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The usefulness of the Flash Style Libre system in glycemic control in children with type 1 diabetes during summer camp

Przydatność systemu Flash FreeStyle Libre w kontroli glikemii u dzieci z cukrzycą typu 1 podczas obozu letniego

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Abstract
Type 1 diabetes requires the patient to be very involved in the treatment process, especially in terms of proper self-control. The new method of non-invasive glycemic control by scanning is an attractive alternative for patients requiring multiple measurements due to the high dynamics of glycemic changes. **The aim of the study** was to evaluate the usefulness of Flash FreeStyle Libre in glycemic control in children during summer camp on the basis of the participants' completed questionnaire and on the basis of the assessment o the suitability of the system performed by medical staff based on a comparative analysis: glycemia by sensor and glucometer. **Material and Methods.** A study using the new Flash FreeStyle Libre glycemic control system was conducted at a seaside summer camp for children with diabetes at the seaside. The study included 75 children (32 boys and 43 girls), in mean 13.4 (SD 4.6) years old, with an average duration of diabetes of 6.5 (SD 4.5) years and mean HbA_1c of 7.81% (SD 2.05). All camp participants were provided with Libre sensors, however, routine glucose control measurements with therapeutic decisions was made using traditional glucose meters. On the last day of the camp, after the removal of the sensors, a satisfaction survey was conducted to assess with a new self-monitoring method and a comparative analysis of the glucose results from the sensor with the personal glucose meters – MARD, MAD, and clinical errors on the Clarke Error Grid were calculated. **Results.** In the Libre user's survey, wearing comfort and ease of installation were described as very good / good by 86% and 94% of the respondends, respectively. Ease of reading blood glucose by scan was positively evaluated by 92% of the respondents, 95% of the subjects did not report any side effects. The sensor remained intact for 14 days in 46 children (62%), which value was the basis for the statistical calculations. Comparative analysis of glucose results obtained from Libre measurements performed with glucose meters (3143 measurements) showed a relatively good MARD index – 18.22% on average, with a large individual variation (6.36–29.51%). Clarke Error Grid showed that 75.2% (2309) of the results were in Zone A (Acceptable Errors) and 95.81% (3012) in Zone A and B (Non-Negative Errors). **Conclusion.** Libre user's satisfaction survey revealed that most of the respondents rated the cooperation with Flash FreeStyle Libre positively. The relatively good results of Libre in comparison with glucose meters have confirmed the usefulness of this method of monitoring glucose in summer camps for children with diabetes.

Key words
type 1 diabetes, Flash FreeStyle libre continuous glucose monitoring system, quality of life, FGM, CGM

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Streszczenie
Cukrzyca typu 1 wymaga od chorego dużego zaangażowania w proces leczenia, w tym szczególnie w zakresie prowadzenia właściwej samokontroli. Nowa metoda nieinwazyjnej kontroli glikemii metodą skanowania jest atrakcyjną propozycją dla chorych wymagających wielokrotnych pomiarów z powodu dużej dynamiki zmian glikemii. **Celem** naszej pracy była ocena przydatności systemu Flash FreeStyle Libre w kontroli glikemii w warunkach obozu letniego dla dzieci z cukrzycą na podstawie autorskiej ankiety wypełnianej przez uczestników oraz oceny przydatności systemu przez personel medyczny drogą analizy porównawczej stężenia glukozy: sensor/glukometr. **Materiał i metody.** Badanie z zastosowaniem nowego systemu kontroli glikemii Flash FreeStyle Libre przeprowadzono podczas letniego obozu nad morzem dla dzieci chorych na cukrzycę. Badaniem objęto 75 dzieci (32 chłopców i 43 dziewcząt) w wieku 13,4 (SD 4,6) lat ze średnim czasem trwania cukrzycy wynoszącym 6,5 (SD 4,5) lat i średnią HbA_1c 7,81% (SD 2,05). Wszystkim uczestnikom obozu założono czujniki Libre, jednakże rutynową kontrolę glikemii z podejmowaniem decyzji terapeutycznych prowadzono przy użyciu tradycyjnych glukometrów. W ostatnim dniu obozu po zdjęciu sensorów przeprowadzono ankietę oceny satysfakcji z nowej metody samokontroli oraz analizę porównawczą wyników stężenia glukozy z sensora z glukometrami osobistymi – obliczono wskaźniki MARD, MAD oraz błąd kliniczny na siatce błędów Clarka. **Wyniki.** W ankiecie użytkownika Libre komfort noszenia oraz łatwość zakładania sensora opisano jako bardzo dobry/dobry odpowiednio w 86% oraz 94%. Łatwość odczytu glikemii przez skanowanie była oceniona pozytywnie przez 92% ankietowanych, 95% badanych nie zgłosiło żadnych objawów niepożądanych. Sensor pozostał nienaruszony przez 14 dni u 46 dzieci (62%), co stanowiło podstawę przeprowadzonych obliczeń statystycznych. Analiza porównawcza wyników glikemii uzyskanych z pomiarów Libre z glukometrami (3143 pomiary) wykazała stosunkowo dobry wskaźnik MARD – średnio 18,22%, z dużym indywidualnym zróżnicowaniem (6,36–29,51%). Kliniczna ocena dokładności pomiarów na siatce błędów Clarka wykazała, że 75,2% (2309) wyników znalazło się w strefie A (błędy akceptowalne) oraz 95,81% (3012) wyników w strefach A i B (błędy niegroźne). **Wnioski.** Ankieta satysfakcji użytkownika Libre wykazała, że większość badanych oceniła pozytywnie współpracę z systemem Flash FreeStyle Libre. Stosunkowo dobre wyniki porównania systemu Libre z glukometrami potwierdziły przydatność tego sposobu monitorowania glikemii w warunkach letniego obozu dla dzieci z cukrzycą.
Słowa kluczowe
cukrzyca typu 1, system monitorowania glikemii Flash Libre, jakość życia, FGM, CGM

