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Contemporary Practice in Paediatrics

Usage of Continuous Glucose Monitoring System in Paediatric Patients with Type 1 Diabetes in Hong Kong

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Abstract

Purpose: The aim of this study is to analyse the usage of Continuous Glucose Monitoring System (CGMS) among paediatric population with type 1 diabetes in Hong Kong. ***Methods:*** Data was retrieved from the Hong Kong Childhood Diabetes Registry. Paediatric patients with type 1 diabetes with active follow-up in Hospital Authority in 2018 were included. ***Results:*** Three hundred and sixty patients were included in the analysis. Only 38 patients (10.6%) were regular CGMS users. The mean HbA1c of regular users was significantly lower than that of the non-regular CGMS users (7.4±1.2% vs. 8.5±1.9%; *P*=0.0003). The difference was still significant after adjusting for age, use of insulin pump and parents' occupations (*P*=0.038). The regular usage of CGMS was associated with younger age, use of insulin pump and higher socioeconomic position. ***Conclusions:*** The overall usage of CGMS among paediatric patients with type 1 diabetes in Hong Kong was relatively low.

Key words *Continuous Glucose Monitoring System; Paediatrics; Type 1 diabetes*

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Introduction

Regular self-monitoring of blood glucose is a crucial part of diabetes management to optimise glycaemic control and to prevent long-term complications.[1] In the past, self-monitoring of blood glucose mainly referred to finger-stick blood glucose measurement. With the advancement of technologies, another modality of monitoring, continuous glucose monitoring system (CGMS), has been gaining its place in the management of diabetes.

CGMS consists of three components, [i] the sensor which measures the glucose level in the interstitial compartment every 5-15 minutes, [ii] the transmitter which transfers the glucose information to the receiver, and [iii] the receiver that collects and stores the data. The users can make use of the data to aid the diabetes management. A standardised CGM metrics for clinical care has been formulated from the recent Advanced Technologies & Treatments for Diabetes (ATTD) consensus in 2019. A unique matrix generated from CGMS includes an important parameter called time-in-range (TIR), which is a more informative indicator than haemoglobin A1C (HbA1c) level in reflecting the overall glycaemic control.[2] In addition to TIR, CGMS also provides data on glycaemic excursions throughout the day. The magnitude and frequency of intra- and inter-day glucose variation could not be reflected by HbA1c or regular self-monitoring of blood glucose using finger prick four to six times a day.

CGMS has been implemented clinically in paediatrics since 1999.[3] After the first publication in 2001 showing its benefits in improving the glycaemic control in children with diabetes,[4] its usage has been growing over the past two decades.[5] Many international consensus guidelines have been published regarding the use of CGMS.[6,7] However, the implementation of this technology has not been described locally. The aim of our study is to analyse the usage of CGMS in our local paediatric population with type 1 diabetes (T1DM) and to compare the clinical features between the regular CGMS users and non-regular CGMS users.

Method

Data was retrospectively retrieved from the Hong Kong Childhood Diabetes Registry. The registry was set up in 2016. It involves all the paediatric departments managing children with diabetes mellitus in the Hospital Authority (HA), which governs all the public hospitals and specialist outpatient clinics in Hong Kong. The registry included the clinical information of all childhood diabetes diagnosed from 2008 onwards. The methodology on data collection was described previously.[8]

Paediatric patients who were diagnosed with T1DM at the age of less than 18 years, on or before 31 December 2018 and with active follow-up in HA in the year of 2018 would be included in this study. Diabetes mellitus is defined according to International Society for Paediatric and Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines 2014.[9] The type of diabetes was determined by the physician-in-charge according to the individual's clinical history and laboratory results. Patients having alternative diagnosis other than T1DM, or diagnosed at the age of 18 years old and above, on or before 31 December 2018, or patients who are not actively followed up by HA were excluded from the study.

A standardised data collection form including the basic demographics, clinical diagnoses, medical history, information with respect to glycaemic control including HbA1c, number of episodes of significant hypoglycaemia requiring attendance to emergency departments and diabetes ketoacidosis (DKA), treatment regimens, and details on the self-blood glucose monitoring modalities in the year 2018 were filled out by the physicians-in-charge for each patient and the information was entered into the database of the registry.

