ORIGINAL ARTICLE

Use of Ambulatory Glucose Profile for Improving Monitoring and Management of T2DM

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Abstract

Aim: To demonstrate glycemic variability in type 2 diabetic patients and consequent control of the same.

Methods: 108 patients with type 2 diabetes with an HbA1c level of 7.5-8.5% were selected for the study. A Freestyle Libre Pro AGP sensor was applied to the patients after explaining the patient about the same. Next, they were called for follow up at 3rd, 7th, 11th and 14th days. Based on the readings and graph obtained, diet and treatment changes were made on various follow-up days. The sensor was removed at the end of 14 days.

Results: Out of the 108 subjects, 106 completed the study. There were no adverse device effects. 98 patients had therapy changes while the rest had diet and lifestyle modifications. The mean HbA1c decreased from 7.96% to 7.03% by the end of 15 days. The glycemic variability curves helped in recognizing and treating masked or asymptomatic hypoglycemic events. It also graphically shows intervals of optimal and sub-optimal glycemia.

Conclusion: AGP is one of the most recent, innovative developments that are being used to monitor Glycaemic variability in DM patients. AGP is generated from the Flash Glucose Monitoring device which is like a CGM device attached to the patient for a maximum period of 14 days, which checks the ISF glucose at every 15 minutes. We are able to get a Glycaemic variability curve, a median, a modal, various percentiles and statistical data generated through this.

AGP study in the patient provides the doctor with an opportunity to have a complete glycemic picture of the patient l. It offers a reliable, predictive, standardized visualization of the glucose data. We were able to not only reduce the Glycaemic variability but were also able to improve their Quality of Life by reducing the frequency of hypos. The data lead to breaking of the clinical inertia and provided a valuable insight into Glycaemic patterns. The achievement of near to normal Glycaemic status at the end of 14 days reflected the use of AGP as an interventional tool.

Introduction

Diabetes mellitus is estimated to rise 171 million (2.8%) in 2000 to 366 million (4.4%) in 2030.[1] due to lack of awareness and proper patient education diabetes is usually poorly controlled and there still are many undiagnosed sub-clinical cases of diabetes.[2] SMBG forms an integral part in diabetes care and management. A good metabolic control can be achieved by a combination of regular blood glucose monitoring, good patient education and appropriate treatment. HbA1c has been used to assess a good glycemic control. However, it has been seen that it is a poor predictor of glycemic variability. For example a patient with HbA1c of 7% may experience significant glucose fluctuations.[3] increased glucose variability is associated with oxidative stress which plays a significant role in the pathogenesis of diabetic complications.[4]

Figure 1 shows the AGP sensor and the reader

The Ambulatory Glucose Profile consists of a small, round sensor – around the size of a 10 rupee coin that has to be applied on the back of the arm; it measures the interstitial blood glucose every 15 minute with the help of a small filament that is inserted subcutaneously. The glucose readings can be obtained by a reader. Each result shows ISF glucose value, showing the glycemic trend of the patient. It functions for a maximum of 14 days.

Figure 2 represents five curves of AGP represents five curves which demonstrate the median level of control and provide an index of variability in control at every hour of a typical day, both inter as well as intraday variability.[5]

The following study has been done to show the glycemic variability in apparently well controlled type 2 diabetic patients and consequent decrease in the glycemic variability with` appropriate dietary and medical

Fig. 1: AGP sensor and reader

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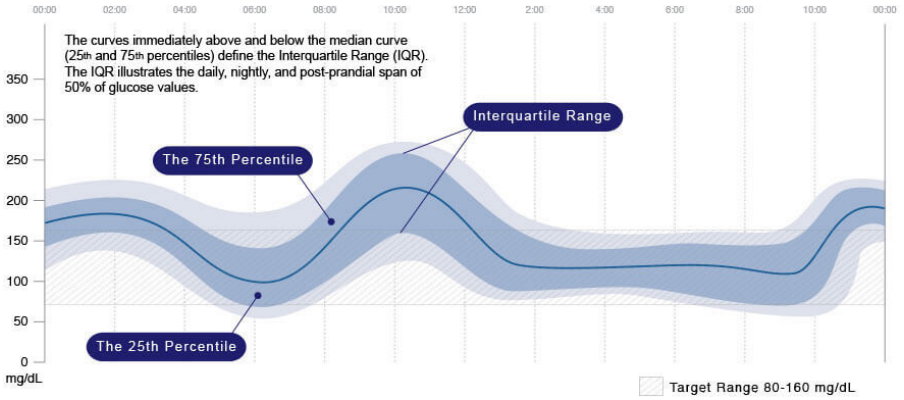

Fig. 2: AGP graph depicting median, 10th to 90th percentile and 25th to 75th percentile graphs

management. Thus, it can be used as a comprehensive tool to understand the patient's metabolic fluctuations.

