## Monthly use of a real-time continuous glucose monitoring system as an educational and motivational tool for poorly controlled type 1 diabetes adolescents

Głowińska-Olszewska B\*, Tobiaszewska M, Łuczyński W, Bossowski A

Department of Paediatrics, Endocrinology, Diabetology with Cardiology Division, Medical University of Bialystok, Poland

\* CORRESPONDING AUTHOR: Department of Paediatrics, Endocrinology, Diabetology with Cardiology Division, Medical University of Bialystok, Waszyngtona 17, 15-274 Bialystok, Poland Tel./Fax: +48 85 7450 730
e-mail: bglowinska@poczta.onet.pl (Barbara Głowińska-Olszewska)

Received 29.10.2012 Accepted 10.06.2013 Advances in Medical Sciences Vol. 58(2) 2013 • pp 344-352 DOI: 10.2478/ams-2013-0024 © Medical University of Bialystok, Poland

## ABSTRACT

**Purpose:** Experience with the use of real-time continuous glucose monitoring systems (RT-CGMS) in teenagers with type 1 diabetes mellitus (T1DM) is limited. We aimed to assess the possibility of glycaemic control improvement and to characterize the group of adolescents, who may gain long-term benefits from the use of the RT-CGMS.

**Methods:** Forty T1DM patients, aged  $14.6\pm2.1$  years, with diabetes duration 7.4 $\pm3.6$  years and initial HbA<sub>1</sub>c  $9.3\pm1.5\%$  were recruited. The analysis was based on one-month glucose sensors use, combined with the thorough family support. Patients were analysed in groups according to baseline HbA<sub>1</sub>c: below and above 7.5%, and 10.0%. Comparison between patients with or without improvement in HbA<sub>1</sub>c after 3-month follow-up was also performed. Patients' satisfaction based on the questionnaire was assessed.

**Results:** HbA<sub>1</sub>c level in entire study group decreased after three months, from  $9.3\pm1.0\%$  to  $8.8\pm1.6\%$  (P<0.001). In the group with HbA<sub>1</sub>c improvement, reduction was the highest:  $9.0\pm1.3\%$  vs.  $8.0\pm1.2\%$  (P<0.001). Only the group with initial HbA<sub>1</sub>c>10% did not achieve significant improvement:  $11.2\pm0.5\%$  vs.  $10.9\pm1.1$  (P=0.06). In satisfaction questionnaire the lowest scores (negative opinion) were reported by group of patients with initial HbA<sub>1</sub>c above 10%, while the highest scores (positive opinion) were found in the group with improvement of HbA<sub>1</sub>c after 3 month follow-up.

**Conclusion:** Short-term use of CGMS RT, united with satisfaction questionnaire, performed in poorly controlled teenagers with T1DM, can be useful in defining the group of young patients, who can benefit from long-term CGMS RT use in metabolic control improvement.

Key words: diabetes type 1, adolescents, real-time continuous glucose monitoring, metabolic control, education

## INTRODUCTION

Despite the increased use of multi dose insulin injection therapy (MDI), continuous subcutaneous insulin infusion (CSII) and the introduction of new insulin analogues among patients with diabetes, patients with type 1 diabetes mellitus (T1DM) often do not achieve the target metabolic control recommended by the Diabetes Control and Complications Trial (DCCT) more than 15 years ago [1]. In theory, selfmonitoring of blood glucose levels coupled with intensive and extensive ongoing education could help to achieve therapeutic aims. However, the snapshot nature of self-monitoring and limited number of measurements that are carried out during the day restrict the influence of self-monitoring of blood glucose. Only few patients measure glucose levels several times a day, after meals or overnight. As a result, postprandial hyperglycaemias or asymptomatic nocturnal hypoglycaemias are frequent [2,3].

Recently introduced into clinical practice real-time continuous glucose monitoring systems (RT CGMS), offering a longer-term ongoing display of interstitial glucose levels, allow to improve glycaemic control, prevent unrecognized high and low blood glucose values, and improve blood glucose pattern management through self-analysis. The system has the potential to revolutionize treatment of type 1 diabetes [4-9]. Several studies performed so far, have demonstrated the effectiveness of RT CGMS and high level of satisfaction with treatment mainly in adults with T1DM, using continuous glucose monitoring for a longer period of time [10-16]. Research in the pediatric population is not as common and has shown less effectiveness than in adults [11, 16-18]. The landmark Juvenile Diabetes Research Foundation Study showed a significant reduction of HbA.c level only for patients over 25 years of age [16].

Pediatric patients are more likely to use CGMS only if from the beginning they and their attendants express a high degree of new method acceptability and improvement of life quality [18,19]. As with any medical technology, RT CGMS may not be appropriate for every patient. Baseline assessment of patient's ability to effective use of system and analysis of opinions on the quality of life and willingness to continue to use, can help precisely determine target group of CGMS users. This seems a better approach than indiscriminate usage of glucose sensors in an unselected group of patients with diabetes who do not want or are not able to take advantage of continuous information about glucose level [18, 20].

In Poland the CGMS system is not reimbursed and most polish families cannot afford continual expenses associated. Studies on RT CGMS use among Polish pediatric patients with type 1 diabetes are limited. The study by Tucholski et al. [21] showed almost physiological glycaemic profiles in very young, 8 yrs old children with well-controlled type 1 diabetes. Considering the difficulties with CGMS adaptation by young patients [16, 22], and commonly known problems with acceptance of chronic illness, frequent lack of motivation and worsening metabolic control at the time of adolescence, the attempt to use RT CGMS, precisely in this extremely difficult group of patients – teenagers with diabetes type 1, seems to be a challenge.