DKA was defined according to ISPAD Consensus Guidelines 2014 as hyperglycaemia with blood glucose >11 mmol/L, venous blood gas pH <7.3 or bicarbonate <15 mmol/L and ketonaemia or ketonuria.[10] Regular CGMS user was defined as those using CGMS for more than or equal to 80% of the time in the study period. Intermittent users referred to those using CGMS less than 80% of the time but at least once every six months. Rare users referred to those who used CGMS for at least once in the year of 2018 but less frequent than once every six months. Non-regular users included intermittent and rare users, as well as all remaining patients who had never used CGMS before. Patients' socioeconomic position (SEP) was assessed using their parents' occupations. The parents' occupations were categorised into 'professionals' or 'non-professionals' according to International Standard Classification of Occupations (ISCO-08).[11]

Statistical Analysis

Descriptive statistical analysis was performed on the study population. The data was presented as frequency (percentage) for categorical variables and mean ± standard deviation (SD) for continuous variables. Student's t-test was used for the comparison of continuous variables between groups (regular CGMS users vs. non-regular CGMS users). HbA1c between these two groups were compared using logistic regression model after adjusting for potential confounders. Dichotomous variables would be compared by chi-square test. The level of significance was defined as $P<0.05$. All statistical analyses were performed using Stata (StataCorp. 2015. Stata Statistical Software: Release 15.1 College Station, TX: StataCorp).

Ethics

This study had the approval of the Ethics Committees of all the clusters under HA. The informed consents from all children's parents or guardians and adolescents aged ≥16 years according to local regulations for active patients were obtained.

Results

Three hundred and sixty patients fulfilled the inclusion criteria and were included for analysis in the study. The mean age was 13.9±4.1 years old and 41.9% were male. The mean duration of diabetes was 5.0±3.0 years.

Fifty-six patients (15.6%) had ever used CGMS in the year of 2018 and 38 patients (10.6%) were regular users. The usage of CGMS in paediatric T1DM patients in 2018 was summarised in Figure 1.

The mean age in regular CGMS users was younger at 11.6±4.1 years when compared to the non-regular users at 14.1±4.1 years old. The mean duration of illness was shorter among the regular CGMS users than the non-regular users (4.1±2.8 years vs. 5.1±3.0 years). Compared with the non-regular user group, the regular users had higher SEP. There was also higher percentage of insulin pump users in the regular user group. The demographics and clinical characteristics of the CGMS users and non-users were summarised in Table 1.

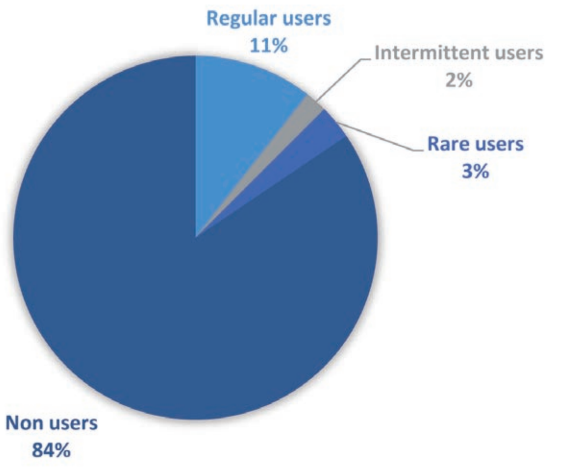

Figure 1 CGMS uptake in paediatric T1DM patients in 2018.

The mean HbA1c of regular CGMS users was significantly lower than that of the non-regular users (7.4 ±1.2% vs 8.5±1.9%, P=0.0003) as shown in Table 2. The difference was still significant after adjusting for age, use of insulin pump and SEP (P=0.038).

Among regular CGMS users, there were 4 reported episodes (4 patients) of DKA while 22 episodes (19 patients) were reported in non-regular CGMS users in the study period. However, the difference was not statistically significant (P=0.260). Regarding the number of episodes of significant hypoglycaemia requiring attendance to emergency department or admission, none was reported among the regular CGMS users, while two were reported in the non-regular users group. Nevertheless, the difference was not statistically significant (P=0.628).

Discussion

In this retrospective cross-sectional study, we found that only 15.6% of children with T1DM in Hong Kong had ever used CGMS; and that the percentage of regular CGMS users was only 10.6%. As shown in Figure 2, the observed rate was much lower than that in other developed countries. The use of CGMS has been increasing all over the world in parallel to its improved accuracy and growing evidence on its use with better glycaemic outcomes.[12] According to the data in the United State T1DM Exchange Clinic Registry and the Prospective Diabetes Follow-Up Registry (DPV) from Germany and Austria in 2016, the CGMS usage among paediatric T1DM patients were 19% and 22% respectively.[5,13] Looking at our closer counterpart, Korea, the percentage of CGMS users among patients younger than 20 years was 18.7% in 2019.[14] One important factor boosting its use is probably related to the reimbursement on the cost of the device. The cost of CGMS device is not inexpensive - it ranges from HKD 1,100 to HKD 3,000 per month. Without funding or subsidy, it would be challenging to encourage its use, especially in the low socioeconomic groups. This is consistent with our observation that CGMS usage was associated with higher

Table 1 Demographics and clinical characteristics of regular vs. non-regular CGMS users

