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Consensus for the use of flash glucose monitoring in the Colombian adult population with type 1 and 2 diabetes mellitus

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Abstract

Introduction: in Colombia, the Clinical Practice Guidelines for the treatment of patients with type 1 (DM1) and type 2 (DM2) diabetes do not mention the use of flash glucose monitoring, as this system was not available. The objective of this study was to establish a set of recommendations for the use of intermittent flash monitoring in Colombia.

Methods: the group of experts consisted of eight Colombian physicians from different cities within Colombia, with expertise in the management of patients with DM1 and DM2; a certified diabetes nurse educator; a patient with DM1; and a methodological expert. Using the Zoom Enterprise video conferencing application (Zoom Video Communications, San Jose, California), the group generated questions through the Metaplan method, then carried out a systematic literature search and evidence review. The recommendations were made according to the degree of evidence and strength of the recommendation, following the GRADE method.

Results: clinical recommendations were made for: a) patients with DM1 and hypoglycemia; b) patients with DM1 and poor metabolic control; c) patients with insulin-treated DM2; d) pregestational diabetes; e) quality of life; and f) inpatient use.

Conclusions: this consensus's clinical recommendations guide clinical decision making with regard to the use of intermittent flash monitoring in patients with diabetes in various clinical settings. **(Acta Med Colomb 2022; 47. DOI: https://doi.org/10.36104/amc.2022.2239).**

Keywords: *type 1 diabetes mellitus, type 2 diabetes mellitus, continuous glucose monitoring, capillary self-monitoring, hypoglycemia.*

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Introduction

The everyday assessment and recording of glucose levels is essential in achieving good metabolic control in patients with T1DM and those with type 2 diabetes mellitus (T2DM) who use insulin (1). This glucose self-monitoring has been available in clinical practice for approximately three decades using capillary measurement with glucometers.

Recently, alternative or complementary methods have emerged based on the use of a subcutaneous glucose sensor which can produce more measurements per day (2). This large amount of information can create a tracing reflecting the behavior of glucose 24 hours a day, which is why this technology has been termed "continuous glucose monitoring" (CGM) (3).

There are various devices which use real-time CGM (rt-CGM) or retrospective CGM. Patients can use real-time CGM to recognize dangerous glucose levels and take immediate corrective action, which is not possible with retrospective CGM. The clinical situations in which retrospective CGM methods are recommended are usually different from those in which real-time monitoring is recommended (2). In Colombia, rtCGM is only available as part of an integrated treatment system which includes continuous insulin infusion. This is a very expensive system and is restricted to a limited type of patients.

Other parts of the world have rtCGM which is not integrated with insulin pumps (4) and can be used in a certain group of patients who do not need the integrated pump but who are insufficiently controlled with capillary self-monitoring. This *sui generis* technology availability situation in Colombia results in only the most elementary and inexpensive or most sophisticated and expensive technology being available, with no intermediate element, limiting the adoption of diabetes technology recommendations produced in other countries with more therapeutic alternatives.

Recently in many countries around the world, including Colombia, an intermittent glucose monitoring system has become available, an alternative to those already mentioned, known as flash glucose monitoring (5). This technology can be considered more complete as well as more costly than capillary glucose self-monitoring (glucometer readings), but cheaper and, to a certain extent, more clinically limited than rtCGM alone or integrated with an insulin pump (3, 6).

Flash glucose monitoring is a system consisting of a glucose sensor inserted in the skin over the triceps muscle, and a reader for scanning. This system constructs a glucose tracing over time from individual readings made every 15 minutes. The sensor is factory-calibrated and can be used for up to 14 days. Its use has spread significantly over the last two years, replacing capillary glucose recording, as it provides more frequent readings without the need for finger pricks. This device reports the glucose trend through arrows showing the direction of the change, and provides retrospective information on the behavior of glucose over several days, which allows the effect of medications, exercise or other variables to be evaluated, aiding interpretation and treatment adjustments (5).

In Colombia, the Clinical Practice Guidelines for managing patients with T1DM (7) and T2DM (8) do not mention the use of flash glucose monitoring as this system was not available when the guidelines were drafted. With the introduction and availability of this monitoring option in the Colombian market and the possibility of its inappropriate use, evidence-based consensus recommendations were generated by Colombian clinical experts.