Therefore the objective of this study was to assess shortterm use of real time continuous glucose monitoring and system acceptance by adolescents with T1DM. Thus, this study attempts to answer the question whether on the basis of the results of one month use of RT CGMS, connected with thorough education and support, in conjunction with the satisfaction questionnaire, it is possible firstly to improve metabolic control and secondly to characterize this group of adolescents, who may gain long-term benefits.

## PATIENTS AND METHODS

#### Patients

Forty-four T1DM patients were enrolled into the run-in phase. Four of the 44 withdrew during this phase due to lack of acceptance of the system. RT CGMS four week trial has been conducted in the other subjects. A total of 40 patients with diabetes type 1 were included into the entire study, 19 boys and 21 girls, aged mean 14.6±2.1 vrs. Mean diabetes duration was 7.4±3 yrs and HbA,c level before the study was 9.3±1.5%. Primary eligibility requirements were: age between < 18 yrs and  $\ge 10$  yrs, diabetes duration above 1 year, exogenous insulin requirement at least 0.5 j/kg and insulin pump therapy for at least 0.5 year. Exclusion criteria were: lack of cooperation with therapeutic team, difficulties in education and in use of knowledge in daily life (based on the opinion of the doctor). Initial HbA,c level was not inclusion/ exclusion criterion. We enrolled patients who have never used time continuous glucose monitoring system before but expressed their willingness to participate in the study. Our patients used RT CGMS device in two options: sensor augmented pump or Guardian RT (Medtronic), when insulin pump was without sensor option.

#### Study design

The patients/caregivers were put on a 4-week trial following appropriate technical training as well as training on substantive decision-making related to the received information. The devices and sensors were used following the manufacturer instructions. Patients also received the written instruction of operating system with telephone numbers to diabetology team involved into the study. Patients were supplied with 4-5 sensors, the device and sensors were ensured by the clinic, at no costs to the family. The sensor was changed every 6-7 days, depending on skin sensitivity and sensor activity. First sensor was inserted by medical staff. After first and last sensor usage the obtained data were uploaded to the computer and analyzed together with diabetologist. All analyses were done with use of a computer program Care Link Pro (Medtronic). Proper adjustments to insulin therapy, diet and physical activity were discussed these both times. During the study, patients led a normal life; they had a possibility of making changes in therapy based on sensor real-time records by themselves or prior telephone consultations. They measured glucose level 4 times a day using the glucometer and entered the results into CGMS device for calibration. Based on the results of continuous glucose monitoring obtained from Care Link Pro records we compared glycaemia data for the first and last sensor: mean blood glucose, standard deviation (SD), minimum and maximum glucose level, area under the curve (AUC) for glucose level < 70 mg/dL and >140 mg/dL.

Subsequently, patients and parents filled out a questionnaire survey on various aspects of the use of

CGMS [based on reference 17]. Participants answered the questionnaire questions just after completion of sensors usage, but before second measurement of HbA,c level. The survey included 31 questions grouped into several modules and related to: technical problems, calibration, new knowledge, quality of life, alarms and willingness to continue using the system. Answers were prepared in the 5 point Likert scale, where 1 means-strongly agree, 2 - agree, 3 - neutral, 4 – disagree, 5 – strongly disagree. Items were positively worded (agreeing corresponds to more satisfaction) or negatively worded (agreeing corresponds to less satisfaction). Mean score for positively worded questions was reversed so that higher score always corresponds to more satisfaction. In the conclusion of questionnaire, mean score for the group of questions above 3 means positive result (satisfaction), 3.0 means neutral answer, below 3 - means negative result (lack of satisfaction).

Glycated hemoglobin was measured, using HPLC method, on the first day of the study and after three month follow-up. Based on the HbA<sub>1</sub>c level patients were divided into the following groups: with initial HbA<sub>1</sub>c level above and below 7.5%, above and below 10.0% and patients whose HbA<sub>1</sub>c level decreased after 3-month follow-up (by at least 0.5%) vs. not decreased.

Basic characteristic of the entire study group and selected subgroups is presented in *Tab. 1.* The study was approved by the Bioethical Committee of the Medical University of Bialystok, Poland. Parents and children were informed about the nature of the study and have given their written consent.

#### Statistical analysis

Paired t-test was use for comparison between studied parameters of first and last sensor usage during one month follow-up, as well as to assess difference between HbA<sub>1</sub>c levels at the beginning and after 3 month follow-up of study within one subgroup. To assess differences between two groups at the same time of the study t-student test was used. The results are presented as mean±SD. Statistical significance was determined at P<0.05 level. All calculations were made using Statistica 9.0 StatSoft (Kraków, Poland).

