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How often patients on insulin therapy measure postprandial glycemia and modify insulin doses accordingly? From an on-line survey in insulin-treated diabetes patients in Spain

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ABSTRACT

Introduction: Controlling postprandial glycemia (PPG) is important to achieve optimal glycemic control, but few studies have evaluated how often is measured and evaluated.
Objectives: To evaluate how often patients on insulin therapy measure PPG and modify insulin doses accordantly. As secondary objectives, we evaluated the factors conditioning elevated PPG and associated issues.
Material and methods: Cross-sectional observational study based on a web-based survey from an unselected sample of adult insulin-treated patients. A p-value of < 0.05 was significant.
Results: 1251 patients (68% women, 38.9 ± 13 years [mean ± SD], body mass index (BMI) 24.2 ± 4.2 kg/m^2, diabetes duration 17.4 ± 12.8 years, insulin dose 38 ± 18 IU) participated, 1104 with autoinmmune disease (AD) and 147 with non-autoinmmune diabetes (NAD). 59% of patients had HbA1c $\leq$ 7%, 92.7% of patients with AD and 55.8% with NAD were attended by specialists ($p < 0.001$). People with AD did more often blood glucose monitoring (BGM) ($p < 0.0001$) and used continuous glucose monitoring systems (CGMS) ($p < 0.0001$). 90.1% with AD and 68.0% with NAD received instructions on measuring PPG ($p < 0.001$), and more with AD received specific training to change the treatment (87% vs. 61.2%, $p < 0.0001$) and

Abbreviations: ADA, American diabetes association; AD, autoimmune-diabetes; BMI, body mass index, BGM, blood glucose monitoring; CGMS, continuous glucose monitoring systems; EASD, European association for the study of diabetes; FPG, fasting plasmatic glycemia; HbA1c, glycated hemoglobin; IDF, International diabetes federation; LADA, latent autoinmmune diabetes in adults; NAD, non-autoimmune diabetes; PPG, postprandial glycemia; PPH, postprandial hyperglycemia; T1DM, type 1 diabetes; T2DM, type 2 diabetes

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were more proactive. However, more with NAD discussed their postprandial glucose levels with their healthcare team during clinical visits (92.5% vs. 74.1%, $p < 0.0001$). Regarding bolus administration, 88.6% with AD and 68.7% with NAD injected the insulin bolus before meals ($p < 0.001$).

Conclusions: Patients with AD determine PPG more frequently. Diabetes type, follow-up setting, number of injections and CGMS use were the most important predictive factors for PPG measurement. Diabetes education programs should address how to best monitor PPG and appropriate corrective actions.

1. Introduction

Achieving optimal glycemic control is necessary in all people with diabetes to avoid long-term chronic diabetes complications [1]. From interventional studies, reducing glycated hemoglobin (HbA1c) plays a major role in preventing the development and progression of chronic complications [2]. However, in many cases, elevated postprandial glycemia (PPG) is the rate-limiting factor to achieve optimal glycemic control. According to Monnier et al. [3], the relative contribution of PPH on the HbA1c values is higher in those patients with closed to normal glycemic control, whereas basal hyperglycemia is more relevant in patients with elevated on HbA1c values.

Currently, there is no consensus on the definition of postprandial hyperglycemia (PPH) in the literature. Different scientific societies use diverse definitions of PPH in their guidelines. According to the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), the PPG target 1–2 h post-meal should be less than 180 mg/dL while the International Diabetes Federation (IDF) recommends a PPG target of less than 160 mg/dL [1,4].

Traditionally, the emphasis in diabetes treatment has been focused on targeting on HbA1c and bringing fasting plasma glycemia (FPG) under control. Recent data suggest that controlling PPG is also important to achieve optimal glycemic control, especially when patients are closed to their individual target, and also in reducing excessive glycemic variability [5,6]. These data raise the importance of giving additional information to clinicians and patients in relation to PPG control. In fact, current development of prandial insulins is focused on finding ultra-rapid acting analogues that can be administered just before meals just to improve PPH [7,8].

