychological harm. Some people may find that self monitoring enables them to understand and take control of their diabetes, many people with diabetes are performing inaccurate or unnecessary tests. There is also no evidence that self monitoring blood testing is better than urine testing.[91,95,97] It may be appropriate for some patients not to monitor their own glucose but to rely instead on regular laboratory estimations of glycemic control. Glucose self monitoring should be performed only when it serves an identified purpose.

This study evaluated a 16-week period of prospectively collected blood glucose meter readings from a population of stable insulin-treated type 2 diabetes patients, comprised mostly of middle-age women with fair glycemic control. All subjects never performed self-monitoring of blood glucose before. There was no difference in glycemic control between pre- and post-prandial monitoring strategies at the end of 8th week in this study. The HbA1c levels were equally reduced by approximately 0.5% from baseline in both groups. There was also no difference in lipid profiles. The pre-prandial strategy appeared to detect more episodes of hypoglycemic readings, whereas the post-prandial strategy appeared to detect more episodes of hyperglycemic readings.

The insulin dosage of the post-prandial group is increased approximately10% more than the pre-prandial group, resulting in a more increasing in body weight.

The negative result of this study that showed no difference between two strategies could be from many possible reasons; 1) the sample size, 2) the duration of study, 3) the treatment algorithm, 4) the subjects' profiles.

The predetermined sample size of this study was calculated by the assumption that at least 0.4% difference of absolute HbA1c level will be observed by the end of study period, and the pool variance of HbA1c would be less than 0.5. In fact, both groups had equal reduction of HbA1c from baseline by approximately 0.5% of absolute HbA1c values. The pool variance of HbA1c of both groups was 1.4, which is much greater than expected. Substitution of the variance of 1.4 to the formula, the sample size for the study increases to 115 per groups. So, it is possible that the negative result of this study could be from an inadequate sample size.

The duration of study since randomization was 8 weeks. In fact, subjects from both groups received the intervention for 10-12 weeks, since SMBG was introduced 2-4 weeks before randomization. The 2-4 weeks run in period was desired for the insulin dosage adjustment and SMBG training. During this training period both pre- and post-prandial monitoring were performed which could affected the subjects' glycemic control. However, both fructosamine which represented a retrospective glycemic control of 2-3 weeks and HbA1c which represented a retrospective of 10-12 weeks were not different. Longer duration of study may be needed to see the differences of two strategies.

Glycemic control at the end of study may not be the sole effect of pre- and post-prandial blood glucose monitoring. The result of blood monitoring was linked to the insulin dose adjustment algorithm. For the pre-prandial strategy, insulin dose adjustment was set to increase or decrease the premixed insulin before the meal. The post-prandial strategy, insulin dose adjustment was set to add rapid acting insulin after the meal. Both insulin algorithms were different and probably incomparable. Post-prandial strategy had a tendency to detect post meal hyperglycemia and required more

insulin than the pre-prandial strategy. The insulin adjustment algorithm was arbitrary set to control the pre-prandial glucose blood level of 100-180 mg/dl and post-prandial blood glucose level of 140-200 mg/dl. Currently, there is no evidence based and no consensus concerning the optimum level of pre- and post-prandial blood glucose.

The subjects recruited in this study were middle age female with fair glycemic control (mean HbA1c was 8.2-8.4%). A lesser degree of HbA1c reduction could be expected compared to the poorer diabetic control group. As shown in DCCT and UKPDS the treatment effects resulted in a reduction of 1-2% of HbA1c by the first year. The higher value of HbA1c, the more reduction was observed.

Finally, the care provided by frequent telephone for ensuring of compliance might affect subjects' life style. This intensive intervention may contribute to the improving of glycemic control besides SMBG in both groups.

Hypoglycemic and hyperglycemic readings were commonly recorded in this study. Interestingly most of these out-of-range readings were asymptomatic. The high proportion of hypoglycemic readings occurred during prelunch, and predinner time and the high proportion of hyperglycemic readings occurred at postbreakfast, and postdinner. Each of the pre- and post-prandial testing strategies captured different proportions of these out-of-range readings. The combinations of testing prebreakfast /prelunch and prelunch/predinner captured the highest yield of hypoglycemic readings. The combinations of testing postbreakfast/postdinner captured the highest yield of hyperglycemic readings.

There was only few literatures looking at the yield of combining multiple testing times to detect hypoglycemic or hyperglycemic readings. Findings from this study suggest that twice-daily testing strategies with fasting time combined with one of pre- and post-meal samplings can capture a substantial proportion of hypo- and hyper-glycemic readings, and present a reasonable alternative to four-times daily testing which is recommended for type 1 diabetes. Random pre- and post-meal strategies is probably an optimal strategy for capturing both hypoglycemic and hyperglycemic readings.