Introduction

Type 1 diabetes requires patients to be greatly involved in the treatment process, and to cooperate closely with a diabetes team in order to adapt the therapy to current needs. Essential elements of the control of diabetic treatment are: ongoing monitoring of blood glucose, retrospective assessment of glycemia and regular hemoglobin A_{1C} testing. The proper glycemia self-control is necessary to obtain satisfactory results of the therapy, and provides an opportunity to avoid the acute and chronic complications [1,2]. Patients treated with by multiple daily insulin injections or continuous subcutaneous insulin infusions must perform numerous measurements of the glucose level every day to control the daily glycemic profile and undertake appropriate treatment. In case of children with unstable type 1 diabetes with frequently occurring episodes of hypoglycemia or in children who are not aware of such episodes, who particularly often should check the glucose level, a valuable complement to glucose self-control are continuous glucose monitoring systems (CGM), which not only present glucose level and the trend of its dynamic changes, but also offer emergency alerts [3].

A novelty in this field is the newly available Flash FreeStyle Libre system manufactured by the Abbott company. It is an innovative glucose measurement system, designed for adults and children older than 4 years evaluates glycemia both at the time of the scan as well as retrospectively and contimuously. The measurements can be performed in a comfortable and discreet way, with no need to prick oneself and calibrate the device. The device potentially allows for a much more accurate assessment of changes in the concentration of glucose, more accurate registration of the dynamics of changes in blood glucose after meals, during physical activities, as well as assessing the twenty-four-hour glycemia profile [4].

The aim of the study was to evaluate the usefulness of Flash FreeStyle Libre in glycemic control in children during a summer camp on the basis of questionnaires filled by participants and assessment of usefulness of the system by medical staff, based on a comparative analysis of the value of glycemia measured by sensor/glucometer.

Material and Methods

The study using the Flash FreeStyle Libre in glycemic control was conducted at a summer camp for children with diabetes from across Poland, organized by the Society for Children and Youth with Diabetes in Gliwice. All of the participants of the summer camp at the seaside were invited to test the devices provided by the Society. The study included 75 children (32 boys and 43 girls), aged 6.2 to 16.5 years, mean 13.4 years old (SD 4.6), with an average duration of diabetes of 6.5 (SD 4.5) years and mean HbA_1c of 7.81% (SD 2). Children from different diabetes centers in Poland participated in the camp. All participants were treated with intensive functional insulin therapy: 62 by using an insulin pump, 13 by using pens. The medical staff, who supported children with diabetes during the camp, consisted of diabetologists and pediatricians related to Upper Silesian Child Health Centre in Katowice and a student from The Students Scientific Association at the Dept. of

Children's Diabetology of the Medical University of Silesia. The study was approved by Bioethical Committee of the Medical University of the Silesia (CDF / 0022 / KB1 / 87/16).

On the second day of the stay, after obtaining the written consent of the parents / guardians to participate in the study, the medical staff fixed the Libre sensors in the location indicated by the Abbott Company (back side of the arm) using a special applicator. Glucose measurements were carried out in parallel by the Libre reader and traditional Contour Link or AccuChek Performa personal glucometers, yet the treatment decisions were made on the grounds of glucometer results. The glucose level was monitored routinely during the day as required: fasting, before meals, during exercise (trips, when playing on the beach, in the sea), at night, and always when the children were feeling bad. Measurements of blood glucose on personal glucometers and Libre readers were recorded in medical documents. The appliances were regularly checked by medical personnel and, if necessary, sensors were additionally protected against preterm detachment. The sensors were removed on the last day of the stay,14 days after they were fixed, and the place where the sensor was located was carefully viewed by medical personnel.