Several epidemiological studies have suggested an association between fluctuations in PPG and cardiovascular risk in patients with prediabetes and type 2 diabetes (T2DM) [9,10]. However, intervention studies have not shown that selective control of PPH is associated with any cardiovascular benefits [11]. On the other hand, recent studies in T2DM have revealed that postprandial glycemic excursions is associated with cognitive impairment [12], increased risk of some tumors [4] and endothelial dysfunction [10]. But association of PPH with diabetes chronic complications is not well established [13]. Despite these considerations, from a clinical point of view it remains relevant to offer all patients individualized treatment goals for fasting and PPG levels in order to reduce the deleterious effects of PPH. Another important issue to take into consideration are the costs derived from PPH. According to a study conducted by Brod et al. [14], the costs are higher because of higher health resources consumption related to more frequent health provider visits and increased risk of chronic complications.

More recently, the widespread use of continuous glucose monitoring systems (CGM) has revealed that patients experience excessive glucose excursions more frequently than expected, because patients don't usually measure PPG. In fact, these findings suggest that available rapid-acting insulin analogues used are not quick enough to control PPG. Then, there is a demand of developing ultra-fast acting insulin analogues such as faster aspart to solve this unmet need [8].

Despite all the aforementioned considerations, there is a lack of studies that have evaluated how often patients measure PPG, which factors influence PPH, how subjects respond to PPH and what they do to avoid or solve these situations. Recently, a web-survey on this topic performed in Germany, UK and USA has been published [14]. In this survey, very few patients measured PPG and even less made some changes to solve it. This aspect is particularly important for patients with diabetes on insulin treatment.

Due to the scarce available data regarding PPH control in our country, we perform a national on-line survey to know the real situation on PPH control in Spain. The main objective of this study was to evaluate how often patients on insulin therapy measure PPG and modify insulin doses accordantly. As secondary objectives, we evaluated which factors have an influence on PPH, how important is PPG for patients, if patients discussed PPG values during clinical visits and their association with overall glycemic control.

2. Methods

2.1. Study design

It was a cross-sectional observational study performed on a web-based survey. An unselected sample of adult patients (≥18 years-old) with diabetes on prandial insulin-treatment

were invited to participate. The web-based survey was conducted in Spain between February and September of 2018. All the data were self-reported.

2.2. Study population

To be eligible for the survey participants were required to have any type of diabetes (type 1 diabetes, type 2 diabetes, MODY or LADA) and be treated with prandial insulin-treatment with or without oral antidiabetic agents. Any modality of insulin therapy (basal plus, basal bolus, premixed insulin with 2–3 daily injections or continuous subcutaneous insulin infusion [CSII]) are accepted. The main exclusion criteria were younger than 18 years-old, pregnancy, severe hepatic insufficiency, advanced renal impairment, psychological disturbances, or treatment with corticosteroids or immunesuppressants.

The study protocol was in accordance with the Helsinki Declaration and was approved by the Ethics Committee for Clinical Research of the University "Hospital Fundación Jiménez Díaz", Madrid, Spain.

Participants did not receive any payment to collaborate on this survey.

2.3. Survey development

To develop the survey, an analysis of data from a pilot semi-structured survey with 30 participants was used. The final survey consisted of 12 questions. Time estimated to complete the survey was approximately 20 min.

A multisource informant strategy was used to recruit participants. The survey was available on the website of the Diabetes Foundation https://www.fundaciondiabetes.org/ and the Canal Diabetes website https://www.canaldiabetes.com/. The web-based survey was finally administered to initial respondents to a formal invitation if they met the inclusion criteria and signed electronically the informed consent to participate.

All the participants' data and their answers were handled as anonymous.

2.4. Survey variables

Survey items were designed to assess demographic information, diabetes status and different aspects of glucose management. Demographic variables included age, gender, size, weight, place of residence and educational level.

Diabetes status included type of diabetes (type 1 diabetes, type 2 diabetes, MODY or LADA), disease diagnosed before 40 years-old or not, duration of diabetes, insulin treatment since diagnosis, insulin modality (basal bolus, basal plus, premixed, CSII), number of insulin injections per day, insulin type, total insulin daily dose, estimated mean FPG (<70 mg/dL, 70–140 mg/dL, 140–180 mg/dL, >180 mg/dL), last HbA1c (<6.5%, 6.5–7%, 7–8%, 8–9%, >9%), and level of follow-up (primary care, tertiary care or both).

