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A Comparative Study of Two Glycemic Control Methods (SMBG vs. CGM) in Children and Adolescents Aged from 4 to 18 Years with Type 1 Diabetes

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Abstract

Background: Considering the prevalence of diabetes in children and also the effect of good control of blood sugar and hemoglobin A1C (as a long indicator of glucose control) on reducing the complications of diabetes, this study was done to compare two glycemic control methods in children and adolescents with T1DM.

Method: The CGM device was connected to the patients once every three months for 4 to 7 days and the number of hypoglycemic events per month and their average HbA1C and average daily dosage of insulin were collected before and after installing the CGM device. Statistical tests were performed in SPSS software.

Result: The results showed that the use of CGM leads to more decrease in the number of hypoglycemic cases, in comparison to SMBG. The percentage change in the number of hypoglycemic cases was not statistically significant with any of the factors of the patient's age, gender and duration of diabetes. In addition, the results showed that the use of CGM leads to a greater decrease in HbA1C levels, when compared to the SMBG.

Conclusion: The mentioned decrease, not related to age, sex, and duration of diabetes, might be due to the increase in patients' insight into their disease and how to control their level of blood sugar; and on the other hand due to increase in the doctor's insight into the patient's abilities in self-monitoring blood sugar but CGM did not reduce the patients' daily insulin dosage.

Key Words: Continuous Glucose Monitoring (CGM), Glycemic Control, Glycosylated HemoglobinA (HbA1C), Self-Monitoring of Blood Glucose (SMBG), Type 1 Diabetes Mellitus (T1DM).

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1- INTRODUCTION

Diabetes mellitus (DM) is the most important health problem worldwide (1) and is a common, chronic, metabolic disease characterized by hyperglycemia as a cardinal biochemical feature. The major forms of diabetes are differentiated by insulin deficiency vs. insulin resistance: type 1 diabetes mellitus (T1DM) results from deficiency of insulin secretion because of pancreatic β-cell damage; type 2 diabetes mellitus (T2DM) is a consequence of insulin resistance occurring at the level of skeletal muscle, liver, and adipose tissue, with various degrees of β-cell impairment (2). T1DM is the most common endocrine-metabolic disorder of childhood and adolescence, with important consequences for physical and emotional development. Individuals with T1DM confront serious lifestyle alterations, including an absolute daily requirement for exogenous insulin, the need to monitor their own glucose level, and the need to pay attention to dietary intake (3). Morbidity and mortality stem from a constant potential for acute metabolic derangements and from long-term complications. Potential acute complications include the development of hypoglycemia related to insulin excess or hyperglycemic ketoacidosis from insulin deficiency. Long-term complications typically manifest in adulthood and are related to the adverse effects of chronic hyperglycemia and associated metabolic abnormalities on tissues and organ systems. This can result in microvascular diseases such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as ischemic heart disease and arterial obstruction with gangrene of the extremities (4, 5). The prevalence of type 1 diabetes in children is about 2 per 1000 (6). One of the programs that have recently been considered by researchers is the diabetes self-management program. Self-management is an active and practical process that is led by the patient and includes specific activities in order to achieve the goals of disease management (7). The goal of diabetes self-management in children and adolescents is to control blood sugar, prevent Potential acute complications including the development of hypoglycemia related to insulin excess or hyperglycemic ketoacidosis from insulin deficiency, and to increase the quality of life of diabetic patients. Self-management is generally an important way to maintain and improve the patient's behaviours and health status (8). Immediate control of blood sugar is possible through self-monitoring of blood glucose (SMBG). The procedure is such that the patient must measure his blood sugar himself at certain times of the day with a glucometer and a needle (lancet). The SMBG detects blood glucose levels at a specific time and, therefore, cannot expose continuous fluctuations in blood sugar of the patient. Lack of continuous monitoring of SMBG is more common, especially in children and adolescents, which means that in patients, especially in the mentioned groups, measuring SMBG is more difficult and causes treatment disruptions (9, 10). As a method of continuous blood sugar control, continuous glucose monitoring (CGM) provides patients with a set of glucose measurements that can be used to adjust their treatment regimen (11). Technological developments in recent years have improved the CGM device in terms of accuracy and ease of use and, as a result, more successful implementation. Therefore, it can be a desirable treatment method, especially in children and adolescents with type 1 diabetes (12). CGM provides insight and self-awareness about the changes in our patient's blood sugar that occur between BS glucometers, which leads to improved knowledge and better control of the patient's blood sugar. For professionals, it reveals a better glycemic pattern of the patients' blood sugar (without patient intervention), and determines the changes in the patients' nocturnal blood sugar levels in response to exercise, insulin, stress, and lifestyle; and for patients, it makes the daily control of diabetes more convincing. On the other hand, the information obtained from this method can be helpful in designing an individualized diabetes