## RESULTS

#### Effect of RT CGMS on HbA<sub>1</sub>c level

HbA<sub>1</sub>c level in entire study group has significantly decreased after three months from  $9.3\pm1\%$  to  $8.8\pm1.6\%$  (P<0.001). In the group of children with optimal metabolic control (HbA<sub>1</sub>c<7.5%), mean HbA<sub>1</sub>c level decreased from  $7.2\pm0.2\%$ to  $6.7\pm0.2$  (P=0.006), and in the group with non-optimal metabolic control (HbA<sub>1</sub>c>7.5%), mean HbA<sub>1</sub>c level after 3 month follow-up decreased from  $9.8\pm1.2$  to  $9.3\pm1.1$  (P=0.003). When the cut-off point for the initial HbA<sub>1</sub>c level was fixed at 10% it appeared that children with initial HbA<sub>1</sub>c below 10% improved metabolic control: decrease from  $8.5\%\pm0.8\%$  vs. 7.9±1.0 (P=0.002), while the group with the poorest control, HbA<sub>1</sub>c>10%, did not achieve any significant improvement: 11.2±0.5% vs. 10.9±1.1 (P=0.06). Then, the group of children which HbA<sub>1</sub>c level decreased at least by 0.5% after 3 month

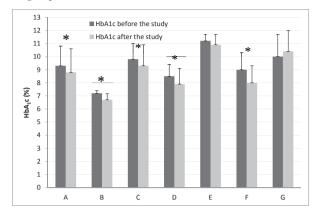
	Study group	HbA <sub>1</sub> c before the study		HbA <sub>1</sub> c before the study		Improved HbA <sub>1</sub> c after 3 month follow-up	
		<7.5%	≥7.5%	<10%	≥10%	Yes	No
Number of patients	40	10	30	28	12	27	13
Age (years)	14.6±2.1	15±1	14.5±2	13.9±2	16.2±2*	14.4±2	15.1±1
Gender (boys/girls)	19/21	4/6	15/15	15/13	4/8	15/12	4/9
Height (m)	1.6±0.1	1.7±0.1	1.6±0.1	1.6±0.1	1.6±0.0	1.6±0.1	1.7±0.0
Body mass (kg)	59±9.9	64±3.8	58±10	57±2	64±10*	58±10	62±8
Body mass index (kg/m <sup>2</sup> )	21.6±3.1	21±1.8	21.8±3	21±2.4	23±4	22±3	21±2.4
SDS-BMI	0.6±1.0	0.3±0.8	0.7±1	0.5±0.8	0.9±1.3	0.8±1	0.2±0.8
Diabetes duration (yrs)	7.4±3.6	6.5±2.7	7.6±3.8	6.5±3	9.4±4*	7±4	8±2.2
HbA <sub>1</sub> c (%) before study	9.3±1.5	7.2±0.2	9.8±1.2*	8.5±0.9	11.2±0.5*	9.0±1.3	10±1.7

Table 1. General characteristics of the entire study group and subgroups selected on the basis of the HbA, c level.

\*P < 0.05 - comparison among subgroups considering the analyzed issues the statement of the statement of

Data are presented as mean  $\pm SD$ 

Figure 1A. Mean  $HbA_1c$  levels before the study and after 3 month follow-up of observation after the study in the selected subgroups.

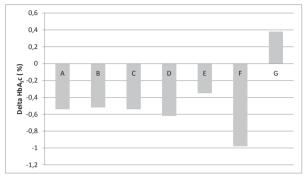


\*P<0.05

follow-up (27 patients, 67%) was compared with group which HbA<sub>1</sub>c level has not changed or increased. In the group with improvement, HbA<sub>1</sub>c decreased from  $9.0\pm1.3\%$  to  $8.0\pm1.2\%$  (P<0.001). The group with no improvement in HbA<sub>1</sub>c had already at beginning of the study significantly worse metabolic control:  $10.0\pm1.7\%$  vs.  $9.0\pm1.3\%$  (P=0.054), and that difference has grown much more after three month follow-up:  $10.4\pm1.4$  vs.  $8.0\pm1.2\%$  (P<0.001) (*Fig. 1*).

# Parameters of glucose variability during first and last sensor use periods

In the entire study group we found significant improvement in the parameters of glucose variability at the end of the sensor usage period. We noticed decrease of: mean glycaemia, SD of mean glycaemia, maximum glucose value and AUC for hyperglycaemia, while minimum glucose value increased, and AUC for hypoglycaemia did not change (*Tab. 2*). Similar improvements in parameters of glycaemic variability were noticed for almost all groups divided according to HbA<sub>1</sub>c level. The largest favourable changes were reported in groups with HbA<sub>1</sub>c>7.5%, below 10% and in the group with improvement of HbA<sub>1</sub>c after 3 month follow-up (*Tab. 3*). Figure 1B. Delta  $HbA_1c$  in the selected study subgroups between  $HbA_1c$  before the study and after 3 month follow-up of observation.



A - The entire study group

B - Group with initial HbA<sub>1</sub>c below 7.5%

C - Group with initial HbA<sub>1</sub> c above 7.5%

D - Group with initial HbA c below 10.0% E - Group with initial HbA c above 10.0%

F - Group with improvement of HbA<sub>1</sub>c level after 3 month follow-up of the study

G - Group without improvement of  $HbA_1c$  level after 3 month follow-up of the study

#### The results of satisfaction questionnaire

Results of the questionnaire showed, that the system is generally well accepted by adolescents with T1DM. Almost all groups of questions gained positive score in the entire study group, the highest positive score was for the wish to use more frequently the device in the case where the system is reimbursed: 4.3 points, the lowest score received calibration of the system: 3.0 points. When we compared subgroups of patients divided according to initial HbA,c level or improvement of HbA,c level after the study it appeared, that those with the worst metabolic control and those without improvement reported less satisfaction than children with better metabolic control or those with improvement after the study. The lowest scores were reported by group of patients with initial HbA<sub>1</sub>c above 10%: 2.4 point for calibration, 3.5 points for new knowledge, and 4.0 for wish to use more frequently the device, while the highest scores was reported by the group with improvement of HbA<sub>1</sub>c after 3 month follow-up: 3.3 point for calibration, 4.0 for new knowledge,

*Table 2.* Results of the continuous glucose monitoring in the entire study group. Comparison between first and last sensor usage.