However, testing strategies will be based on the individual's risk for hypoglycemia or hyperglycemia.

The mean blood glucose results from the four daily conventional testing times, fasting (prebreakfast), prelunch, predinner, and prebedtime, as well as three postmeal times, were each significantly correlated with HbA_{1c} measured at the end of the 8-week and 16-week monitoring period. The correlation coefficients between HbA_{1c} and the means of the four once-daily testing strategies ranged from 0.65 to 0.72 (all statistically significant). Combination of fasting and one pre-meal or fasting and one post-meal testing resulted a better correlation (r = 0.79, 0.78) with HbA1c value.

The readings obtained from once daily or twice daily pre- and post-prandial testings were almost as highly correlated with HbA_{1c} as readings obtained from four-times or more daily testing. For patients performing once-daily testing, a rotating strategy (alternating testing times on successive days) could explain more of the variance in HbA_{1c} than any of the fixed once-daily testing strategies. The rotating once-daily testing strategy also captured nearly one-third of the out-of-range readings, suggesting that patients testing once daily should obtain readings from different times of day. The twice-daily testing strategies explained a significant amount of the variance in HbA_{1c} and captured a substantial proportion of hypoglycemic and hyperglycemic readings. Measuring fasting/predinner readings appeared to be the best overall twice-daily testing strategy because the correlation with HbA_{1c} was high (r = 0.79) and these measurements captured the statistically highest yield of hypoglycemic and combined out-of-range readings. By rotating the timing of the twice-daily strategies, we explained more of the variance in HbA_{1c} than any of the fixed twice-daily strategies, but the yield in capturing out-of-range readings decreased by ~ 10%. However, the rotating strategies, particularly alternating prelunch/predinner with prebreakfast/bedtime readings, are intuitively appealing because medication adjustments can target glucose readings at different times of day.

The relationship between HbA_{1c} value and self-monitoring frequency was investigated in a study in England of 290 type 2 diabetic patients treated with insulin; no association was found. A study in Missouri of 61 type 2 diabetic patients who self-monitored found no difference in mean GHb values based on the frequency of testing. Among 115 patients treated with oral agents at a Veterans Administration Medical Center in Arizona, glucose control was independent of the number of blood glucose test strips dispensed. Some reports have questioned the efficacy of self-monitoring in patients with type 2 diabetes. In contrast, the importance of self-monitoring in patients with type 1 diabetes is more certain, and an increased frequency of self-monitoring is generally associated with decreased HbA_{1c} values for these patients. The dissociation between fasting and daytime glycemia appears to explain the failure of conventionally treated type 2 patients in the United Kingdom Prospective Diabetes Study (UKPDS).

Self-monitoring is considered to be a tool to guide patient and physician action with respect to changes in diet, physical activity, and use of antihyperglycemic medication. Both patient and physician action are needed to change diabetes management when hyperglycemia is evident. Patients with differing levels of insulin resistance and ß-cell reserve may respond differently to self-monitoring and changes in diabetes control regimens. In this study, the improving glycemic control of the subjects could be explained by changing of their life-style such as diet and activities in addition to the changing of insulin therapy. The true impact of self-monitoring could be assessed in a randomized clinical trial with pre-established guidelines for how glucose monitoring results would be used to facilitate achievement of glycemic target.

There were some limitations to this study to be considered. Subjects were predominantly middle–age female with type 2 diabetes, and all were using premixed insulin twice daily. Results may not be applicable in other populations, especially for patients treated with diet alone or oral hypoglycemic agents or other insulin regimens. The postmeal glucose excursions captured by postprandial readings are hypothesized to better explain glycemic control, and results from these testing times may be better correlated with HbA_{1c} in some reports. In this study, there is no difference in glycemic

control between pre- and post-prandial monitoring strategies. Since many of hypoglycemic readings were asymptomatic. This study design, however, was consistent with the ADA objective of using SMBG to detect asymptomatic hypoglycemia. Medications can be adjusted based on the timing and frequency of these hypoglycemic readings, potentially preventing symptomatic episodes. Without these monitoring data, we may have under estimated their occurrence.

The results of this study may have implications for glucose-monitoring strategies. Although the ADA recommends blood glucose meter testing frequently enough to assess glycemic control and reduce the risk of hypoglycemic events, testing compliance is often poor. The majority of subjects in the Chulalongkorn Diabetic Clinic are testing less than once daily. When testing infrequently, patients often obtain only morning fasting readings. Although these values can be correlated with glycemic control, combinations of fasting with pre-and post-meal readings were much better correlated with HbA_{1c}.