Methods

Part of the group who developed the clinical practice guidelines for diagnosing, treating and following patients with type 1 diabetes mellitus over the age of 15 in Colombia, based at Pontificia Universidad Javeriana in Bogotá, acted as the coordinating group for producing the recommendations for the use of flash glucose monitoring, through a panel of experts armed with the best available evidence (9-11). A coordinating group was responsible for selecting the experts; conducting the search for, evaluation and synthesis of the evidence; and preparing the evidence to decision (EtD) framework. The coordinating group was also responsible for creating the questionnaires; ensuring the flow of information between experts during the iterative process of consults and their respective feedback; analyzing the responses in each round and preparing the subsequent questionnaires; and constructing the consensus document.

The group of experts was made up of eight Colombian physicians from various Colombian cities who were experts in the management of patients with T1DM and T2DM, a nurse who was a certified diabetes educator, a patient diagnosed with T1DM and a methods expert (11). Experts were defined as Colombian endocrinologists with at least five years of clinical experience with T1DM or T2DM in adult patients and with indexed publications related to these conditions. The participants reported their conflicts of interest in writing, using a form.

To identify the questions, an initial meeting was held in which the questions produced by the coordinating group were communicated to and rephrased by the group of experts using the Metaplan method, and subsequently definitively established by consensus.

Once the questions were produced, a systematic search of the literature was performed in PubMed using the MESH terms for each question and subsequently applying effectiveness, values and preferences, and economic evidence filters, with priority given to systematic reviews or meta-analyses and high-quality primary studies. Using the EtD data presentation form (12, 13), the body of evidence for each outcome of interest was summarized. Evidence on patient preferences and values regarding the outcomes defined in the PICO strategy was integrated into this same EtD form (14). Once the EtD forms were completed, a general meeting on the Zoom videoconference application (Zoom Video Communications, San Jose, California) was held to produce the recommendations using the nominal group method of personal interaction between the experts. Finally, ongoing email contact was maintained until the definitive written guidelines were approved (15).

The recommendations are presented according to the degree of evidence and strength of the recommendation, following the GRADE tool. Consensus was defined as a minimum agreement of 80% of the experts with the suggested recommendation (eight of ten). Each consensus member drafted a declaration of conflicts of interest, and these are available as an annex. The sponsor did not influence the design or development of this consensus, and it was paid for through an unconditional grant from Pontificia Universidad Javeriana in Bogotá.

Question 1

Does flash glucose monitoring in patients over the age of 18 with type 1 diabetes mellitus and a low risk of hypoglycemia (defined as the absence of severe hypoglycemia or having a normal awareness of hypoglycemic symptoms) reduce hypoglycemia compared

with self-monitoring with capillary glucose measurement with or without a structured educational program?

Summary of the evidence

A randomized, controlled, non-blinded study (IMPACT) was found which included 328 adult patients with T1DM with an HbA1c on admission equal to or less than 7.5%. The mean daily hypoglycemic time was evaluated, which went from 3.38 hours to 2.03 hours at six months (with a mean change of -1.39 hours) in the intervention group and from 3.44 hours to 3.27 hours in the control group (-0.14 hours). The difference in means between the groups was -1.24 (SD 0.239; p<0.0001), equal to a 38% reduction in hypoglycemic time in the intervention group. Thirteen adverse events related to the device were reported, although none were serious (16).

Several articles were found evaluating the effectiveness of flash glucose monitoring (17-20). However, as these studies did not have a comparator (they were single-arm studies), the methodological score was low.

Expert panel discussion

The evidence for the intervention of interest is limited to one controlled, randomized and multicentric study; three prospective studies but with a single arm; one retrospective study; and, regarding the effect of a structured education program, one open, randomized and controlled study. The IMPACT clinical study was not blind, but the panel recognizes the difficulty in blinding this type of intervention. The direction of the effect coincides in both the clinical study as well as the observational studies, which suggests that flash glucose monitoring reduces the risk of hypoglycemia in this population. In addition, the evidence suggests that flash glucose monitoring increases treatment satisfaction and has a similar safety profile to capillary glucose measurement. The group considers that a structured education program and periodic assessment of adherence should be emphasized as good clinical practice. The quality of the evidence was low to moderate.

Recommendation

Flash glucose monitoring is recommended over self-monitoring with capillary glucose measurement in patients with T1DM and a risk of hypoglycemia, but without unperceived or severe hypoglycemia, ideally together with a structured educational program.