program and can be used as an educational tool to improve the patients' motivation and to encourage them to cooperate with their doctor. But which patients and with what characteristics benefit from CGM? They might include those with the following characteristics: 1- Elevated HbA1c levels. 2- Nocturnal hypoglycaemia (low blood glucose) and hypoglycemic unawareness. 3- Postprandial hyperglycemia (high blood glucose). 4- Fluctuating glucose levels or logbooks not reflecting HbA1c. 5-Poor glycemic control (patients who desire better control). 6- Pregnant women with diabetes. 7- Children with diabetes. 8- Patients who test infrequently.

Finally, the use of CGM can reduce the mean HbA1c and reduce the number of nocturnal hypoglycemia and the annual DKA of diabetic patients (8). Other criteria for monitoring diabetes include hemoglobin HbA1C. Although the blood Glucose Monitoring (SMBG) is a Baseline form of glucose monitoring, HbA1C is the Golden Standard for assessing glycemic control. Considering the prevalence of diabetes in children and also the effect of good control of blood sugar and hemoglobin A1C (as a long indicator of glucose control) on reducing the complications of diabetes, this study was done to compare the two glycemic control methods in children and adolescents with T1DM.

2- METHOD AND MATERIALS

This study is a type of asynchronous controlled clinical trial (self-control), i.e. Pre-test / Post-test control group design. The study population consisted of all children and adolescents with T1DM who referred to the pediatrics endocrinology clinic of Loghman Hospital during 2014-2019 (recent 5 years) to perform care and control their disease with the following inclusion criteria: 1-Age between 4 to 18 years; 2-Type 1 diabetes; and 3-Duration of the disease, more than one year.

In this regard, a total of 6 variables were entered into the study, including age, sex, and duration of diabetes, number of hypoglycemic events per month, mean HbA1C, and average daily dosage of insulin.

According to the type of study (clinical trial) before the start of the project, the patients' parents signed the forms indicating their consent to participate in the study and to install a CGM device on their children; and all patients' information remained confidential. Then, in order to find out the feasibility of this research, as well as the shortcomings and problems in the design for its implementation, and to estimate the sample size and the standard deviation of the dependent variables, a pilot study was performed on 11 samples. The sample size for the main project was set at 28 people. The sampling method was non-probabilistic (non-random) and available (Constitutional) and the data collection technique was observational. The CGM device was connected to the patients once every three months for 4 to 7 days. The Medtronic iPro 2 system, which is actually a kind of Retrospective or Professional CGM, was used and the number of hypoglycemic events per month, the average HbA1C, and the average daily insulin dose of 3 patients, before and after implanting the CGM device, were collected within 5 years (from 2014 to 2019), using the patient records. the daily blood sugar record book (Logbook), the results of HbA1C tests, the information obtained from the CGM device, and the CGM information form (log sheet). It should be noted that the type of insulin used by the patients was Regular-NPH or Novorapid-Lantus and the method of injecting insulin into the body of the patients (Insulin Delivery Mode) was Multiple Daily Injection (M.D.I) and none of the patients in this study used an insulin pump to inject insulin into their bodies.