A paper questionnaire was developed to evaluate the Libre system. The questionnaire was completed personally by the tested persons or by their legal guardian (if the child was too young to complete the questionnaire by themselves). It included closed questions (single or multiple choice) as well as open ones. The survey was conducted immediately after the sensors were removed from the arms of the patient involved in the study. The questionnaire is shown in Table I.

In order to assess the application of the Libre system in an objective manner, the glucose value measured with the use of the Flash method was compared with traditional measurements performed with Contour Link glucometers – patients' personal glucometers paired to insulin pumps (reading from pump memory) or Contour Link/AccuChek Performa glucometers used routinely by the camp medical staff (camp card data). The analysis concerned the glucose levels measured using the Flash glucose monitoring systems which remained in place intact for 14 days, with no significant skin lesions after removal of the sensor (46 readings – 61.3%). Absolute values of the measurements of the glucose level in the interstitial fluid were compared with the blood glucose level (readings parallel in time, to an accuracy of five minutes). The following indexes were calculated: MARD (Mean Absolute Relative Difference) and MRD (Mean Relative Difference), and clinical error on the Clarke Error Grid. Statistical calculations were performed using the R language and the Error Grid Analysis package, based on the methodology commonly used for this purpose and described in the literature [5].

Results

According to the survey concerning users' satisfaction with the Libre system, the vast majority of the respondents assessed (in a five-point scale: very good/good/neutral/poor/very poor) the comfort of wearing and the ease of putting on the sensor as very good or good (86% and 94% respectively). The ease of glucose reading by scanning was evaluated positively by 92% of the respondents (including over 69% – very good and 23% – good). Despite difficult conditions at the camp, in the case of more than half of the children (62%), the sensor remained in place intact for 14 days. In the remaining ones, the sensor came off earlier during the physical exercise, changing of clothes and other daily activities zamieić na or during other daily activities, and, in two cases, the sensor was removed due to the reader failure. 95% of the respondents did not report any adverse events during the installation of the sensor – bleeding, mild pain, or bruising occurred in 5% of the children. In 38% of the respondents the skin lesions were observed in the place where the sensor was removed. The most common events were minor changes in the form of itching (16 persons), less frequent were: swelling (3), rash (2), erythema (2), callosity (1), bruising, (1) and abscess (1). The level of pain while putting on and wearing the sensor was evaluated as 79% smaller than in the case of pricking a finger with a glucometer, and almost all respondents (92%) felt that it was easier to measure the glucose level with the use of Libre than with a glucometer. According to the users, the compatibility of measurements performed with the use of Libre and a glucometer was as follows: nearly half of the users assessed it as very good/good (10% and 38% respectively), and 33% as poor/very poor (25% and 11% respectively). However, it is noteworthy that the children compared mainly the glucose level measured with a glucometer and through a sensor without taking into account a delay in the measurements by sensor in relation to the measurement of capillary blood (which is a natural phenomenon resulting from the assessment method). When asked about their willingness to apply the Libre system in the future, most participants responded the vast majority positively – 82%. In the open-ended question the respondents pointed to the inconvenience of using extra protection to keep the sensor on the skin in the course of intense physical exercise during a summer camp by the sea. They suggested the need to improve the accuracy of reading of the glucose level in cases of hyperglycemia and hypoglycemia. During such moments, differences between the glucometer and sensor readings increased, which could result in poor decisions made in order to control glycemia, if the treatment had to be based only on the sensor. For some of the respondents, it is a condition that must be fulfilled before they start using the Libre device permanently. The ability to observe the trend arrows and chart, which allow for better visualisation of the direction of glycemia, was assessed very positively. The young people also suggested that it would be more beneficial and convenient for them to be able to transmit the current glucose level to their smartphones.

Detailed replies to questions of the treatment satisfaction questionnaire are shown in Figure 1.

The objective evaluation of the compatibility of the Libre system readings with personal glucometers based on 3143 measurements of glucose level (46 children for 14 days) showed

Table I. Libre user's questionnaire form
Tabela I. *Kwestionariusz dla użytkowników Libre*