RECOMMENDATION. LOW-MODERATE CERTAINTY OF THE ESTIMATED EFFECTS.

Question 2

Does flash glucose monitoring in patients over the age of 18 with type 1 diabetes mellitus and a high risk of hypoglycemia (defined as asymptomatic hypoglycemia and/or a history of severe hypoglycemia) reduce hypoglycemia when compared with capillary glucose self-monitoring together with a structured education program, or with real-time continuous glucose monitoring, or with insulin pump therapy integrated with a real-time continuous monitoring system?

Summary of the evidence

A controlled, randomized pilot study and its extension study were found. This clinical trial included 40 patients with T1DM and a high risk of hypoglycemia. The subjects were randomized to rtCGM or flash glucose monitoring. The authors established the change in hypoglycemic time (<60 mg/dL) as the primary outcome and changes in the Gold score and the Hypoglycemia Fear Survey (HFS-II) as additional outcomes. The difference in the average hypoglycemic time was 4.3% in favor of rtCGM. When the study began, 90% (18/20) of the subjects in the rtCGM group and 85% (17/20) of those in the flash glucose monitoring group had a Gold score ≥ 4; after eight weeks of treatment, this percentage lowered to 60% (12/20) in both groups. No episodes of severe hypoglycemia were reported during follow up in either group (21). In a different article, the authors extended the follow up for eight weeks, in which all patients were assigned to flash glucose monitoring. They found a significant reduction in the percentage of hypoglycemic time (<54 mg/dL) after changing to rtCGM (5.0 [3.7–8.6] vs. 0.8 [0.4–1.9], P <0.001). As a secondary outcome, there was also an improvement in time in range (22).

No evidence was found for the capillary glucose measurement plus structured education program comparator.

Expert panel discussion

The available evidence is from a study with a small sample size and without intervention blinding. The random assignment is unclear and there are inaccuracies in the data. This gives it a risk of serious bias and inaccuracy. In addition, it should be noted that the study did not report severe hypoglycemic episodes during the eight weeks of follow up in the intervention or the control group. The panel considers the finding of improved perception of hypoglycemic symptoms in most patients both in the rtCGM group as well as the flash monitoring group to be important. However, the reduction in hypoglycemic time was statistically greater in the rtCGM group, which suggests superiority of this treatment in this specific group of patients. The availability of alarms in rtCGM might explain the advantage of these devices in this type of patients with a diminished response to hypoglycemia. New versions of the flash glucose monitoring device, which are not available in Colombia, include alarms, but there are no publications yet in this type of population.

Recommendation

In patients with T1DM with a high risk of hypoglycemia (defined as the presence of asymptomatic hypoglycemia and/or a history of severe hypoglycemia), the use of rtCGM, integrated or not integrated with an insulin pump, is recommended over the use of flash glucose monitoring or capillary glucose measurements.

Recommendation. Low certainty of the estimated effects.

Question 3

Does flash glucose monitoring in patients over the age of 18 with type 1 diabetes mellitus and an HbA1c greater than 7% improve glycemic control compared with capillary glucose self-monitoring?

Summary of the evidence

No direct evidence was found regarding the question of interest. Indirectly, the FLASH study was found which included the population, intervention and outcomes of interest, but not the comparator. This controlled, multicenter clinical trial compared the impact of a specific structured education program known as "FLASH" on flash glucose monitoring users compared with the usual care (23). All study participants used flash glucose monitoring and were randomized to the structured education program consisting of four 90-minute sessions over six weeks (Table 1).

The primary outcome was the change in HbA1c after six months of follow up. The percentage of time in range and treatment satisfaction were assessed as secondary outcomes. After six months of follow up, HbA1c improved in both groups, both the group with the educational intervention (-0.28%, 95% CI -0.16, -0.40%) as well as the control group (-0.11%, 95% CI 0.00, -0.22%). However, HbA1c decreased more in the intervention group (-0.17%; 95% CI -0.01, -0.33%; p = 0.033). This difference persisted in the sensitivity analysis after adjusting for age, sex, and duration of the diabetes. As a secondary outcome, the time in range between 70 and 180 mg/dL was evaluated, which increased significantly by 3.8% (95% CI -7.0, -0.5, p=0.027) in the intervention group (23). In addition, the subjects who received structured education reported more frequent use of the trend arrows for daily insulin dose adjustments compared with the control group (69.6% vs. 54.6%, p = 0.003) and a more frequent assessment of the glucose levels after downloading the information in the computer (71.0% vs. 38.5%, p = 0.030) (23).