	Regular CGMS users	Non-regular CGMS users	*P*-value*
N	38 (10.6%)	322 (89.4%)	
Sex, n (%)			0.307
Female	25 (65.8%)	13 (34.2%)	
Male	184 (57.1%)	138 (42.9%)	
Ethnicity, n (%)			0.010
Asians	33 (86.8%)	310 (96.3%)	
Non-Asians	5 (13.2%)	12 (3.7%)	
Mean age (years)†	11.6 ±4.1	14.1 ±4.1	<0.001
Mean age ± SD§			
Parents' occupations, n (%)‡			0.005
At least one is professionals	11 (28.9%)	39 (12.1%)	
Both are non - professionals	27 (71.1%)	283 (87.9%)	
Duration of illness			0.067
<5 years	26 (68.4%)	170 (52.8%)	
≥5 years	12 (31.6%)	152 (47.2%)	
Use of insulin pumps	5 (1.6%)	5 (1.6%)	<0.001

*Chi-square test was used to compare the patients' characteristics of the two groups
†Two-sample student's t-test was used for comparison of the mean age of the two groups
§SD denotes Standard deviation
‡Jobs' natures were classified according to International standard classification of occupations ISCO-08

Table 2 Glycaemic outcomes in paediatric T1DM patients in regular and non-regular CGMS users*

	Regular CGMS users	Non-regular CGMS users	*P*-value
Number, N (%)	38 (10.6%)	322 (89.4%)	
Mean HbA1c in 2018 [Mean% ± SD%†]	7.39% ± 1.20%	8.45% ± 1.86%	0.0003

*Two-sample student's t-test was used to compare the mean HbA1c between the two groups, df=355, t=3.43, p=.0003
† SD denotes Standard deviation

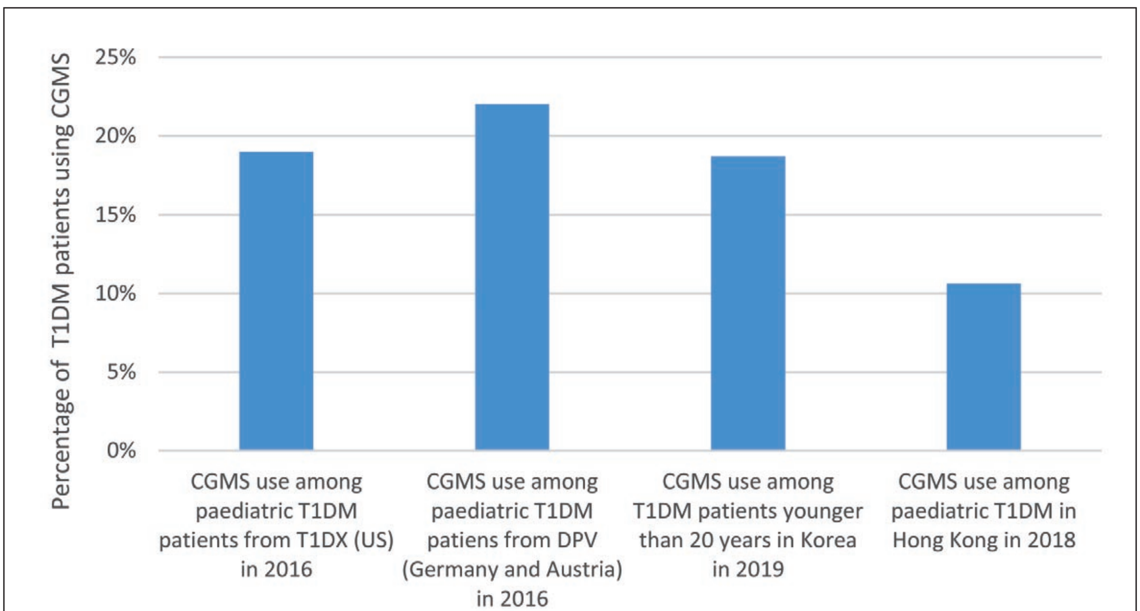

Figure 2 CGMS uptake in different countries.

socioeconomic position. In the U.S., Germany, Austria and recently Korea, insurance coverage and government subsidies on CGMS had contributed to the increased usage of this technology.[5,14] Since Hong Kong has a heavily subsidised health care system and health insurance is not mandatory, and the fact that CGMS is not covered for paediatric patients with T1DM under HA in 2018, this partly explained the relatively low usage of CGMS in Hong Kong.[15]

Apart from the funding limitations, patients' access to CGMS is also influenced by both patients' and parents' willingness to start this new diabetes technology, as well as clinicians' attitudes towards its use and benefits. Hassles of wearing a device all the time on the body, body self-image and inadequate medical support were reported as some of the reasons for patients not using CGMS.[15] On the other hand, while clinicians have a crucial role in recommending or approving the new diabetes technology for their patients, different clinicians might have varied points of view towards this relatively new technology.[16] The initiation of CGMS also requires intensive technological support and guidance. The clinicians would need to be familiar with the system before introducing this technology to their patients. As in 2018, there were no local guidelines regarding the use of CGMS. Although there are many international guidelines formulated on the use of CGMS, a clear local guideline tailored to local situations would facilitate its implementation locally. Further studies would be needed to delineate the actual barriers to regular CGMS use in our locality and possible solutions to increase its usage.