Some experts recommended that the frequency of monitoring should depend on the patient's current glycemic control. Most people with type 1 diabetes should test four or more times a day to obtain information needed to maintain near-normal levels of blood glucose. For patients with type 2 diabetes, monitoring can be less intensive if insulin is not part of their medical regimen and if HbA_{1c} values are less than 7%. If HbA_{1c} is higher than 7%, monitoring of pre-prandial and post-prandial blood glucose levels is necessary to determine the best treatment regimen. Regardless of the therapy, frequent monitoring is one of the keys to optimal glucose control. The goals for glycemic control, adapted from the recommendations of the American Diabetes Association. A lesser frequency of SMBG may suffice if the patient is still able to secrete substantial amounts of insulin (e.g., recent onset of type 1 DM and most cases of type 2 DM). In these patients glycemic goals often can be met. SMBG may be used in these patients to assess temporal patterns so that the morning or evening doses of insulin and/or oral agents can be appropriately increased or decreased. Once therapy is optimized and

glycemic control has stabilized, the frequency of monitoring often can be decreased substantially, particularly in people with type 2 diabetes.

Even when patients perform regular blood or urine tests and religiously record the results in their home monitoring diaries, we may not rely on the accuracy of these measurements. Despite appropriate training, almost half of patients testing their blood may obtain inaccurate results through poor technique[114] and, although portable blood glucose meters have become much simpler to use, most of them are not yet foolproof.

As well as technical inaccuracies, deliberate falsification of results is common across all age groups and social classes. By asking patients to use blood glucose meters with a hidden memory, researchers showed that the results recorded in home monitoring diaries were often lower than the actual readings. Patients frequently omitted to record high readings and made up extra results so that it appeared that they had tested more frequently than they had in reality.[135] Many patients abandon self monitoring tests if their purpose is not clear.[137] Home glucose monitoring should be performed only if it serves an identified purpose that is clear to both the patient and the nurse or doctor.

Most people with diabetes feel guilty that they do not test often enough.[108] This can be avoided if an individual home monitoring plan is agreed. This should include the method, timing, and frequency of tests and a review date. Regular reviews of the plan will prevent unnecessary testing after the need for tests has passed and will also lessen the guilt experienced by patients who fail to comply with the testing regimen recommended by their nurse or doctor. The patient should be able to perform the test accurately, according to the manufacturer's instructions, and must know what results to expect and what action to take if the results are outside the desired range. The method of monitoring should depend on the purpose of monitoring and the patient's manual dexterity, visual and cognitive ability, and personal preference.

5.2 Summary

- Self monitoring of blood glucose can improve glycemic control in insulin treated type 2 diabetic subjects.
- No difference between pre- and post-prandial monitoring in term of glycemic control and lipid profiles.
- Pre-prandial monitoring is better than post-prandial monitoring in term of detecting hypoglycemic readings and convenience for insulin dosage adjustment.
- Post-prandial monitoring is better than pre-prandial monitoring in term of detecting hyperglycemic readings, which encourage the changing of their life-style such as diet and activities
- The readings obtained from once daily or twice daily pre- and post-prandial testing were almost as highly correlated with HbA_{1c} as readings obtained from four-times or more daily testing.
- The results of this study support the hypothesis that both pre- and post-prandial glucose monitoring, in combination with fasting blood glucose measurements, can significantly improve the glycemic control is type 2 diabetes subjects who require insulin therapy.

5.3 Recommendation

Self monitoring of blood glucose enables patients treated with insulin to take control of their diabetes, allowing them to adjust their insulin dosage or diet in the light of their results, especially in relation to exercise, illness, or dietary changes. For these people, the ability to take an instant measurement of blood glucose and act on the result is helpful. It justifies both the inconvenience of carrying around the testing equipment and the discomfort of the test itself.

Frequent monitoring is one of the keys to optimal glucose control. A lesser frequency of SMBG may suffice if the patient is still able to secrete substantial amounts of insulin (e.g., most cases of type 2 DM within 5-years duration). In these patients glycemic goals often can be met using less complex insulin regimens. SMBG may be used in these patients to assess temporal patterns (i.e. does glucose concentration rise/fall during the day vs. during the night) so that the morning or evening doses of

insulin can be appropriately increased or decreased. Once therapy is optimized and glycemic control has stabilized, the frequency of monitoring can be decreased substantially. If the patient's social situation, medical condition, or motivation would discourage or preclude efforts at achieving near-normoglycemia, then the frequency of SMBG should be utilized in relation to the patient's willingness or ability to obtain the needed information.

Because the accuracy of SMBG is instrument- and user-dependent[59], it is important for health care providers to evaluate each patient's monitoring technique, both initially and at regular intervals thereafter. In addition, optimal use of SMBG requires proper interpretation of the data. Patients should be taught how to use the data to adjust food intake, exercise, or pharmacological therapy to achieve specific glycemic goals. Health professionals should evaluate at regular intervals the patient's ability to use SMBG data to guide treatment.