Expert panel discussion

After evaluating the impact on metabolic control of flash glucose monitoring in controlled clinical trials, the results are inconclusive (24). However, the data from the descriptive studies (25-33) report an improvement in HbA1c and TIR levels which, in the panel's opinion, could highlight the role of cointerventions such as patient education. The consensus panel considers that the integration of an educational program such as DAFNE (Table 2) would be desirable to improve the results of the monitoring device, in line with the Colombian clinical practice guidelines for T1DM patients over the age of 15 (7).

There is a relationship between the number of measurements and TIR (31). However, there is no recommendation regarding the optimal number of daily scans; these have ranged from eight to 14 scans per day in the studies (23-33).

In conclusion, according to the available evidence, the panel recommends that the use of glucose monitoring devices in patients with T1DM and poor metabolic control always be accompanied by frequent scanning and data interpretation, along with the necessary education to help the patient adjust his/her treatment (23, 35) and modify his/her lifestyle (36).

Recommendation

1. ***Compared with capillary glucose measurement, the expert panel suggests using flash glucose monitoring in individuals over the age of 18 with a T1DM***

Table 1. *Summary of the FLASH education program: purpose, content and objective (23).*

Session	Objective	Content	Objectives
First week.	Information regarding the motivation for using flash glucose monitoring.	General information regarding flash glucose monitoring. Understanding the trend arrows.	Classification of the device characteristics. Personal motivation.
Second week	Recognition of glucose patterns	Analyzing glucose values and trends.	Introduction to the six AGP modules Modules 1 & 2: Basic AGP concepts. Discussion about glucose data collection and the software for data analysis.
Fourth week	Treatment adjustments based on recognized AGP patterns.	Use of data to recognize glucose patterns and adjust treatment.	Modules 3-6: Interpreting the AGP and treatment adjustments. Concept discussion and reinforcement, with personal examples.
Sixth week	Review of treatment adjustments.	Dealing with the barriers to reaching goals.	Reinforcement of lessons learned. Preparation of a long-term management plan.

diagnosis and poor metabolic control, ideally combined with a structured "FLASH"-type educational program, along with the DAFNE education.

SUGGESTION. VERY LOW CERTAINTY OF THE ESTIMATED EFFECTS.

2. ***The expert panel considers that flash glucose monitoring offers conditions which strengthen the role of education in T1DM (physical activity, trend interpretation, time in range, etc.), facilitating structured education.***

RECOMMENDATION PRODUCED BY EXPERT CONSENSUS.

Question 4

Does flash glucose monitoring in insulin-dependent patients with type 2 diabetes mellitus improve metabolic control (glycosylated hemoglobin, time in range) and/or improve the quality of life compared with capillary glucose monitoring?

Summary of the evidence

One controlled, randomized clinical trial was found involving 224 adults with T2DM on intensive insulin therapy, which compared the interventions specified in this question (REPLACE). The primary outcome was the difference in HbA1c at six months. Secondary outcomes were hypoglycemia and patient satisfaction. At the end of the study there were no differences in HbA1c between the groups. A subgroup analysis found a greater decrease in HbA1c in patients under the age of 65 who were assigned to flash glucose monitoring (0.53% vs. 0.20) (p=0.301). The hypoglycemic time under 70 mg/dL decreased 0.47 h/day ± 0.13 (p = 0.0006), and time under 55 mg/dL decreased 0.22 ± 0.07 h/day (p = 0.0014), in both cases favoring flash glucose monitoring compared with the control group. No serious adverse events related to the device occurred (37).

In the REPLACE study, total treatment satisfaction was greater in the flash glucose monitoring group (DTSQ 13.1 ± 0.50 vs. 9 ± 0.72; P<0.0001) compared with capillary glucose measurement. The satisfaction with treatment results evaluated with the Diabetes Quality of Life Questionnaire (DQoL) showed a significant improvement in the intervention group (-0.2 ± 0.04) compared with the control group (0.0 ± 0.06); P=0.0259 (37).