1	How do you evaluate the comfort of using the sensor for 14 days? (circle the appropriate answer)				
	0 very poor	1 poor	2 neutral	3 good	4 very good
2	How do you evaluate the ease of putting on the sensor?				
	0 very poor	1 poor	2 neutral	3 good	4 very good
3	Have you noticed any adverse effects when putting on the sensor ?				
	yes / no	which (please specify): acute pain, bleeding, other			
4	How do you evaluate the ease of glucose reading by scanning?				
	0 very poor	1 poor	2 neutral	3 good	4 very good
5	Has the sensor remained intact in place for 14 days?				
	yes / no	circumstances of losing the sensor.....			
6	Have you noticed any skin lesions in the place of the sensor after its removal?				
	swelling	yes	no		
	itching	yes	no		
	rash	yes	no		
	erythema	yes	no		
	callosity	yes	no		
	bruising	yes	no		
	bleeding	yes	no		
	other				
7	How do you evaluate the compliance of Libre measurements with parallel glucometer results?				
	0 very poor	1 poor	2 neutral	3 good	4 very good
8	How do you estimate the level of pain when putting on the sensor and wearing the Libre device, compared with the pain when pricking your fingers (standard glucometer)?				
	0 more painful	1 equally painful	2 less painful		
9	How do you evaluate the ease of glucose measurement by the Libre device compared with a traditional glucometer?				
	0 more difficult	1 the same	2 easier		
10	Would you like to use the Libre system during routine control of glucose level in the future?				
	yes	no			
REMARKS:					
.....					
.....					
Thank you for filling in the questionnaire. ☺					

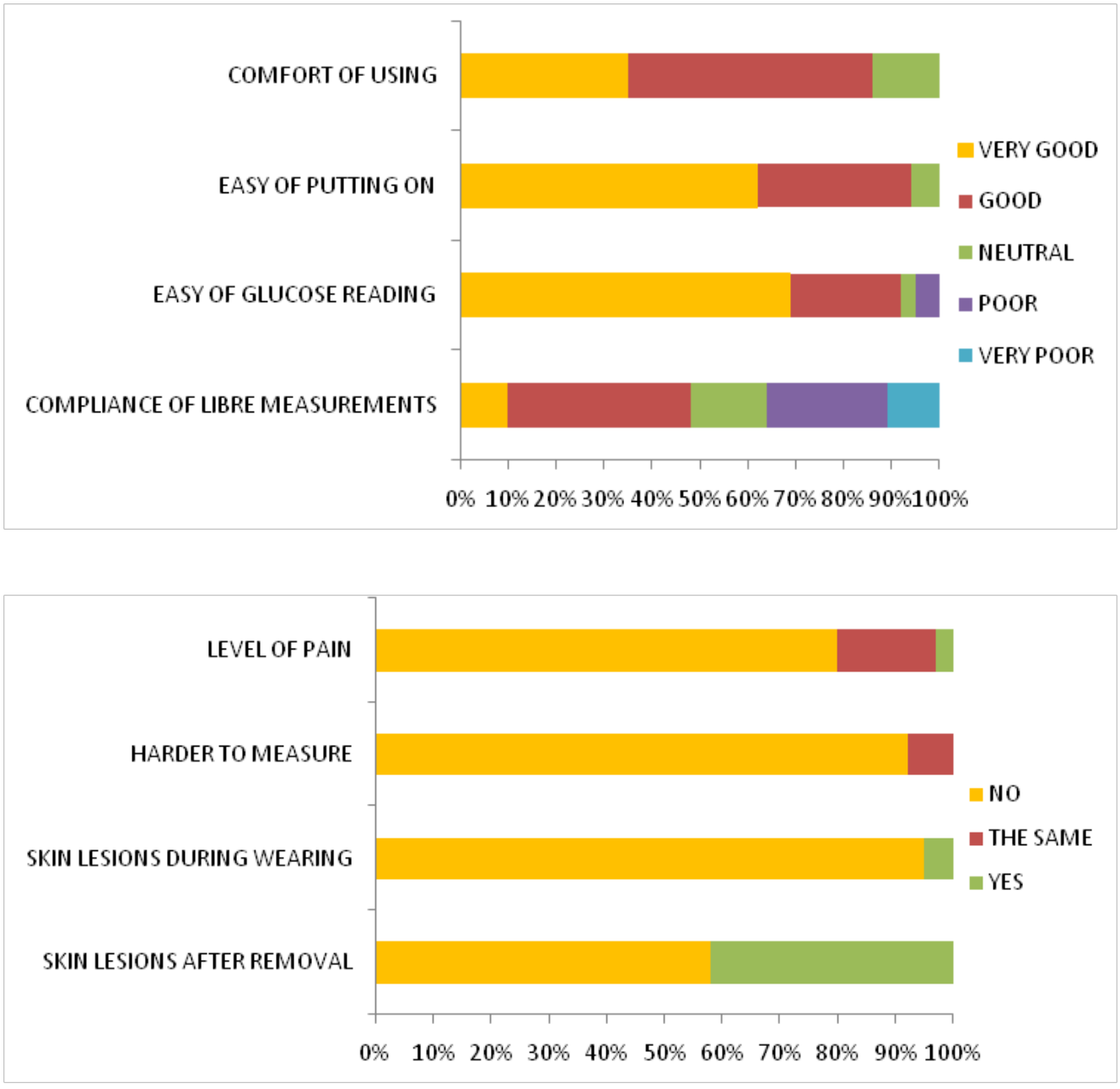

Fig. 1. Users' evaluation of the Libre system
Ryc. 1. *Ocena systemu Libre przez użytkowników*