Glucose management measurements included frequency of capillary blood glucose determinations (1–3, 3–7, 7–21, more than 21 times per week); given recommendations or not to assess postprandial glucose; frequency of postprandial glucose determinations (never, rarely [1–2 times per month], occasionally [1–2 times per week], frequently [>2 times per week but not daily], daily); use of CGM; timing of prandial insulin administration (before, with, of after meals, or not fixed); preferred area of bolus insulin administration (arms, thighs, abdomen, any area); changes of needles for insulin injection (with each injection, every day, 1 time per week, with each insulin pen, every 2–3 injections); knowledge about suitable postprandial glucose levels; given recommendations about treatment modifications in case of inappropriate postprandial glucose levels; treatment modifications in case of unsuitable postprandial glucose levels (never, rarely [1–2 times per month], frequently [>2 times per week but not daily], daily); repeat or not capillary blood glucose determinations after treatment changes; assessment with health care team eventual treatment changes and knowledge about the relevance of postprandial glucose assessment (not relevant, possibly, confident).

2.5. Statistical analysis

The sample size was chosen based on a previous analysis plan and to ensure that comparisons could be made between selected aggregated groups of patients, i.e. autoimmune (Type 1 diabetes and LADA) and non-autoimmune diabetes (type 2 diabetes and MODY). Continuous variables were shown as mean and standard deviation, whereas categorical variables were presented as frequency (%). All statistical analyses were carried out using IBM SPSS statistical software 23 version. T-tests were used for comparison of means between two groups. Chi-square was used to test for significant associations between categorical variables. All analyses were conducted by diabetes type (autoimmune vs non-autoimmune diabetes). A p value of less than 0.05 was considered statistically significant.

3. Results

3.1. Sample description

A total of 1251 subjects completed the survey, mostly with autoimmune diabetes (88.3%). 1104 of participants had autoimmune diabetes (type 1 diabetes or LADA) and 147 had non-autoimmune diabetes (type 2 diabetes or MODY). Descriptive parameters by aggregated diabetes type are shown in Table 1.

As expected, participants with autoimmune diabetes were significantly younger, were also younger at diagnosis and started earlier insulin therapy. In addition, they were significantly thinner, used less total daily insulin doses and less premixed insulins. The duration of diabetes was similar in the two groups.

Overall glycemic control as expressed by HbA1c levels were similar in patients with autoimmune or non-autoimmune diabetes. Distribution of patients by HbA1c cut-offs of those with autoimmune diabetes were [n, (%)]: <6.5%, 268 (24.3%); 6.5–7%, 383 (34.7%); 7–8%, 348 (31.5%); 8–9%, 79 (7.2%); >9%, 26 (2.4%). Regarding those with non-autoimmune diabetes, numbers and percentages were

Table 1 – Patient demographic and diabetes characteristics by aggregated diabetes type.

Variable	Autoimmune diabetes (n = 1104)	Non-autoimmune diabetes (n = 147)	*p value*
Age (years),	38.9 (13)	58.9 (10)	p < 0.0001
Gender (male, %)	39.7	68.0	p < 0.0001
BMI (kg/m^2),	24.2 (4.2)	28.9 (6.2)	p < 0.0001
Diabetes duration (years)	17.4 (12.8)	16.1 (9.6)	NS
Diagnosis of diabetes before 40 years, %	88.2	42.2	p < 0.0001
Total daily insulin dose (IU)	38 (18)	42 (25)	p = 0.01
Insulin treatment since the diagnosis, %	92.2	27.2	p < 0.001
Premixed insulin, %	26.5	58.5	p < 0.001

*p < 0.05. Data presented as means ± (SD), counts or frequencies (%). NS = not significant; SD = standard deviation; BMI = body mass index.

[n, (%)]: <6.5%, 29 (19.7%); 6.5–7%, 45 (30.6%); 7–8%, 58 (39.5%); 8–9%, 11 (7.5%); >9%, 4 (2.7). A higher percentage of patients with autoimmune diabetes had an HbA1c lower than 7% (p = 0.05).