An analysis of the use of healthcare resources for all causes seen during the six-month treatment period in REPLACE, based on the United Kingdom NHS costs, showed that the flash glucose monitoring system is affordable compared with eight capillary glucose measurements in patients with poorly controlled T2DM on intensive insulin therapy, along with a decreased use of healthcare resources and reduced long-term hypoglycemic complications (38). *Ontario Health Technology* (39) conducted a systematic review of economic studies and analyzed the budget impact of public financing of flash glucose monitoring in patients with T1DM and T2DM who need intensive insulin therapy. The five-year budget impact analysis found that flash glucose monitoring has a net budget impact of 11.7 million per year in T2DM and 30.9 million dollars at five years.

Table 2. *DAFNE-type education program (34).*

Characteristics	Description
Main objective	To help patients diagnosed with T1DM lead as normal a life as possible, maintaining stable blood glucose levels and reducing the risk of complications.
Target population	Adults (>17 years) diagnosed with T1DM
Content	· Carbohydrate count · Adjusting basal insulin · Rules for adjusting the prandial (or mealtime) insulin · Correcting hypo or hyperglycemia · How to manage glucose levels during exercise · Adjusting insulin during illness
Modality	On-site or virtual.
Schedule for the on-site modality.	Option A: five days from Monday through Friday from 9 am to 5 pm Option B: one day a week for five weeks. Weekly follow up after the course by a muldisciplinary group.
Schedule for the virtual modality.	The online course requires five weeks to complete and weekly video call support.
Staff who teach the course	A nurse or nutritionist certified in diabetes education.
Benefits	Improved glycemic control, decreased hypoglycemia, improved quality of life

Expert panel discussion

The REPLACE study showed no difference in glycemic control between flash glucose monitoring and the intervention in the total population, but did show a difference in those under 65 years old. For the expert panel, this finding has the limitations inherent in subgroup analyses, but could produce hypotheses that need to be evaluated in new clinical studies. The lack of a structured program to identify and treat the glycemic disorders found in the ambulatory glucose profile (AGP) or during scanning could explain the differences between REPLACE and real-life studies which show a clear improvement in HbA1c. These studies show a correlation between the number of scans and the HbA1c reduction, suggesting the decisive role of patient education and adherence. The decreased hypoglycemia shown in the REPLACE study seems to confirm what has been found in the use of flash glucose monitoring in T1DM, in which the decreased risk of hypoglycemia did not depend on a structured education program. The consensus panel considers that the evidence could change significantly over the

next few years and eventually clarify the inconsistencies found in the effect of this technology on glycemic control in patients with T2DM. It should be noted that, in patients with complex insulin regimens and self-monitoring, the REPLACE study suggests benefits in the domains of patient preference and cost.

Recommendation

1. ***The expert panel suggests using flash glucose monitoring in patients with T2DM treated with an intensive insulin regimen with poor glycemic control despite the use of capillary self-monitoring with multiple measurements and a structured education program. Very low certainty of the estimated effects.***

RECOMMENDATION PRODUCED BY EXPERT CONSENSUS.

Question 5

Does flash glucose monitoring in patients with pregestational diabetes mellitus improve metabolic control metrics (time in range, time above range and time below range) and/or reduce maternal and fetal complications when compared with other glucose monitoring modalities such as capillary glucose measurements, real-time continuous glucose monitoring or subcutaneous insulin infusion integrated with a real-time continuous glucose monitoring system?

Summary of the evidence

No clinical studies were found comparing flash glucose monitoring with other monitoring alternatives and evaluating the outcomes specified by the consensus group. As indirect evidence, in 2018, Scott published a prospective multicentric study in 13 centers in the United Kingdom and Austria (40) using flash glucose monitoring in pregnant women, showing the safety and precision of the device in this population. This study included women diagnosed with T1DM (32.4%), T2DM (14.9%) or gestational diabetes (52.7%). Altogether, 39.2% were in their second trimester and 60.8% were in their third trimester, and the study included data from 74 women over the age of 18 with more than 12 weeks of gestation. The authors excluded patients with moderate or advanced kidney disease, a history of diabetic ketoacidosis within the previous six months, an allergy to adhesives, a history of preeclampsia or HELLP syndrome (hemolysis, elevated transaminases and thrombocytopenia) and the use of tocolytics for treating preterm labor during the current pregnancy. A total of 5,031 paired capillary glucose measurements and sensor readings were analyzed. The overall mean absolute relative difference (MARD%) was 11.8%. Altogether, 88.1 and 99.8% of the flash glucose monitoring results fell within Zone A and Zones A and B of the Clarke error grid, respectively, when compared with capillary glucose measurements (40). The sensor's precision was not affected by the type of diabetes, pregnancy trimester, body mass index or type of insulin (40).