Mean, standard deviation, median, and interquartile range were used to describe

continuous quantitative data; and frequency and percentage were used to describe qualitative data. The normality of continuous quantitative data distribution was assessed using the Shapiro-Wilk test. Wilcoxon, Mann-Whitney, paired t-test, and independent t-test were used for comparisons. The percentage of changes in each of the main dependent variables was calculated. Pearson and Spearman's correlations were calculated to examine the linear relationship between age and duration of diabetes with the percentage change. Statistical tests were performed in SPSS software version 25. The significant level for all statistical tests was considered as 5%.

3- RESULTS

In this study, a total of 28 patients with diabetes were studied. The mean age of the patients was 9.92 years with a standard deviation of 3.22 years, the age range of patients was 4.5-17.08 years. 15 patients (53.6%) were male and 13 (46.4%) were female. **Fig. 1** shows the patients' distribution based on gender.

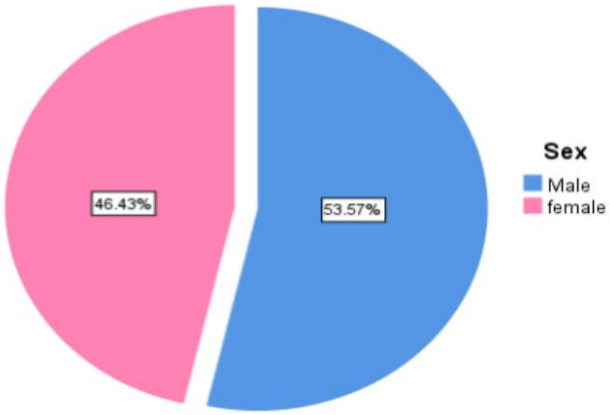

Fig. 1: Sexual distribution of the patients

The mean age of the boys was 9.93±2.91 years, and the mean age of the girls was 9.91±3.66 years. There was no statistically significant difference between the mean ages of girls and boys (p=0.989). **Fig. 2** shows the age distribution of patients by gender.

The median duration of disease in all patients was 2 years with a interquartile range of 1.85 years. The median duration of disease was 2 years for boys with a interquartile range of 2.20 years; and for girls, the median duration of disease was 2 years with a interquartile range of 1.75 years. There was no statistically significant difference in the distribution of diabetes duration between the two genders (p=0.555). **Fig. 3** shows the distribution of the duration of diabetes between the two genders.

As **Table 1** represents, the median of monthly hypoglycaemia occurred at the beginning of the study was 10.5 times with an interquartile range of 7; and the median of monthly hypoglycaemia happenings after CGM was 4 times with an interquartile range of 4.5. Therefore, the number of hypoglycaemia attacks among the patients had a significant decrease (p <0.001) after CGM. Also, the number of hypoglycaemia attacks decreased by more than 67% among 50% of patients, after CGM compared to the beginning of the study. Also, the percentage of changes in the number of hypoglycaemic cases was not significantly related to any of the factors of patients 'age (p=0.529), patients' gender (p=0.235), and duration of diabetes (p=0.731) (**Fig. 4**).

As shown in **Table 2**, the median of HbA1c measurements at the beginning of the study was 9.10 with an interquartile range of 1.67; and after GCM, the median of HbA1c measurements was 7.10 with an interquartile range of 1.15. There was a statistically significant decrease in hemoglobin A1C level after CGM (p <0.001), so that after CGM this decrease was more than 18.7 in 50% of the patients, compared to the beginning of the study. Also, the percentage of changes in HbA1C level was not significantly related to any of the factors of patients 'age (p=0.786),

patients' gender (p=0.739), and duration of diabetes (p=0.456) (**Fig. 5**).

The mean daily dosage of insulin at the beginning of the study was 33±17.96 U and after using CGM was 32.75±16.94 U. Mean reduction in the mean daily dosage of insulin after CGM use, was -0.250±5.21 U, which was not statistically significant (p=0.802).