Regarding academic education level, patients with autoimmune diabetes had significant higher education level (p = 0.001), with more percentage of patients with university studies (38.3% vs 24.5%) and master/PhD (14.9% vs 3.4%).

More patients with non-autoimmune diabetes were followed up by primary care physicians (n = 65, 44.2%), but only few of those with autoimmune diabetes (n = 81, 7.3%). By contrast, 1.023 (92.7%) patients with autoimmune diabetes and 82 with non-autoimmune diabetes (55.8%) were attended by specialists, and these differences were significant (p < 0.001).

3.2. *General glucose and insulin management*

Frequency of capillary blood glucose measurements is shown in Table 2. People with autoimmune diabetes checked more times their capillary blood glucose (p < 0.0001). In addition, as expected, more patients with autoimmune diabetes used CGM than patients with non-autoimmune diabetes, either continuously (33% vs 10.9%) and intermittently (22.7% vs 15%) (both, p < 0.0001).

There were more patients with non-autoimmune diabetes who changed the needles with each injection (42.9% vs 37.3%, p < 0.001), but also still even more who changed the needle only with the change of insulin pen (19.7% vs 7.3%, p < 0.001). Asking about changes of needles for insulin injection 4 patients with non-autoimmune diabetes and 170 patients with autoimmune diabetes (in this last case because they were on treatment with CSII) did not respond to this question.

3.3. *Postprandial glucose management*

More patients with autoimmune (90.1%, n = 995) and non-autoimmune diabetes (68.0%, n = 100) recognized that measure PPG has been recommended by their healthcare team, being this difference significant (p < 0.001). Regarding the frequency of postprandial glucose determinations, the data are shown in Fig. 1.

While the 88.6% of patients with autoimmune diabetes and 68.7% with non-autoimmune diabetes injected the insulin bolus before meals, there were still 8.8% with autoimmune diabetes and 9.5% with non-autoimmune diabetes who administered the insulin after meals. In addition, 2.6% and 21.8% with autoimmune and non-autoimmune diabetes, respectively, changed usually the time of bolus administration. Interestingly, patients with autoimmune diabetes, when compared with non-autoimmune diabetes, were significantly more likely to inject insulin bolus before meals, p < 0.001.

The preferred site of injection of prandial insulin for autoimmune diabetes patients were into abdomen in 54% (596), arm 9.4% (104), thigh 7.7% (85) or indifferent in 25.7% (284). For patients with non-autoimmune diabetes the preferred sites for injection were into abdomen in 53.7% (79), arm 12.2% (18), thigh 9.5% (14) or indifferent in 16.3% (147). Only 35 patients with autoimmune diabetes and 12 patients with non-autoimmune diabetes did not declare the preferred site for rapid insulin injection. Although the percentage of injection in the abdomen was similar, patients with autoimmune diabetes changed the injection site more frequently (p = 0.005).

Most patients (92.6%, n = 1.022) with autoimmune diabetes and 70.1% (n = 103) patients with non-autoimmune diabetes answered that they knew about the appropriate postprandial glucose values (p < 0.0001). In addition, 87% (n = 961) in the first group and 61.2% (n = 90) in the second group affirmed that they had received specific training to change the treatment in case of high or low postprandial glucose levels, being this difference significant (p < 0.0001). But, asking about modification of treatment, patients with autoimmune diabetes were more proactive in doing changes in treatment regarding their postprandial glucose levels (p < 0.0001) (Table 3). Only 21 patients in autoimmune diabetes group and 19 patients in non-autoimmune diabetes group did not respond to the question.

Most patients with autoimmune diabetes (87.4%, n = 965) recognized that they used to repeat postprandial glucose measurements if they made changes in treatment as compared to only 60.5% (n = 89) patients with non-autoimmune diabetes (p < 0.0001).

The majority of patients with autoimmune diabetes (92.5%, n = 1.021) and 74.1% (n = 109) with non-autoimmune diabetes discussed their postprandial glucose levels with their healthcare team during clinical visits (p < 0.0001). Based on their experience, the importance given by the patients about the relevance of assessing the postprandial glucose levels

Table 2 – Frequency of home blood glucose measurements by aggregated diabetes type.