The CONCEPTT study (41) is a controlled clinical trial which showed the usefulness of rtCGM added to standard care, compared with self-monitoring using capillary glucose measurements, in pregnant patients with T1DM treated with multiple insulin doses, and its impact on perinatal outcomes such as reduction in the number of newborns diagnosed with large for gestational age (LGA), neonatal hypoglycemia or admission to neonatal intensive care. In addition, it showed a significant reduction in HbA1c, greater time in range (63-140 mg/dl), less time in hypoglycemia (<63 mg/dL) and reduced glycemic variability.

Kristensen's observational study described a population of pregnant women with T1DM who used rtCGM or flash glucose monitoring at any time during gestation. In a subanalysis of this study there were no trimester-specific differences in time in range (63-140 mg/dL) nor in time above range (>140 mg/dL) between rtCGM and flash glucose monitoring. In addition, a clear trend towards improved glycemic control was shown as gestational age advanced, both in women treated with rtCGM as well as in the group treated with flash glucose monitoring (42). However, the women who used rtCGM had less hypoglycemic time.

Finally, a Cochrane systematic review was found comparing different glucose monitoring modalities in pregnant women with pregestational diabetes, but which did not include the CONCEPTT study results. This review did not find any publication using intermittent flash-type monitoring as an intervention, either. The analysis of the various glucose monitoring methods showed no differences in maternal and neonatal outcomes, but it should be noted that few studies were included, these were of very low quality, and the study interventions varied with regard to type and time of use during gestation.

Expert panel discussion

Population studies report that only 15% of pregnant women achieve the HbA1c goal at the beginning of pregnancy, and despite multidisciplinary management with biweekly follow up in specialized clinics, only 40% of women with T1DM reach the HbA1c goal after pregnancy week 24 (41, 43). Maternal hyperglycemia is associated with maternal and fetal complications (44, 45).

The National Institute for Health and Care Excellence (NICE) recommends that blood glucose levels be assessed four to eight times per day to help achieve the glucose goals without increasing the number of hypoglycemic events (40, 46, 47). Strict metabolic control reduces the risk of macrosomia and thus all the risks it entails (48). However, the physiological changes during pregnancy (increased ef-

fective circulating volume, increased plasma exchange and anemia) decrease the reliability of Hb1AC (44), which in addition does not provide information regarding acute glycemic excursions; thus, the presence of hyperglycemia or hypoglycemia in the course of the day cannot be evaluated (49). Therefore, daily capillary monitoring is essential. The panel considers that flash glucose monitoring should be used continuously throughout most of the pregnancy, as opposed to its intermittent use during only a few weeks, especially in patients with pregestational T1DM. These recommendations are based on an expert recommendation due to the very low quality of evidence, and may change substantially as new evidence emerges.

Recommendations

1. ***The use of rtCGM is recommended over flash glucose monitoring in patients with pregestational type 1 diabetes mellitus outside of the pregnancy goals (HbA1c >6.5%).***

RECOMMENDATION. LOW CONFIDENCE IN THE ESTIMATED EFFECTS.

2. ***The continuous use of flash glucose monitoring is suggested over self-monitoring with capillary glucose measurements in patients with pregestational T1DM outside of the pregnancy goals (HbA1c >6.5%) who do not have access to rtCGM.***

VERY LOW CERTAINTY IN THE EVIDENCE - RECOMMENDATION PRODUCED BY EXPERT CONSENSUS.

3. ***Flash glucose monitoring is suggested over capillary glucose measurements in patients with pregestational T2DM or gestational diabetes who have persistently poor metabolic control despite standard nutritional and pharmacological treatment or in whom fetal complications, such as macrosomia, are suspected.***

VERY LOW CERTAINTY IN THE EVIDENCE - RECOMMENDATION PRODUCED BY EXPERT CONSENSUS.

Question 6

What is the impact of flash glucose monitoring on quality of life or patient-reported outcomes in patients over the age of 18 with T1DM and T2DM treated with insulin?