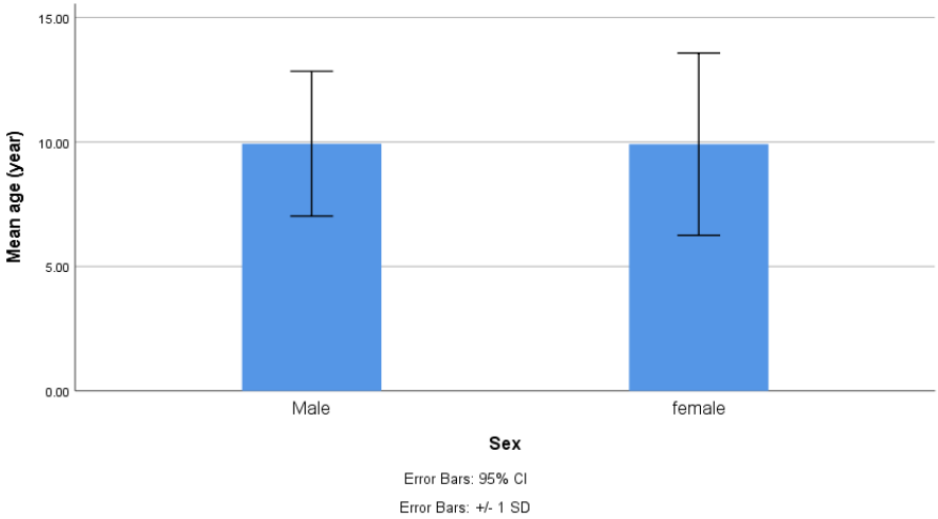

Fig. 2: Age distribution of patients according to their gender

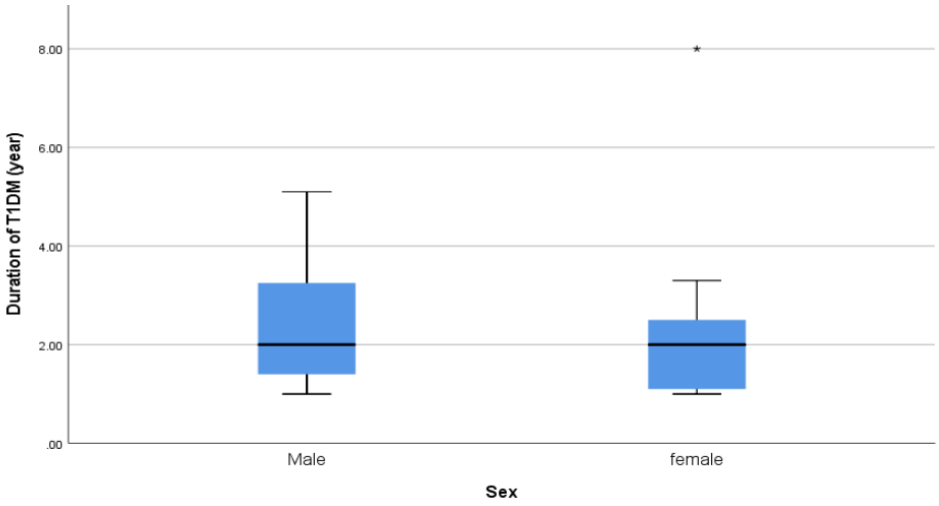

Fig. 3: Distribution of duration of type 1 diabetes based on their gender

Table-1: Description and comparison of the number of hypoglycemic cases before and after using CGM

	Median	Interquartile range	P-value
Before CGM	10.5	7	<0.001
After CGM	4	4.5	
Percentage of changes	-66.76%	30.80%	