	Autoimmune diabetes (n = 1104)	Non-autoimmune diabetes (n = 147)	*p value*
Never	0.2%	0%	NS
1–3 times per week	1.5%	16.3%	p < 0.001
3–7 times per week	3.5%	17.7%	p < 0.001
7–21 times per week	13.6%	32.7%	p < 0.001
>21 times per week	81.2%	33.3%	p < 0.001

*p < 0.05. Data presented as frequencies (%). NS = not significant.

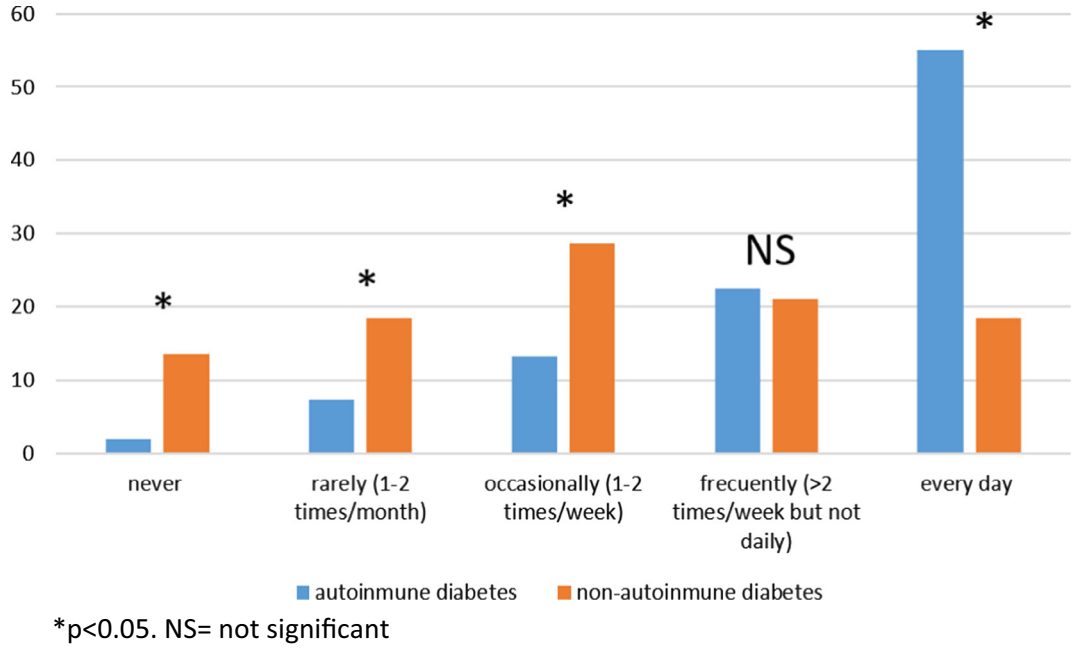

Fig. 1 – Frequency of postprandial glucose determinations according to aggregated diabetes type. *p < 0.05. NS = not significant.

Table 3 – Frequency of changes in insulin dosing after checking PPG by aggregated diabetes type.

Frequency	Autoimmune diabetes (n = 1,104)	Non-autoimmune diabetes (n = 147)	*p value*
Never	2.7%	19.7%	p < 0.001
1–2 times per month	8.5%	21.1%	p < 0.001
>2 times per week, not daily	26.4%	18.4%	p < 0.001
Daily	60.4%	27.9%	p < 0.001
Not response	1.9%	12.9%	

*p < 0.05. Data presented as frequencies (%). NS = not significant.

are represented in Fig. 2. Autoimmune diabetic patients were more confident in the importance of measuring postprandial glucose levels (p < 0.0001).

4. Discussion

We present the results of a Spanish nationwide on-line survey that was developed in order to know in our environment the importance of PPH and the concerns and behavior of patients with PPH. Consistent with prior studies [15], this survey shows that PPH is a real challenge in diabetes management among insulin-treated people with autoimmune and non-autoimmune diabetes. In this unselected on-line sample of insulin-treated adults with diabetes, only 50.7% measured their PPG, despite it was recommended by HCP and PPG measurement was considered relevant for most of them (95%). Bearing in mind the well-known importance of PPH, few patients measure PPG and even less do some changes to control it. This fact is particularly important for patients with diabetes on insulin treatment.