Entire stu	P value	
First sensor	Last sensor	(t-student paired test)
168±33	144±22	< 0.001
61±14	53±14	0.002
51±12	47±6	0.04
356±74	329±67	0.001
43±26	25±16	< 0.001
0.58±0.6	0.53±0.5	0.59
	First sensor           168±33           61±14           51±12           356±74           43±26	168±33       144±22         61±14       53±14         51±12       47±6         356±74       329±67         43±26       25±16

347

	HbA <sub>1</sub> c before the study						
	<7.5% (n=10)			≥7.5% (n=30)			
	First sensor	Last sensor	Р	First sensor	Last sensor	Р	
Mean glucose (mg/dL)	127±9.8	126±8	0.8	178±29*	149±23*	< 0.001	
SD of mean glucose (mg/dL)	46±6	44±3	0.28	64±13*	55±3*	< 0.001	
Minimum glucose level (mg/dL)	42±2	48±5	0.045	53±13*	47±5	< 0.001	
Maximum glucose level (mg/dL)	279±26	291±14	0.14	375±70*	339±71	< 0.001	
AUC>140 mg/dL	14±5	13±3	0.15	50±24*	28±17*	< 0.001	
AUC<70 mg mg/dL	0.9±0.4	0.6±0.2	0.2	0.4±0.6*	0.4±0.5	0.4	
	HbA <sub>1</sub> c before the study						
	<10% (n=28)			≥10% (n=12)			
	First sensor	Last sensor	Р	First sensor	Last sensor	Р	
Mean glucose (mg/dL)	161±30	142±23	< 0.001	184±36*	151±21	< 0.00	
SD of mean glucose (mg/dL)	59±11	53±14	0.03	66±18	52±14	0.03	
Minimum glucose level (mg/dL)	47±7	46±5	0.4	59±17*	50±7	0.06	
Maximum glucose level (mg/dL)	356±82	331±68	0.009	355±54	326±67	0.09	
AUC>140 mg/dL	38±22	24±17	< 0.001	55±31	27±16	< 0.00	
AUC<70 mg/dL	0.6±0.5	0.6±0.4	0.48	0.4±0.6	0.4±0.5	1	
	Improved HbA <sub>1</sub> c level after 3 month follow-up						
	Yes (n=27)			No (n=13)			
	First sensor	Last sensor	Р	First sensor	Last sensor	Р	
Mean glucose (mg/dL)	164±37	138±21	< 0.001	175±22	158±21*	< 0.00	
SD of mean glucose (mg/dL)	60±15	51±14	0.01	62±12	57±11	0.06	
Minimum glucose level (mg/dL)	49±13	46±5	0.13	53±10	50±7*	0.1	
Maximum glucose level (mg/dL)	344±57	317±55	0.003	380±90	354±82	0.15	
AUC>140 mg/dL	41±29	21±15	< 0.001	47±18	33±17*	< 0.001	
AUC<70 mg/dL	0.7±0.6	0.6±0.5	0.43	0.3±0.3*	0.3±0.3	0.57	
Results of RT CGMS are presented as mean	±SD						

Table 3. Results of the continuous glucose monitoring considering comparison between first and last sensor usage – the analysis in selected subgroups.

Results of RT CGMS are presented as mean  $\pm SD$ 

P-difference between first and last sensor within a single selected subgroup (paired t-student test)

\*P < 0.05 - significant difference between two selected subgroups, considering the same sensor usage (first or last)

#### Table 4. Questionnaire results in the subgroups of patients – the analysis of selected issues.

	Entire study group	HbA <sub>1</sub> c before the study		HbA <sub>1</sub> c be the study	HbA <sub>1</sub> c before the study		Improved HbA <sub>1</sub> c level after 3 month follow-up	
		<7.5%	≥7.5%	<10%	≥10%	Yes	No	
Technical problems	3.8	3.9	3.8	3.9	3.4	3.9	3.7	
Problems with calibration	3.0	3.2	2.9*	3.2	2.4*	3.3	2.6*	
New knowledge about diabetes	3.7	3.8	3.8	4.0	3.5*	4.0	3.5*	
Quality of life	3.9	4.0	3.9	4.1	3.4	4.2	3.6*	
Usefulness of alarms	3.7	3.6	3.7	3.7	3.5	3.6	3.7	
The wish to use system if reimburse is provided	4.3	4.5	4.2*	4.3	4.0*	4.4	4.3	

\* P < 0.05 -comparison among groups considering the analysed issues (HbA<sub>1</sub>c>7.5% vs <7.5%, HbA<sub>1</sub>c < 10% vs > 10%, improvement in HbA<sub>1</sub>c after 3 month follow-up: yes vs no).