It was observed that the mean age of regular CGMS users was younger in our study. This was consistent with the findings from other overseas cohorts.[13] Younger children experienced greater glycaemic variation[17] and they cannot volunteer symptoms of hypoglycaemia[18] which can be readily picked up by CGMS. These could explain the relatively higher popularity of CGMS in younger paediatric patients.

CGMS was introduced to our locality around a decade ago. The percentage of regular CGMS use among paediatric T1DM patients was 10.7% in 2018. The pace of CGMS uptake in Hong Kong was actually not too slow at this initial stage. Comparing to the U.S., the first real-time CGMS was introduced since 2004,[19] and that overall CGMS uptake in paediatric population was only 4.6% in 2014,[20] which was not high in the initial years as well. However, the rate grew substantially in subsequent years. As CGMS was introduced into Hong Kong later than other counties, this might explain the relatively lower uptake rate in 2018.

In our study, regular CGMS usage was shown to be associated with lower HbA1c when compared to non-regular CGMS users. While causality on CGMS use and better glycaemia control could not be concluded from our cross-sectional observational study, our findings were consistent with several large-scaled randomised-controlled trials.[12] The landmark study published by the Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group in 2008 had shown that, regular use of CGMS was associated with improvements in HbA1c across different age groups.[21,22] Similarly, a randomised clinical trial published recently had also demonstrated a significant improvement in glycaemic control as reflected by the reduction of HbA1c from 8.9% to 8.5% after 26 weeks of CGMS use.[23] All these studies support the use of CGMS in improving the glycaemic control in children with T1DM.

Even though there are lots of advantages with CGMS, with the current technology, most CGMS models cannot totally replace finger-stick blood glucose monitoring. The accuracy of CGMS is commonly measured by mean absolute relative difference (MARD). MARD is calculated by averaging the absolute values of the relative difference between the sensor readings of CGMS and a series of reference blood glucose samples.[24] A MARD value of 10% is generally regarded as an acceptable accuracy for its safe use in diabetic management including the adjustment of insulin dosage.[25] Over the past decade, the accuracy of CGMS has improved with MARD in the range of 8% to 14%.[26] In other words, the accuracy of some CGMS models need further improvement before they could entirely replace finger-stick glucose monitoring. On the other hand, the accuracy of CGMS is affected by the rate of fluctuations in glucose level, hypoglycaemia or use of certain medications like acetaminophen.[27-29] In these situations, confirmation with glucometer reading would be necessary. Therefore, rather than over-reliance on CGMS on the exact glucose readings at a certain time point, it is more useful to provide information on the glucose trend, as well as the rate of its change as presented by the 'trend arrows'.[30] Patients should understand these limitations and potential pitfalls of CGMS so as to fully utilise the technology.

There are several limitations of our study. As a retrospective study, some important information relating to CGMS usage was not available. These include patients' reasons for not using CGMS, information on household income and insurance coverage, as well as attitude of our local health care professionals towards the use of CGMS. All these factors would significantly affect the uptake of this technology in our local population.

The Hong Kong Hospital Authority has launched the 'Paediatrics Diabetes Enhancement Program with CGMS support' in 2020. This program aims to improve the control of high-risk paediatric patients with T1DM through empowerment of glycaemic control and diabetes technology. Patients fulfilling the enrolment criteria would be supplied with certain number of CGM sensors per year, depending on different enrolment indications. At the same time, a local guideline on CGMS for healthcare professionals - 'Continuous Glucose Monitoring System: Practice Guide for Diabetes Nurse' was published in October 2019.[31] It is believed that both initiatives would positively influence the trend of CGMS usage in the coming years.

Further study would be needed to assess the trend of CGMS usage, overall glycaemic control and quality of life of our local children with T1DM after the implementation of the above measures in the future.

Conclusion

The overall usage of CGMS among paediatric patients with T1DM in Hong Kong is relatively low when compared to other parts of the world. Regular CGMS use was associated with better glycaemic control with lower HbA1c. Further studies would be required to delineate and tackle the barriers to regular CGMS usage in Hong Kong, and to monitor the trend of the use of this diabetes technology over the years.

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Declaration

The authors declare no potential conflict of interests relevant to this paper to disclose.

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