Overall glycemic control as expressed by HbA1c levels was similar between groups but a higher percentage of patients

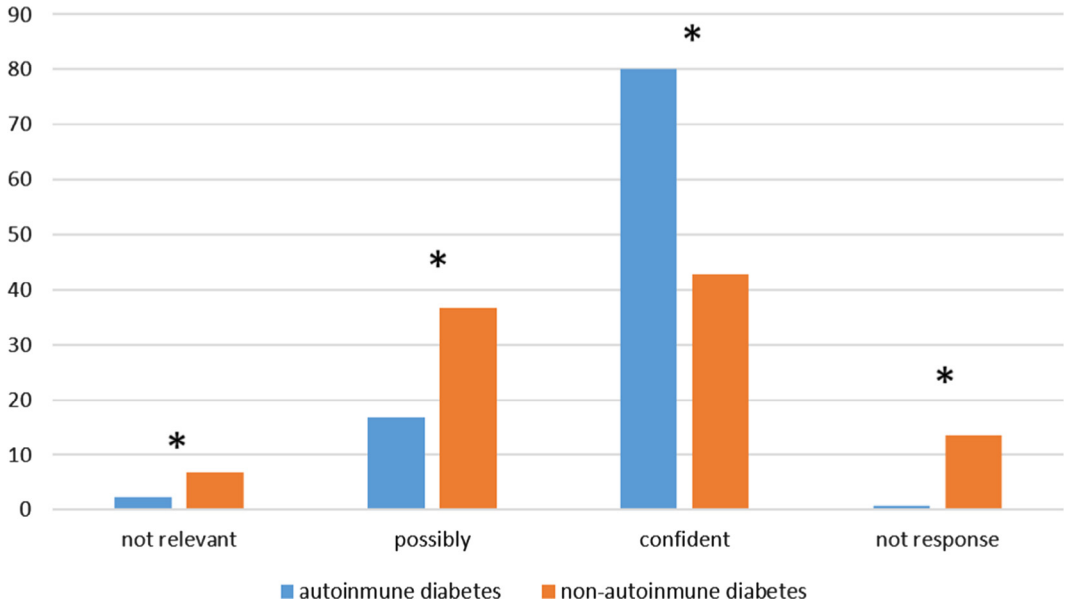

Fig. 2 – Importance of PPG determination according to aggregated diabetes type. *p < 0.05. NS = not significant.

with autoimmune diabetes achieved an HbA1c $\leq$ 7%. Recently, an online survey reported a mean (SD) self-reported most recent A1C value at last test across countries participants (USA, Canada, the UK, Germany, Spain, and Mexico) between 6.8% (1.3) and 7.3% (1.6), with over half of respondents (57%) reporting an HbA1c level of at least 7.0% [16].

From a cohort retrospective study, in a tertiary university hospital in Catalonia and collected in 1994, mean (SD) HbA1c in patients with T1D diabetes 5 years before and in the last year were 7.8% (0.9) and 7.7% (1.1), respectively (7.3% [1.5] in those given CSII) [17]. Regarding T2DM, a Spanish cross-sectional study including more than 3 million T2D patients showed a mean (SD) HbA1c value of 7.15% (1.5), and 56% of the subjects had HbA1c values $\leq$ 7% [18].

Brod et al. [14] performed also a survey on PPH with 906 respondents completed the survey. PPH was frequent among patients with T1DM and T2DM; 61.9% of respondents had experienced PPH, and no differences were found by diabetes type. In our study, 26.4% of subjects changed their insulin dose after measuring PPG more than 2 times per week in the autoimmune diabetes group and 18.4% percent in the non-autoimmune group. The percentage was higher when they measured the PPG daily, 60.4% in the autoimmune diabetes group vs 27.9% in non-autoimmune diabetes. These data are similar to those reported by Brod et al., were 62% of respondents with PPH took insulin bolus based on the glucose levels readings.