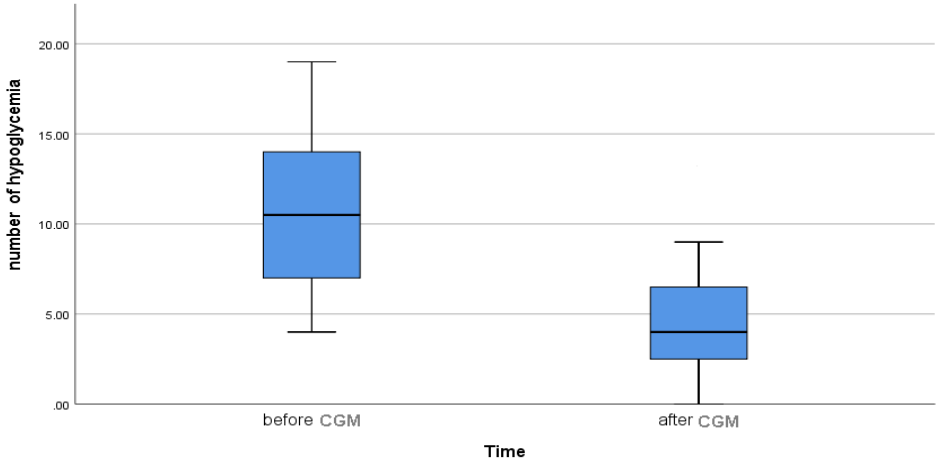

Fig. 4: The number of hypoglycaemia attacks, before and after using CGM

Table-2: Description and comparison of mean hemoglobin A1C before and after CGM use

	Median	Interquartile range	P-value
Before CGM	9.10	1.67	<0.001
After CGM	7.10	1.15	
Percentage of changes	-18.68%	12.19%	

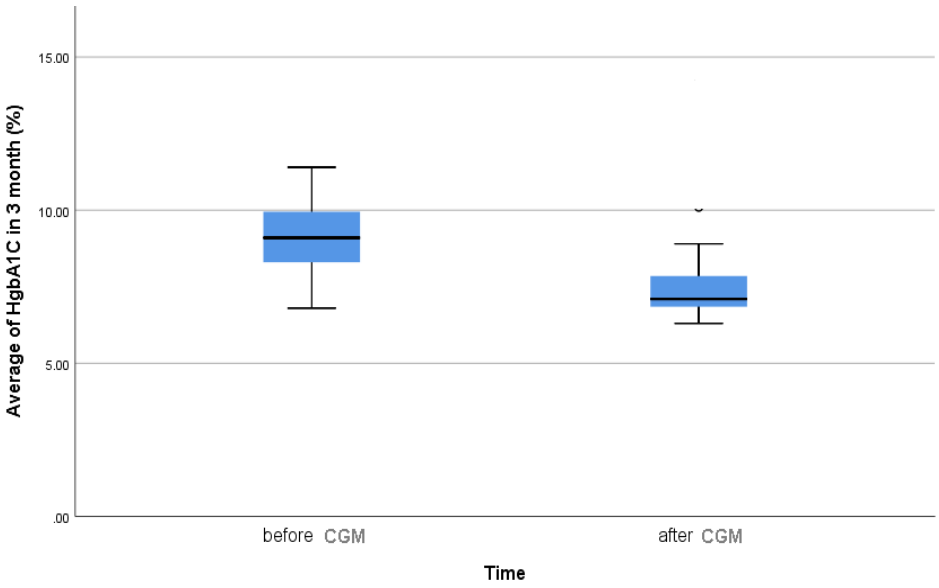

Fig. 5: The mean hemoglobin A1C, before and after using CGM

The mean percentage of changes in the mean daily dosage of insulin was 5.76±13.04 percent among girls and -0.409±16.54 percent among boys. There was no statistically significant difference in the percentage of changes in the average daily dosage of insulin between boys and girls (p=0.289). Also, there was no statistically significant relationship between the percentage of changes in the average daily dosage of insulin after CGM

with age (p=0.145) and duration of diabetes (p=0.230).

4- DISCUSSION

In this study, a total of 28 patients with diabetes were studied. The mean age of the patients was 9.92 years with an age range of 4.5-17.08 years. 15 patients (53.6%) were male and 13 (46.4%) were female. The mean age of the boys was 9.93±2.91 years and the mean age of the girls was 9.91±3.66 years. There was no statistically significant difference between the mean ages of girls and boys (p=0.989). The median duration of the disease in all patients was 2 years with an interquartile range of 1.85 years. The median duration of the disease was 2 years for boys with an interquartile range of 2.20 years; and for girls, the median duration of the disease was 2 years with an interquartile range of 1.75 years.