Results of the questionnaire are presented as mean score for the selected group of questions. Mean score for the group of questions above 3 means positive result (satisfaction), 3.0 – means neutral answer, below 3 – means negative result (lack of satisfaction), with maximum possible score 5 and minimum 1.

4.2 for quality of life and 4.4 points for wish to use the system more frequently (*Tab. 4*).

Children from our study group used two CGM devices – sensor augmented pump (n=22) and Guardian RT, when their pump was without sensor option (n=18). As the comparison of the two methods was not the aim of the study we did not show the results. However, it is noteworthy to mention that the two groups did not differ in baseline and follow-up HbA<sub>1</sub>c level, as well as in satisfaction questionnaire results (data not shown).

## DISCUSSION

The main finding of our study is that in the group of teenagers, even with poor baseline metabolic control, it was possible to improve significantly level of HbA<sub>1</sub>c. Study design assumed intensive and frequent cooperation between patient/caregivers with diabetology team, connected with education and current changes in the diabetes treatment regimens. By such approach we wanted to expand new resources of motivation to take care for the disease. Therefore, significant decrease in HbA<sub>1</sub>c of at least 0.5% was reported in the majority: 27 (67%) subjects after 3 month follow-up. These children have been separated as a subgroup and compared with those whose HbA<sub>1</sub>c levels did not improve. It is worth noting that a group of adolescents with improvement in HbA<sub>1</sub>c had at baseline unsatisfactory high level of glycated haemoglobin.

Further analysis of selected subgroups of patients allowed concluding that improvement in metabolic control is possible independently of initial level of HbA<sub>1</sub>c, until it reaches values above 10%. The system was well accepted by most of the participants of the study, and the highest satisfaction was reported in the groups with better initial HbA<sub>1</sub>c, and in the group where significant improvement was achieved. Parameters of glycaemic variability improved mostly in teenagers with initial HbA<sub>1</sub>c above 7.5%, but below 10.0% and in the group with improvement in HbA<sub>1</sub>c level.

#### Effect of RT CGMS on HbA<sub>1</sub>c level

In adolescents with type 1 diabetes, good metabolic control is a major challenge, because fluctuations in blood glucose levels are often unpredictable, even in patients treated with CSII. It can lead to that many patients may make wrong decisions related to treatment. Patients' and their caregivers' fear of hypoglycaemia can lead to a conscious avoidance of strict metabolic control [23, 24].

The primary endpoint of most studies on the CGMS was the reduction in HbA<sub>1</sub>c level [16, 25-27]. Long-term studies have demonstrated the possibility of improving HbA<sub>1</sub>c in young adults, the impact in the age group below 18 years was not significant. The authors emphasized the decrease of the frequency of use of the sensor with the duration of the study and less frequent use of sensors in the group of youngsters [16]. However, the results of another study showed the possibility of very strict glycaemia control in 11 yrs old children where they achieved HbA<sub>1</sub>c improvement from 7.1% to 6.8%, with high patient satisfaction and the absence of severe hypoglycemia [17]. The latest STAR 3 Study results confirmed the possibility of sustained improvement of metabolic control in one-year follow-up in the pediatric diabetes population, using sensor augmented pump. It is however noteworthy, that children wore CGM sensor more often and were more likely to reach age-specific HbA,c targets than adolescents [28]. Previously proven possibility of improving metabolic control when replacing insulin therapy from MDI to CSII is higher, when CGMS is used at the same time, especially in patients who use the system in the longer term (> 70% of the time) [29]. Results from our present study add some new data to the field of interest, that the improvement in metabolic control is possible even in about 14 yrs old teenagers, with high level of initial glycated haemoglobin. This population is considered to be very difficult group of diabetic patients. Almost 70% of our patients improved HbA<sub>1</sub>c level by at least 0.5%, what makes clinically significant difference. In general, HbA,c decreases irrespective of the baseline level, indicating that there is no reason to exclude patients on the basis of baseline HbA,c, except for those with a very high HbA,c, in whom other issues regarding treatment and self-monitoring require attending to first.

#### RT CGMS and parameters of glycaemia variability

Variability of blood glucose can cause complications of diabetes, regardless of the level of glycated hemoglobin, and also has a significant impact on quality of life. Fluctuations in blood glucose levels are associated with changes in behavior in children with diabetes [30, 31]. RT CGMS gives a possibility to increase the duration of maintaining glucose level in the target values in both, type 1 and 2 diabetes [32-35]. Danne et al. [32] emphasize, that improvement in glycaemia variability is more pronounced in people over 25 years of age, compared with young adults <25 years, probably because of less predictable way of life of the second group. In our study we have shown that even during the short-term use of glucose sensors, it is possible to improve glycaemia variability parameters in a group of teenagers. Noteworthy, the reduction in glycaemia variability was observed mainly in the groups of patients whose HbA1c decreased in 3-month follow-up, in patients with baseline HbA<sub>1</sub>c level >7.5% and <10.0%. In the analyzed subgroups we showed no improvement in the reduction of time in hypoglycemia. Most previous studies on RT CGMS usage also showed no reduction in this parameter [10, 29]. However, in the latest study by Battelino et al. [36], where the primary endpoint was the time of hypoglycemia, a significant reduction of this parameter was demonstrated during the six-month follow-up in patients with optimal metabolic control, both children and adults.