A Canadian observational study showed that one out three of the patients measured their PPG and for those who did, only one third part were within the recommended target, suggesting that these patients, and probably the responsible physicians, are not aware of the importance of measuring PPG [19]. In our study the 81.2% of autoimmune diabetes patients and the 33.3% of non-autoimmune diabetes patients measured their blood glucose levels more than 21 times per week, so they were warned that PPH was present. In the Brod et al. study [20], more than half of the respondents reported that they knew that they were experiencing PPH because they had measured their blood glucose levels (64.8%) and/or because they didn't feel good (51.9%). However, PPG monitoring was limited among people with T2DM treated with non-insulin therapies [14]. It is important to consider that, the epidemic dimension acquired by T2D is of global concern. As poor control of the disease is a leading cause of death in most developed countries and is associated with micro and macrovascular complications we have to look for implementing both nonpharmacologic and pharmacological interventions to reduce PPH with the same intensity we treat fasting hyperglycemia.

Another important question would be how to re-educate patients to avoid PPH.

The goal will be facilitating health care providers and other interested parties with the information they need to make informed decisions that could help on patient care.

Brod et al. [20] reported that eating fat and sugar were the main causes of PPH (31.2%) and also over-eating in relation to their calculated bolus insulin dose (30.4%). In our study, the predictive factors for PPG measurement and based treatment changes were Type of diabetes, follow-up setting (specialized vs primary care settings), CGM use and number of insulin injections. Duration of diabetes was similar in the two groups, with a mean 17.4 and 16.1 respectively in patients with autoimmune vs non- autoimmune diabetes.

In relation to the setting of follow-up, more patients with non-autoimmune diabetes were followed up by primary care physicians (44.2%) instead of those with autoinmmune diabetes (7.3%). By contrast, 92.7% of patients with autoimmune diabetes and 55.8% with non-autoinmmune diabetes were attended by specialists, and these differences were significant. In Spain, the majority of T1DM patients were diagnosed and controlled in specialized pediatric or endocrinology

settings, while T2D were more frequently followed in primary care settings [17].

Regarding the use of CGM, as expected, more patients with autoimmune diabetes used real-time or intermittent CGM. Use of CGMS allows diagnosis of glycemic variability during the day and between days, and this cannot be detected assessing only HbA1c levels. Thus, for the accurate diagnosis of glucose variability and PPH is necessary to use a CGMS [21]. However, lack of reimbursement of CGMS in the past explain the low use of these systems in most of the regions of Spain, but this will be changed in the near future.

Regarding some educational aspects, 92.6% in the group of autoimmune diabetes and 70.1% in the group of non-autoimmune diabetes answered that they knew the suitable postprandial glucose levels. In addition, 87% in the first group and 61.2% in the second group affirmed that they had received specific training to change the treatment in case of high or low postprandial glucose levels. But, when asking about modification of treatment, patients with autoimmune diabetes were more proactive in doing changes in treatment regarding their postprandial glucose levels. Ongoing educational support in patients with diabetes with refresh sessions is mandatory to extend the benefits of the intervention [22]. Patients should be instructed and motivated to change to a healthier lifestyle with increased physical activity and to switch to a diet with an appropriate caloric intake with a reduction in fat and refined carbohydrates according to their PPG levels [23]. Moreover, previous studies have shown that premeal ingestion of whey protein, as well as altering the macronutrient composition of a meal, reduces PPH [24]. Foods with a lower glycemic index have a positive effect on postmeal glucose and cardiovascular risk factors [25]. Additionally, regular aerobic exercise is the cornerstone treatment for the delay and/or prevention of T2D, due in part to its transient effects on postprandial metabolism and skeletal muscle insulin sensitivity that can last upward of approximately 48 h after the last exercise bout [26]. Group-based education interventions are more effective than individual education during clinical visits, but this aspect was not analyzed in our study. We need to teach patients in self-monitoring of PPG and explain to them how it allows to obtain actual concentrations of their blood glucose with sufficient accuracy. By measuring not only fasting but also postmeal glucose, patients have good feedback on their glucose excursions and can make therapeutic decisions based on those measurement results. The frequency of testing depends on therapeutic modality and individual characteristics such intrinsic hypoglycemic risk, etc. According to PPH we have to select those drugs acting preferentially on postmeal hyperglycemia, but the final choice of drugs should always take into account efficacy for the patient, safety, and cost-benefit issues.