Summary of the evidence

Two published systematic reviews were found. Castellana et al. (50) published a systematic review in 2020 which included 20 studies with more than eight weeks' follow up and evaluated 2,173 patients with T1DM and T2DM with multiple doses or continuous subcutaneous infusion of insulin. The comparator was self-monitoring with capillary glucose measurement (50). The other systematic review was published by Cowart et al. in 2019 and includes nine studies of patients with T1DM and T2DM which also evaluated the previously mentioned glycemic control metrics, overall patient-reported satisfaction, and diabetes-related stress (24). The outcomes reported by the studies varied and are reported in Annexes 1 and 2.

Expert panel discussion

Despite having two published systematic reviews, the results are derived from only a few studies. The results of the IMPACT study on T1DM were analyzed without finding a significant improvement in quality of life. The only thing that showed significant improvement was the global satisfaction results reported by the patients using the DTSQ. Patients with T2DM did report improved quality of life on the DQoL questionnaire and treatment satisfaction on the DTSQ. However, there were no differences in other questionnaires such as the DDS or the Audit of Diabetes-Dependent Quality of Life (ADDQoL). The panel of experts considers that the results are heterogenous and even if the scale domains are analyzed separately, there are different results for each of them. Despite having two published systematic reviews, the results are produced only by the IMPACT study (16) for T1DM and the REPLACE study (37) for T2DM. On that basis, the expert committee considers that using flash glucose monitoring solely to improve the quality of life is not justified, and therefore does not recommend using it for this sole objective.

Recommendation

The panel of experts does not issue a recommendation for the use of flash glucose monitoring as a tool for improving quality of life or other patient-reported outcomes.

VERY LOW CERTAINTY OF THE ESTIMATED EFFECTS.

Question 7

Does flash glucose monitoring improve glycemic control in diabetic patients hospitalized for hyperglycemia, compared with capillary glucose measurements?

Evidence summary

Six studies were found; of these, two studies used flash glucose monitoring. However, none of these studies reported the outcomes of interest. Recently, Galindo published a prospective study of 97 patients diagnosed with T2DM hospitalized in a general ward with an admission glucose level ≥140 mg/dL and <400 mg/dL, no ketoacidosis, and treated with a basal-bolus insulin regimen and blind flash glucose monitoring using the FreeStyle Libre Pro device (51). The primary objective was to evaluate the difference between CGM vs. capillary glucose measurement data. The average glucose was 188.9 ± 37.3 mg/dL

vs. 176.1 ± 46.9 mg/dL, with an estimated difference of 12.8 mg/dL (CI 8.3-17.2); and time in range (between 70 and 180 mg/dL) was 48.4 ± 22.9% for capillary glucose measurement compared with 53.5 ± 28.8% (p≤0.001) for CGM (51). More level 1 (<70 mg/dL), level 2 (<54 mg/dL) and <40 mg/dL hypoglycemic events were detected in CGM users, especially during the night (51). As a secondary objective, the numeric precision was evaluated using the mean absolute relative difference (MARD), showing an acceptable correlation when compared with capillary glucose measurements, except for values under 70 mg/dL. However, this analysis was performed using a very small number of events (51). Regarding clinical precision, 98% of the glucose values were in Zones A and B (51).

In 2017, Ancona published a pilot study of eight patients with T2DM hospitalized in an intensive care unit, seven of whom required vasopressor support. The primary objective was to evaluate the precision and accuracy of flash glucose monitoring in critically ill patients. The flash glucose monitoring readings were consistently lower than the arterial glucose measurements, with a 14% MARD, considering that the reliability of the readings produced by this device was acceptable in the intensive care unit (52).

Expert panel discussion

Hyperglycemia and glycemic variability in the hospital setting is related to adverse events like death, prolonged stay and increased costs (53). Between 12 and 25% of hospitalized patients have a history of diabetes, and 50% of patients admitted to intensive care units have diabetes or prediabetes (54). Various hospital studies have shown the precision and usefulness of CGM for detecting hyper and hypoglycemic events, especially during the night in the general ward (51, 55). The panel of experts considers that these studies focus on the precision of these devices with a short follow up period and small number of patients, which does not allow clinically relevant outcomes like decreased hypoglycemic events, complication rates, mortality or hospital stay to be evaluated. Likewise, the studies which have evaluated the impact of CGM on glycemic control have shown no differences in average glucose compared with capillary glucose measurements.