## The usefulness of short-term use of RT CGMS in quick glucose control and the possibility of metabolic control improvement

The main idea of RT CGMS is individual and long-term use of the system by patients. However some studies showed that even short-term use of its opportunities, in collaboration with a therapeutic team and specific guidelines for the patient, can bring measurable results in terms of increased time on the glycaemia target levels [37]. In one of these several-day studies, usefulness of low-glucose alarms in reducing the incidence of hypoglycemia has been shown [38]. Moreover, another study reported that several times short-term use of RT CGMS is associated with a reduction of HbA<sub>1</sub>c, reduction in meals calories, weight loss, decrease in postprandial glucose levels and increase in time of physical activity in patients with type 2 diabetes [39]. In the group of teenagers, several times use of sensor for only three days, combined with a very intense substantive support (visits every week) were associated with improved HbA,c and the increase of time spent in target glucose range [40]. The results of our study indicate that after thorough training, upon receipt of written instructions and with the possibility of telephone contact, a group of teenagers was able to quickly respond and improve glycaemia parameters. It was also possible to maintain better blood glucose levels in the longer term, which resulted in improved metabolic control. The results of the aforementioned studies and own results show that even short-term use of the RT CGMS, with the strong involvement of medical personnel and the competent use of obtained information may be helpful and effective in solving problems related to diabetes.

## **RT CGMS use and patients' satisfaction**

Using RT-CGMS, in addition to the expectations of concrete results from changes in glycated hemoglobin, is associated with the influence on everyday life. In the modern treatment of chronic diseases the quality of life is of great importance, in addition to basic health problem. Satisfaction questionnaire may help to identify the advantages and disadvantages of the system and make the decision about future usage of the device. In the study by Cemeroglu et al. [20], as in our present research, most of the patients reported a desire to continue using the device, after 4-wk trial. In questionnaire, patients emphasized the possibility of hypoglycaemia prevention and reduced anxiety associated with it, as well as improvement in the quality of life. To the negative features they included, like in our study, technical problems with the sensor. Calibration, which in our study was the most adverse element, was not analyzed in the above-mentioned work. Also, in case of few-months lasting system usage, both children and adults, in majority expressed their satisfaction and improvement in life quality [17,18,41]. Noteworthy, greater satisfaction with the application of the system at the beginning, is associated with more frequent use of sensors in future [18]. In our study,

group of children with improvement in HbA<sub>1</sub>c in 3-month follow-up and with initial glycated hemoglobin below 10%, assessed the influence of using the system on the quality of life and gaining new knowledge about the disease definitely higher compared to others selected subgroups. It is also worth mentioning, that satisfaction questionnaire was filled out just after last sensor usage and before second measurement of HbA<sub>1</sub>c level. So the information about improvement or not in metabolic control did not affect patients' feelings about CGMS. Results from our study showed that one month trial period may help to define the potential patients that may benefit from the device in long run. This may be helpful for parents and diabetologists, where in the situation of lack of reimbursement of the system, like in Poland, to undertake the decision to pay for it at own costs.

Improvement of diabetes control depends on the motivation of the patient to modify his/her diabetes management by using information provided by the system. If the patient is unwilling to do this, use of the device will not lead to improved glycaemia control. Some authors observed, that even with highly motivated subjects and families, the use of CGM did decrease over time. Authors of this report conclude that provision of extra support and encouragement to this patient group early in the incorporation of CGM into care may promote better maintenance of the system over time [18]. RT CGMS requires an extensive and detailed care and counseling support structure and adequate training of the healthcare professionals. With such a new and precise device, a proactive approach is needed to inform the user how to react. The key issue to success seems to identify the appropriate group of patients who can effectively take advantage of the system. Treatment of adolescent with type 1 diabetes is a major problem for the paediatric diabetology team. However, it seems that the difficulties associated with the use of CGMS in adolescents may be at least in a part of this group overcome. The use of the system can help in solving problems associated with the disease and to improve metabolic control also in this challenging group of patients.

#### Limitations of the study

There are certain limitations of our study implicating a careful interpretation of the conclusions. Improvement in HbA<sub>1</sub>c might be due to extra training and attention the diabetes team was giving to patients rather than the direct effect of CGMS, since we did not have control group that went through the same training, motivation and close monitoring without CGMS. However, several studies performed so far with control groups, indicate the additional benefits from CGMS. And in fact, the aim of the study was not to prove the superiority of CGMS over SMBG in improving metabolic control, but to show additional possible profits of new device proposed to adolescents "bored" with traditional glucose measurements, to increase their motivation and educate.

## CONCLUSIONS

Monthly use of RT-CGMS can be useful in decreasing glycaemia variability and in the improvement of metabolic control even in poorly controlled teenagers with type 1 diabetes. For very poorly controlled teenagers (HbA<sub>1</sub>c >10%) the use of this technology is not efficient. Short-term use of CGMS RT, united with satisfaction questionnaire performed in teenagers with diabetes type 1 and their caregivers', can be useful in defining the group of young patients, who can benefit from long-term CGMS RT use in metabolic control improvement.

## REFERENCES

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993 Sep 30;329(14):977-86.

2. Boland E, Monsod T, Delucia M, Brandt CA, Fernando S, Tamborlane WV. Limitations of conventional methods of self-monitoring of blood glucose: lessons learned from 3 days of continuous glucose sensing in pediatric patients with type 1 diabetes. Diabetes Care. 2001 Nov;24(11):1858-62.