a great individual variation in the MARD index: from 6.36 to 29.51 – an average of 18.22%. After dividing the results into a day/night periods, better measurement compliance was observed at night (23.00–7.00). The average value of MARD during the day was: 19.85%, and at night: 15.33%. When comparing absolute values, the Libre measurement often showed higher values. MRD average (Mean Relative Difference) – comparison of the glucose levels between glucometer/Libre was (-9) mg/dl. Clinical evaluation of the sensor readings compared with the glucometer readings with the use of the Clarke Error Grid showed that 75.2% (2309) of the results were in zone A (acceptable errors) and 95.81% (3012) of the results in zone A and B (non-negative errors). The substantive evaluation of the Libre system by the staff was good. The main problem, arising probably from the conditions in which the device was tested, was the spontaneous detachment of the sensor and the need to back the sensor repeatedly with plasters.

Figure 2 shows individual differences of the MARD index and Figure 3 shows the results of the Clarke Error Grid.

Discussion

Self-control of glycemia is an essential tool for an optimal treatment of diabetes in children and adolescents. Currently, due to the positive correlation between the frequency of self-control and metabolic control, it is recommended that each child should control their glycemia at least 6 times a day (usually 6–10), but the frequency and the time of additional measurements should be arranged individually [1,2]. In practice, due to a different course of the disease in patients, physical and mental maturation, physical exercise, infections, accompanying diseases, there may be a lot more measurements – up to a dozen or so a day. In such situations, properly performed self-control becomes a big challenge. Starting from the child's willingness to perform a measurement, time spent on finger pricking and waiting for the result, to proper hygiene of the pricked place. The current development of medical technology does more than just leads to the improvement of metabolic control and better quality of life of patients with diabetes. Continuous glucose monitoring systems have recently become of particular importance in this regard as they not only inform about current glucose concentration but also educate, motivate to action, and warn in case of emergency [6,7]. The Flash Glucose Monitoring (FGM) device, which has been assessed by us, is currently placed between traditional systems of Continuous Glucose Monitoring (CGM) and traditional blood glucometers due to certain differences. When compared with the CGM, the main disadvantage is the lack of real-time alerts during the hypo- and hyperglycemia, and the necessity for active patient's participation in self-control by regular scans, unlike conventional CGM systems, which transmit the glucose level from the electrode to the reader continuously