In patients on intensive insulin therapy, timing of bolus in relation to meals is crucial to control PPH. Few studies have analyzed when people with diabetes administer bolus insulin at mealtime. In our study, patient with autoimmune diabetes, when compared with non-autoimmune diabetes, were significantly more likely to inject the insulin bolus before meals. This fact has practical implications, as new ultra-rapid acting insulins have been developed to specifically address PPH. This is concordant with the results from a survey conducted in Germany, UK and USA [27], where a majority of respondents reported bolus before meals. Also in the study of Datye et al. [28], 65% of patients administered insulin before meals. In addition, in several studies participants who gave insulin prior to meal had significantly lower HbA1c than those who gave insulin during or after meal [28,29]. Also, participants who reported administering insulin during or after meal were more likely to report missing insulin doses and to have ketoacidosis episodes [28]. It is also proved that patients who used bolus dosed before meals were significantly more likely to perceive bolus dose timing as flexible [20]. Currently, after launching of the new ultra-fast acting insulins more flexibility in the timing of bolus dosing is expected [30,31]. A better understanding of bolus dose timing among people with diabetes may improve diabetes education programs for more complex insulin regimens [27].

Lipohypertrophy is the consequence of a bad insulin injection technique and less than recommended change of insulin needles, and may have a major impact on PPG values. Insulin injection technique and needle characteristics play an integral role in patient satisfaction and targeting for metabolic control [32]. In our study, despite more patients with non-autoimmune diabetes changed needles with each injection as compared with those with autoimmune diabetes, still 7.3% of those with non-autoimmune diabetes changed the needles only when they finish insulin pens. A recent systematic review performed by Spanish investigators summarized the available evidence about the safety of reuse disposable needles for subcutaneous insulin injection and found no clear scientific evidence to suggest for or against the reuse of needles [33]. In 2014–2015, the largest international survey of insulin injection technique in patients with diabetes (T1D and mostly T2D) taking insulin was conducted and reported that 80% of patients reuse pen needles and 57% reuse syringes with 27% having lipohypertrophy [34].

This is the first online survey developed in Spain to assess the importance of PPH measurement. One of the strengths of this study is the great number of patients with diabetes who has answered the survey and that it was a nationwide study with representation of different regions in our country. We evaluated not only frequency of PPG measurements but also related features and discussion of the results with HCP during clinical visits.

However, this study has some limitations, which should be taken into consideration. First, in this study all survey data were self-reported. As in every self-reported survey, reporting accuracy could be a concern, as recall bias may have influenced on the results. In addition, as in most studies based on internet surveys, data may be affected by selection bias. People who had access to the internet survey were probably those patients with high intellectual level, with computer and internet access, and more concerned about their disease and the importance of measuring PPG. They measured probably their blood glucose levels more frequently and did more changes after checking their glucose levels.

Another limitation is that the diagnosis of diabetes was not confirmed by a physician, and some of the respondents might have reported a diabetes diagnosis, diabetes type, etc., inaccurately. Finally, we focused only in insulin-treated patients, and therefore we cannot obtain information about

PPG measurements in non-insulin treated people with diabetes. Despite the study limitations, the findings have clinical implications and suggest opportunities to improve diabetes education and care.

5. Conclusions

Patients with autoimmune-diabetes (T1DM and LADA) determine their blood glucose levels more frequently, at least 3 times per day, and half of them, measure blood glucose levels daily as compared with those with non-autoimmune diabetes (T2DM and MODY). In our environment, type of diabetes, follow-up setting (specialized vs primary care settings), use of CGMS and number of injections were associated with the highest probability of PPG measurement.

In addition, in this unselected on-line sample of insulin-treated adults with diabetes, 50.7% measured their PPG, despite this was recommended by HCP, and most of them (95%) considered PPG measurement as relevant.

The results of this study also have implications for improving diabetes education and the day-to-day management of diabetes. Diabetes education programs should address how to monitor PPG, strategies for preventing elevated PPG, and appropriate corrective actions following PPH. Thus, improvements in diabetes education on PPG and its treatment are key to ameliorate overall glycemic control.

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Declaration of Competing Interest

The authors declare no conflict of interest

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.06.007.

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