3. Kaufman FR, Austin J, Neinstein A, Jeng L, Halvorson M, Devoe DJ, Pitukcheewanont P. Nocturnal hypoglycemia detected with the Continuous Glucose Monitoring System in pediatric patients with type 1 diabetes. J Pediatr. 2002 Nov;141(5):625-30.

4. Danne T, Lange K, Kordonouri O. Real-time glucose sensors in children and adolescents with type-1 diabetes. Horm Res. 2008;70(4):193-202.

5. Hermanides J, DeVries JH. Sense and nonsense in sensors. Diabetologia. 2010 Apr;53(4):593-6.

6. Hirsch IB, Armstrong D, Bergenstal RM, Buckingham B, Childs BP, Clarke WL, Peters A, Wolpert H. Clinical application of emerging sensor technologies in diabetes management: consensus guidelines for continuous glucose monitoring (CGM). Diabetes Technol Ther. 2008 Aug;10(4):232-44.

7. Ives B, Sikes K, Urban A, Stephenson K, Tamborlane WV. Practical aspects of real-time continuous glucose monitors: the experience of the Yale Children's Diabetes Program. Diabetes Educ. 2010 Jan-Feb;36(1):53-62.

 Keenan DB, Cartaya R, Mastrototaro JJ. Accuracy of a new real-time continuous glucose monitoring algorithm. J Diabetes Sci Technol. 2010 Jan 1;4(1):111-8.

9. Tubiana-Rufi N, Riveline JP, Dardari D. Realtime continuous glucose monitoring using GuardianRT: from research to clinical practice. Diabetes Metab. 2007 Dec;33(6):415-20. 10. Beck RW, Hirsch IB, Laffel L, Tamborlane WV, Bode BW, Buckingham B, Chase P, Clemons R, Fiallo-Scharer R, Fox LA, Gilliam LK, Huang ES, Kollman C, Kowalski AJ, Lawrence JM, Lee J, Mauras N, O'Grady M, Ruedy KJ, Tansey M, Tsalikian E, Weinzimer SA, Wilson DM, Wolpert H, Wysocki T, Xing D. The effect of continuous glucose monitoring in well-controlled type 1 diabetes. Diabetes Care. 2009 Aug;32(8):1378-83.

11. Beck RW, Buckingham B, Miller K, Wolpert H, Xing D, Block JM, Chase HP, Hirsch I, Kollman C, Laffel L, Lawrence JM, Milaszewski K, Ruedy KJ, Tamborlane WV. Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes. Diabetes Care. 2009 Nov;32(11):1947-53.

12. Bode B, Beck RW, Xing D, Gilliam L, Hirsch I, Kollman C, Laffel L, Ruedy KJ, Tamborlane WV, Weinzimer S, Wolpert H. Sustained benefit of continuous glucose monitoring on A1C, glucose profiles, and hypoglycemia in adults with type 1 diabetes. Diabetes Care. 2009 Nov;32(11):2047-9.

13. Garg SK, Kelly WC, Voelmle MK, Ritchie PJ, Gottlieb PA, McFann KK, Ellis SL. Continuous home monitoring of glucose: improved glycemic control with reallife use of continuous glucose sensors in adult subjects with type 1 diabetes. Diabetes Care. 2007 Dec;30(12):3023-5.

14. O'Connell MA, Donath S, O'Neal DN, Colman PG, Ambler GR, Jones TW, Davis EA, Cameron FJ. Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial. Diabetologia. 2009 Jul;52(7):1250-7.

15. Peyrot M, Rubin RR. Patient-reported outcomes for an integrated real-time continuous glucose monitoring/insulin pump system. Diabetes Technol Ther. 2009 Jan;11(1):57-62.

16. Tamborlane WV, Beck RW, Bode BW, Buckingham B, Chase HP, Clemons R, Fiallo-Scharer R, Fox LA, Gilliam LK, Hirsch IB, Huang ES, Kollman C, Kowalski AJ, Laffel L, Lawrence JM, Lee J, Mauras N, O'Grady M, Ruedy KJ, Tansey M, Tsalikian E, Weinzimer S, Wilson DM, Wolpert H, Wysocki T, Xing D. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med. 2008 Oct 2;359(14):1464-76.

17. Buckingham B, Beck RW, Tamborlane WV, Xing D, Kollman C, Fiallo-Scharer R, Mauras N, Ruedy KJ, Tansey M, Weinzimer SA, Wysocki T. Continuous glucose monitoring in children with type 1 diabetes. J Pediatr. 2007 Oct;151(4):388-93.

18. Weinzimer S, Xing D, Tansey M, Fiallo-Scharer R, Mauras N, Wysocki T, Beck R, Tamborlane W, Ruedy K. Prolonged use of continuous glucose monitors in children with type 1 diabetes on continuous subcutaneous insulin infusion or intensive multiple-daily injection therapy. Pediatr Diabetes. 2009 Apr;10(2):91-6.

19. The Diabetes Research in Children Network (DirecNet) Study Group. Psychological aspects of continuous

glucose monitoring in pediatric type 1 diabetes. Pediatr Diabetes. 2006 Feb;7(1):32-8.

20. Cemeroglu AP, Stone R, Kleis L, Racine MS, Postellon DC, Wood MA. Use of a real-time continuous glucose monitoring system in children and young adults on insulin pump therapy: patients' and caregivers' perception of benefit. Pediatr Diabetes. 2010 May;11(3):182-7.