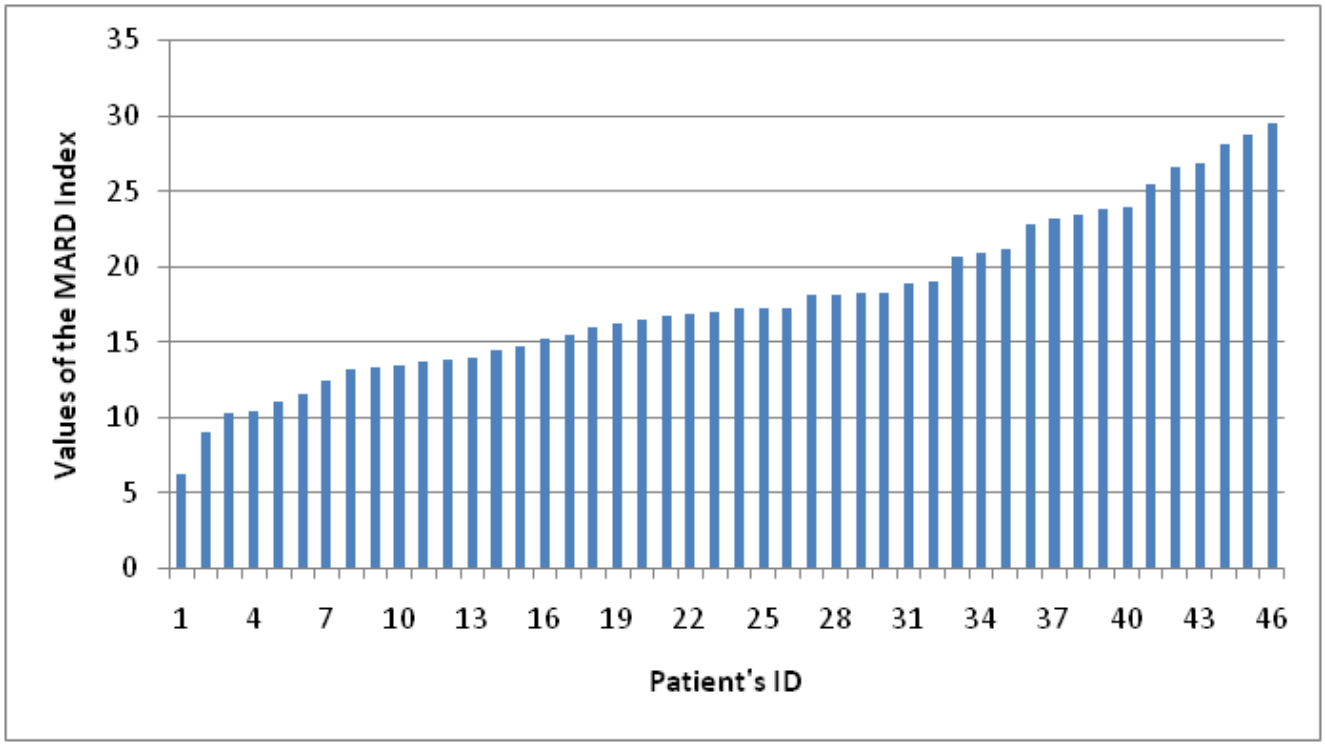

Fig. 2. Individual values of the MARD index (Mean Absolute Relative Difference)
Ryc. 2. *Indywidualne wartości ndeksu MARD*

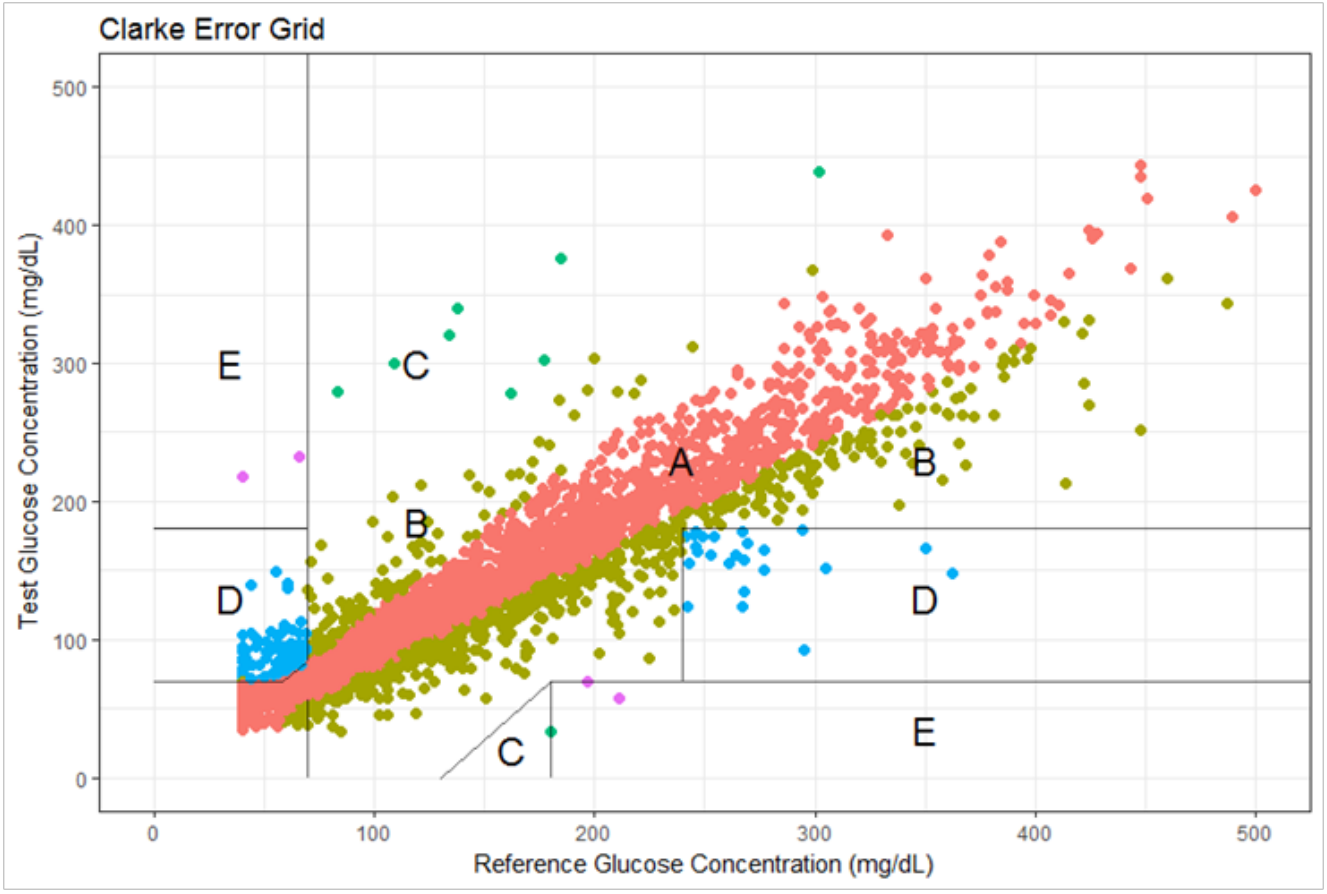

Fig. 3. Sensor accuracy based on the Clarke Error Grid – comparison between sensor and glucometer readings
Ryc. 3. *Dokładność badania na podstawie Clarke EError Grid – porównanie z odczytem w glukometrze*