The panel of experts considers that the implementation of continuous glucose monitoring in the hospital has the potential to decrease the burden of care for hospital nursing staff and facilitates the follow up of patients with complex insulin regimens during hospitalization and after discharge. However, limitations such as making the patient responsible for scanning, the lack of automatic cloud data synchronization, the lack of alarms to alert the healthcare team, the need to transport the device to download data and the lack of cost analyses qualify its implementation in the hospital. Considering the above, there is no evidence to issue a recommendation in favor of or against this intervention.

Recommendation

The expert committee does not issue a recommendation for using flash monitoring to manage hyperglycemia in hospitalized patients.

VERY LOW CERTAINTY OF THE ESTIMATED EFFECTS.

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ABREVIATIONS

ADDQoL: *Audit of Diabetes Dependent Quality of Life***.**

AGP: *ambulatory glucose profile*

CEA: cost-effectiveness analysis

DAFNE: *Dose Adjustment for Normal Eating*

DDS: *Diabetes Distress Scale*

DM: *Diabetes mellitus*

T1DM: Type 1 diabetes mellitus

T2DM: Type 2 diabetes mellitus

DQoL: *Diabetes Quality of Life Questionnaire*

DTSQ: *Diabetes Treatment Satisfaction Questionnaire*

EtD: *Evidence to Decision*

HbA1c: Glycosylated hemoglobin

HFS: *Hypoglycemia Fear Survey*

HRQoL: *Health-related quality of life*

IDF: International Diabetes Federation

CGM: Continuous glucose monitoring

RtCGM: Real-time continuous glucose monitoring

MOOSE: *Meta-analysis Of Observational Studies in Epidemiology*

NHS: *National Health Service*

NICE: *National Institute for Health and Care Excellence*

SF-36: *36-Item Short Form Health Survey*

TIR: time in range

TAR: *time above range*

TBR*: time below range*

NICU: neonatal intensive care unit

ANNEX 1

Outcomes reported by patients with T1DM. Adapted from Castellana et al. (51).

Studies, year. Type of study	Measurement tool	Patient-reported outcomes		
		Positive findings at the end of follow up	Improvement compared with the baseline measurement	Improvement compared with capillary glucose measurements
Al Hayeck, 2017 (2) Prospective study	HFS (children)	-	Yes	-
	PedsQL 3.0 DM Questionnaire	-	Yes	-
Al Hayeck, 2019 (3) Prospective study	Glucose Monitoring Satisfaction Survey	-	Yes	-
Bolinder, 2016 (4) Controlled clinical trial	DDS	-	-	No
	DQoL	-	-	Yes
	DTSQ	-	-	Yes
	HFS	-	-	No
Campbell, 2018 (5) Prospective study	DTSQ (teen)	-	Yes	-
	DTSQ (parent version)	-	Yes	-
Kramer, 2019 (6) Prospective study	DTSQ	-	Yes	-
Landau, 2018 (7) Real-life study	-	-	-	-
Messaaoui, 2019 (8) Real-life study	Likert scale	Yes	-	-
Moreno Fernandez, 2018 (9) Retrospective study	-	-	-	-
Paris, 2018 (10) Prospective study	-	-	-	-

DDS: Diabetes Distress Scale; DQoL: Diabetes Quality of Life Questionnaire; DTSQ: Diabetes Treatment Satisfaction Questionnaire; HFS: Hypoglycemia Fear Survey; FGM: Flash Glucose Monitoring.

ANNEX 2

Outcoomes reported by patients with T2DM. Adapted from Castellana et al. (51).

Studies, year. Type of study	Measurement tool	Patient-reported outcomes		
		Positive findings at the end of follow up	Improvement compared with the baseline measurement	Improvement compared with capillary glucode measurements
Haak, 2017 (37) Controlled clinical trial	DDS	-	-	No
	DQoL	-	-	No
	DTSQ status	-	-	Yes
	DTSQ change	-	-	Yes
Yaron, 2019 (57) Controlled clinical trial	Audit of Diabetes-Dependent Quality of Life	Yes	-	No
	DTSQ status (Hebrew version)	Yes	-	No
	DTSQ change	Yes	-	No

DDS: Diabetes Distress Scale; DQoL: Diabetes Quality of Life Questionnaire; DTSQ: Diabetes Treatment Satisfaction Questionnaire; HFS: Hypoglycemia Fear Survey.