The median number of monthly hypoglycemia at the beginning of the study was 10.5 times with an interquartile range of 7 and the median number of monthly hypoglycaemia after CGM was 4 times with interquartile range 4.5. Therefore, the number of hypoglycemic cases after CGM had a significant decrease among the patients (p <0.001). Also, after CGM, the number of hypoglycemic cases was more than 67% less than at the beginning of the study among 50% of the patients. Also, the percentage change in the number of hypoglycemic cases has no statistically significant relationship with any of the factors of patients 'age (p=0.529), patients' gender (p=0.235), and duration of diabetes (p=0.731). In the study by Langendam et al., It was found that the number of hypoglycemic cases among individuals who used CGM was higher than among those who used SMBG, which differs from the findings of the current study comparing the two groups (13). However, in JDRF's study, it was found that the rate of fluctuation of blood glucose and hypoglycemia was lower in CGM users, and in fact, the use of CGM reduced the number of hypoglycemic cases, which is similar to the results of the current study (14).

The median of HbA1c measurements at the beginning of the study was 9.10 with an interquartile range of 1.67 and the median of HbA1c measurements after CGM was 7.10 with an interquartile range of 1.15. There was a statistically significant decrease in haemoglobin A1C level after CGM (p <0.001); when compared to the beginning of the study, this decrease was more than 18.7 in 50% of the patients. Also, the percentage of changes in HbA1C level was not significantly associated with any of the factors of the patients' age (p=0.786), patients' gender (p=0.739), and duration of diabetes (p=0.456). In a study by Floyd et al., the effect of CGM on reducing HbA1c was greater than that of SMBG. However, in the present study, the impact of CGM use was greater than that of Floyd et al., which may be due to the date of the present study and the improvement of CGM technology (15). However, in a study by Poolsup et al., there was no difference between SMBG and CGM in controlling HbA1C. Their results are inconsistent with those of the current study, which may be due to being independent of the HbA1C level of the study (16).

The mean daily dose of insulin at the beginning of the study was 33±17.96 U and after using CGM, it was 32.75 ±16.94 U. The mean reduction in the mean daily dosage of insulin after CGM use was -0.250±5.21 U, which was not statistically significant (p=0.802). The mean percentage of changes in the mean daily dosage of insulin was 5.76±13.04% among girls and -0.409±16.54% among boys; and the percentage change in the mean daily dosage of insulin between boys and girls was not statistically significant. (p=0.289).

Furtheremore, there was no statistically significant relationship between the percentage of mean changes in the daily dosage of insulin after CGM use, age (p=0.145), and duration of diabetes (p=0.230). Raviteja's study, in alignment with the current study, showed that the use of CGM and SMBG had no effect on the dosage of insulin. In that study, it was found that the use of this method has no effect on reducing the dosage of insulin consumed by the patients (17).

5- CONCLUSION

Based on the findings, it is concluded that the use of CGM with SMBG compared to the use of SMBG alone, reduces the number of monthly hypoglycemic attacks in children with type 1 diabetes, which is unrelated to age, sex, and duration of diabetes. Also, the use of CGM in combination with SMBG causes a further decrease in HbA1C levels than the use of SMBG alone, which was not related to age, sex, or duration of diabetes. But it was due to the increase in the patient's insight towards his disease and how to control his blood sugar level; and on the other hand, it was due to the increase in the doctor's insight towards the patient's abilities in self-management of blood sugar. However, the use of CGM with SMBG did not change the rate of insulin use compared to the use of SMBG alone and did not reduce the dosage of insulin consumed by the patients.

Considering that Retrospective CGM has a function similar to Holter Monitor in the diagnosis, management, and control of type 1 diabetes, it is suggested that Retrospective CGM and the information obtained from this device be used as a complement (rather than as an alternative) to the SMBG method in the management and control of T1DM in children and adolescents. It is also suggested to conduct more studies on the use of CGM in Iran, due to the advancement of technology in future and the possible improvements in CGM method.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGEMENT

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