and automatically without the patient's participation. On the other hand, an important advantage of FGM is the use of factory-calibrated enzyme, which, in practice, means no need for manual calibration of the system by the patients themselves. Despite the differences, the tested system significantly improves, in clinical practice, the process of self-control – it increases the speed (the measurement is reduced to a single scan), discretion (scanning can be done through clothes and the device is not conspicuous) and the hygiene of measurement (no need to injure the skin). Such a situation has a positive effect on the treatment process through increased cooperation in the patient-doctor relationship. In addition, widely available computer programs for reading and analyzing glucose significantly facilitate its documentation and self-analysis of patients' trends and selection of appropriate therapy.

As the FGM Libre system has only been available for a short time, the number of scientific papers assessing the quality and reliability of laboratory measurements, traditional glucometers or comparing FGM Libre with systems existing for a long time is not too large. However, several independent studies conducted in different patients (with type 1 diabetes and type 2 diabetes, in adults and children) confirmed that the measurements by scanning are reliable and are within the limits of permissible error (on the Clarke Error Grid) and MARD indexes amounted to a dozen or so percent, that is they remained at a similar level as in the case of CGM systems which have been available for years [8–11]. The accuracy of measurement is not affected by age, body mass index (BMI), the method of insulin administration or HbA_1c [4,6]. Some studies have confirmed larger differences in comparison with glucometer and capillary blood for lower glucose concentrations [11,12] and during the final days of the sensor operation [4,12]. Some studies [4], but not all of them [6], indicate greater compliance (lower MARD index) with glucometer readings at night – probably because of lower dynamics of glucose fluctuations. Patients evaluating the new measurement method state that the scanning sensor is convenient, fast, very easy, and even easier and less troublesome in comparison with a traditional glucometer [4,6]. Very rarely there may be some temporary skin lesions at the place where the sensor has been located, including: swelling,

pain, erythema, or rash [4,13]. Moreover, there are first reports published, which suggest that permanent use of the sensor may result in a decreased number of hypoglycemias, especially the ones at night, which patients fear the most [13,14].

The research we have conducted using FGM Libre is one of the first ones carried out in a group of children with type 1 diabetes in real-life conditions. The time and conditions of a summer camp, with a completely different lifestyle, different schedule of meals, increased physical activity, and lack of routine control by parents, who know best the individual needs and responses of their children, make it particularly difficult to ensure safe self-control and to achieve effective treatment of diabetes. It is well known that the maintenance of normoglycemia during intense physical exercise is a major therapeutic challenge due to very individual responses [15,16], and the use of constant monitoring may be an alternative tool in safe self-control at this time [17,18]. The difficult conditions in which the Libre sensors were tested in our study (constant contact with the sea, sand, high humidity, high temperature) were, probably in large part, the cause of technical difficulties in keeping the sensor in place and resulted in a shorter service life. On the other hand, the great dynamics of changes of glucose concentration and a very active lifestyle could have caused the considerable discrepancy between the sensor and the glucometer readings observed by certain participants, which is evidenced by relatively high individual variability of the MARD index, and which can be related with the natural delay in such situations. The evaluation of errors on the Clarke Error Grid, obtained in such specific conditions of our study, at 95.81% in zone A and B – as acceptable and harmless mistakes which do not directly affect the behavior of the patient – should be regarded as a relatively high accuracy of the measurement [19,20]. It should be emphasized that the time of testing of the new device was relatively too short to fully learn to interpret the slightly different way of blood glucose control – with the use of additional information in the form of trends, which seems to be more important at the time of high glycemic variability. An algorithm for interpreting and undertaking therapeutic decisions, recently prepared by a group of Polish experts in this field, should be a practical inspiration for patients using CGM / FGM systems and their doctors [21].

Conclusions

The Libre user satisfaction survey revealed that the majority of respondents assessed the cooperation with the Flash FreeStyle Libre system positively. The biggest challenge in the summer camp conditions was the behaviour of the sensor on the skin during the entire of its use. Additionally, in some children the Libre results were at variance with glucometer results, and skin changes (especially itching) were observed after removing the sensor. Despite these drawbacks, the vast majority of patients testing the new device for self-control expressed their willingness to further use the Flash FreeStyle Libre sensor. The comparative analysis of the glycemia results obtained from the sensor/glucometer confirmed the great potential of the glucose monitoring system, even in the difficult conditions of a summer camp for children with diabetes.