21. Tucholski K, Deja G, Skała-Zamorowska E, Jarosz-Chobot P. Evaluation of daily glycemic profiles in well controlled children with type 1 diabetes mellitus using a continuous glucose monitoring system. Pediatr Endocrinol Diabetes Metab. 2009;15(1):29-33.

22. Battelino T. Prolonged use of continuous glucose monitoring: kids do not listen—says who? Pediatr Diabetes. 2009 Apr; 10(2):89-90.

23. Frier BM. How hypoglycaemia can affect the life of a person with diabetes. Diabetes Metab Res Rev. 2008 Feb;24(2):87-92.

24. Thompson CJ, Cummings JF, Chalmers J, Gould C, Newton RW. How have patients reacted to the implications of the DCCT? Diabetes Care. 1996 Aug;19(8):876-9.

25. Bailey TS, Zisser HC, Garg SK. Reduction in hemoglobin A1C with real-time continuous glucose monitoring: results from a 12-week observational study. Diabetes Technol Ther. 2007 Jun;9(3):203-10.

26. Deiss D, Bolinder J, Riveline JP, Battelino T, Bosi E, Tubiana-Rufi N, Kerr D, Phillip M. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. Diabetes Care. 2006 Dec;29(12):2730-2.

27. Hoeks LB, Greven WL, de Valk HW. Realtime continuous glucose monitoring system for treatment of diabetes: a systematic review. Diabet Med. 2011 Apr;28(4):386-94.

28. Slover RH, Welsh JB, Criego A, Weinzimer SA, Willi SM, Wood MA, Tamborlane WV. Effectiveness of sensor-augmented pump therapy in children and adolescents with type 1 diabetes in the STAR 3 study. Pediatr Diabetes. 2012 Feb;13(1):6-11.

29. Raccah D, Sulmont V, Reznik Y, Guerci B, Renard E, Hanaire H, Jeandidier N, Nicolino M. Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study. Diabetes Care. 2009 Dec;32(12):2245-50.

30. Brownlee M, Hirsch IB. Glycemic variability: a hemoglobin A1c-independent risk factor for diabetic complications. Jama. 2006 Apr 12; 295 (14): 1707-8.

31. McDonnell CM, Northam EA, Donath SM, Werther GA, Cameron FJ. Hyperglycemia and externalizing behavior in children with type 1 diabetes. Diabetes Care. 2007 Sep;30(9):2211-5.

32. Danne T, de Valk HW, Kracht T, Walte K, Geldmacher R, Solter L, von dem Berge W, Welsh ZK, Bugler JR, Lange K, Kordonouri O. Reducing glycaemic variability in type 1 diabetes self-management with a continuous glucose monitoring system based on wired enzyme technology. Diabetologia. 2009 Aug;52(8):1496-503.

33. Hirsch IB, Abelseth J, Bode BW, Fischer JS, Kaufman FR, Mastrototaro J, Parkin CG, Wolpert HA, Buckingham BA. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. Diabetes Technol Ther. 2008 Oct;10(5):377-83.

34. Garg S, Zisser H, Schwartz S, Bailey T, Kaplan R, Ellis S, Jovanovic L. Improvement in glycemic excursions with a transcutaneous, real-time continuous glucose sensor: a randomized controlled trial. Diabetes Care. 2006 Jan;29(1):44-50.

35. Rodbard D, Bailey T, Jovanovic L, Zisser H, Kaplan R, Garg SK. Improved quality of glycemic control and reduced glycemic variability with use of continuous glucose monitoring. Diabetes Technol Ther. 2009 Nov;11(11):717-23.

36. Battelino T, Phillip M, Bratina N, Nimri R, Oskarsson P, Bolinder J. Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. Diabetes Care. Apr;34(4):795-800.

37. Garg S, Jovanovic L. Relationship of fasting and hourly blood glucose levels to HbA1c values: safety, accuracy, and improvements in glucose profiles obtained using a 7-day continuous glucose sensor. Diabetes Care. 2006 Dec;29(12):2644-9.

38. Davey RJ, Jones TW, Fournier PA. Effect of shortterm use of a continuous glucose monitoring system with a real-time glucose display and a low glucose alarm on incidence and duration of hypoglycemia in a home setting in type 1 diabetes mellitus. J Diabetes Sci Technol. 2010 Nov 1;4(6):1457-64.

39. Yoo HJ, An HG, Park SY, Ryu OH, Kim HY, Seo JA, Hong EG, Shin DH, Kim YH, Kim SG, Choi KM, Park IB, Yu JM, Baik SH. Use of a real time continuous glucose monitoring system as a motivational device for poorly controlled type 2 diabetes. Diabetes Res Clin Pract. 2008 Oct;82(1):73-9.

40. Halvorson M, Carpenter S, Kaiserman K, Kaufman FR. A pilot trial in pediatrics with the sensor-augmented pump: combining real-time continuous glucose monitoring with the insulin pump. J Pediatr. 2007 Jan;150(1):103-105.

41. Rubin RR, Peyrot M. Treatment satisfaction and quality of life for an integrated continuous glucose monitoring/ insulin pump system compared to self-monitoring plus an insulin pump. J Diabetes Sci Technol. 2009 Nov;3(6):1402-10.