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References

1. *Clinical recommendations regarding management of patients with diabetes – position of the Polish Diabetes Association (PTD) 2017*. Clinical Diabetology, Supplement A, A1-A73.
2. Miller KM, Beck RW, Bergenstal RM, Goland RS et al. *Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A_{1C} levels in T1 exchange clinic participants the registry.* Diabetes Care. 2013, 36: 2009-14.
3. Kovatchev BP, Patek SD, Oritz EA, Breton MD. *Assessing the sensor accuracy for non-adjunct use of continuous glucose monitoring.* Diabetes Technol Ther. 2015; 17: 177-186.
4. Bailey T, Bode BW, Christiansen MP, Klaff LJ, Alva S. *The Performance and Usability of a Factory-Calibrated Flash Glucose Monitoring System.* Diabetes Technol Ther. 2015; 17 (11): 787-794.
5. Clarke WL, Cox D, Gonder-Frederick LA, Carter W et al. *Evaluating the Accuracy of Clinical Systems for Self-Monitoring of Blood Glucose.* Diabetes Care. 1987; 10: 622-628.
6. Rodbarg D. *Continuous glucose monitoring: a review of SUCCESSES, challenges and opportunities.* Diabetes Technol Ther. 2016; 18: 3-13 S.
7. Polonsky WH, Hassler D. *What are the quality of life-related benefits and losses associated with real-time continuous glucose monitoring? A survey of current users.* Diabetes Technol Ther. 2013; 15: 295-301.
8. Edge J, Acerini C, Campbell M, Hamilton-Shield J et al. *An alternative sensor-based method for glucose monitoring in children and young people with diabetes.* Arch Dis Child. 2017; 102 (6): 543-549.
9. Ji L, Guo X, Guo L, Ren Q, N Yu, Zhang J. *A Multicenter Evaluation of the Performance and Usability of a Novel Glucose Monitoring System in Chinese Adults with Diabetes.* J Diabetes Sci Technol. 2017; 11 (2): 290-295.
10. Aberer F, Hajnsek M, Rumpler M, Zenz S et al. *Evaluation of subcutaneous Glucose Monitoring Systems under Routine Environmental Conditions in Patients with Type 1 Diabetes.* Diabetes Obes Metab. 2017; 88: 240-248.
11. Ólafsdóttir AF, Attvall S, Sandgren U, Dahlqvist S et al. *A Clinical Trial of the Treatment Experience and Accuracy of the FreeStyleFlash Monitor Glucose in Adults with Libre Type 1 Diabetes.* Diabetes Technol Ther. 2017; 3: 164-172.

12. Bonora B, Maran A, Ciciliot S, Avogaro A, Fadini GP. *Head-to-head comparison between the flash and continuous glucose monitoring systems in outpatients with type 1 diabetes.* J Endocrinol Invest. 2016; 39 (12): 1391-1399.
13. Haak T, Hanaire H, Ajjan R Hermanns N et al. *Use of Flash Glucose Sensing Technology for 12 months as a Replacement for Blood Glucose Monitoring in Insulin-treated Type 2 Diabetes.* Diabetes Ther. 2017 (3): 573-586.
14. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kröger J, Weitgasser R. *Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomized controlled trial.* Lancet. 2016; 388 (10057): 2254-2263.
15. Robertson K, Riddell MC, Guinhouya BC, Adolfsson P, Hanas R. *Exercise in children and adolescents with diabetes.* Pediatric Diabetes. 2014; 15 (Suppl. 20): 203-223.
16. Riddell MC, Gallen IW, Smart CE, Taplin CE et al. *Exercise management in type 1 diabetes: a consensus statement.* Endocrinol Diabetes Lancet. 2017; 5: 377-390.
17. Riddel MC, Milliken J. *Preventing exercise-induced hypoglycemia in type 1 diabetes using real-time continuous glucose monitoring and a new carbohydrate intake algorithm: an observational field study.* Diabetes Technol Ther. 2011; 13: 819-925.
18. Petruzelkova L, Picková K, Sumnik Z, Soupal J, Obermannova B. *Effectiveness of SmartGuard Technology in the Prevention of Hypoglycemia Nocturnal after Prolonged Physical Activity.* Diabetes Technol Ther. 2017; 19 (5): 299-304.
19. Solnica B. *Distorting factors assay using glucose meters. Error meter.* Diabet. Prakt. 2010; 11, 3: 75-79.
20. Blauw H, Keith Hynes-P, Koops R, DeVries JHA. *Review of Safety and Design Requirements of the Artificial Pancreas.* Ann Biomed Eng. 2016 Nov; 44 (11): 3158-3172.
21. Szadkowska A, Gawrecki A, Jarosz-Chobot P, Myśliwiec M, Zozulińska-Ziółkiewicz D. *Proposals for therapeutic decisions according to glucose trends in patients with type 1 diabetes*, Pediatr Endocrinol Diabetes Metab. 2016; 22, 3: 105-117.