Methods

The study was conducted at Diacare-Diabetes care and Hormone clinic, Ahmedabad, Gujarat. An informed consent was taken from all the patients prior to the application of AGP for the study.

Inclusion criteria: T2D patients with an HbA1c level between 7.5-8.5% of the age group 35-55 years with a diabetes duration of 1 year or more.

Exclusion criteria: Adult and adolescent Type 1 diabetic patients, patients with Gestational diabetes.

Visit Schedule: At visit 1, there was HbA1c estimation and explanation about the AGP device, its mechanism of blood glucose measurement and the graphs obtained thereafter. The subjects were examined and based on the individual patient profile, appropriate dietary and therapeutic changes were done.

After 5 days, at Visit 2, there was anthropometric data measurement (Height, weight, waist and hip circumference), regular general examination (temperature, pulse, blood pressure). After the regular preliminary work up the AGP device was applied.

At visit 3 (day 3) dietary modifications were prescribed based on the patient's hypoglycemic-hyperglycemic variability and diet recall. Major hyperglycemic and/or hypoglycemic episodes were managed by changes in the treatment regimens. Doses of insulin and oral agents were changed or added accordingly.

At visit 4 (day 7), after reviewing the AGP report, pharmacotherapy changes were made in the treatment regimens. OHAs and insulin were either uptitrated or reduced or changed. Insufficient control was managed by initiation of new agents - oral or injectable.

At visit 5 (day 11), the same procedure of reviewing AGP graphs and consequent management of treatment protocol was done.

At visit 6 (day 14), overall change in glycemic variability of the patients blood sugar was noted. Further, patients were explained regarding the changes in improvement of the glycemic variability in comparison to the initial visit. Their diet and therapy changes were reviewed and the AGP sensor was removed.

Fasting, pre-prandial and post prandial blood glucose levels were analyzed. Any hypoglycemic tendencies were noted too. Potential causes of any major hypoglycemia or hyperglycemia was looked for and treated in the first visit. However, in most cases the glycemic pattern were noted and appropriate dietary modifications were made. In the forthcoming visits, dietary modifications were accompanied by pharmacotherapeutical changes. The main consideration during interpreting the AGP data is to evaluate whether the readings are within the target range, shape of the median curve, hypoglycemia pattern and width of the interquartile range.

Results

Out of the 108 subjects, 106 completed the study. Out of the 2 patients who did not complete the study 1 withdrew on their own discretion while the other subject had the sensor fall off before

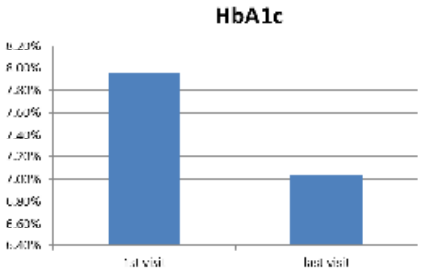

Fig. 3: HbA1c change in the 1st (7.96±1.09%) and the 6th visit (7.03±1.09%).

the completion of 14 days. The mean age of the enrolled subjects was 47.2 ± 7.08 years. Their BMI was 29.52 ± 4.73 kg/m^2 and mean duration of diabetes was 9.2 ± 6.9 years. Clinically relevant hyperglycemia (RBS->350mg/dl) was observed in 35.18% patients and frequent hypoglycemia (<70 mg/dl) in 53.7%.

A1c and sensor glucose values: On the initial visit, the baseline HbA1c calculated of all subjects was 7.96 ± 1.21%. At the end of the study, i.e, at the end of 14 days the HbA1c mean had reduced to 7.03 ± 1.09% (Figure 3).

Dietary and Therapeutic modifications: At least 2 therapy changes were done in 98 (90.74%) patients. Of the 98 patients that underwent the therapy change the mean reduction of HbA1c was 0.78% from baseline. Of the 10 subjects who did not require any therapeutic modifications the mean decrease of HbA1c was 0.33% from baseline.

On the 3rd day, 37 (34.26%) subjects required dietary modifications. Major therapy changes due to significant hyperglycemia and/or hypoglycemia was done in 7 (6.48%) patients. Basal insulin was decreased in 2 (1.85%) patients and OHAs (Pioglitazone, gliptin and $SGLT_2$ inhibitor) were added in 5 (4.62%) patients.

On day 7 and 11, therapeutical changes were made. New OHAs were added in subjects with suboptimal control of blood glucose. Patients who were on insulin had their basal and/or bolus dose increased or reduced based on reviewing the fasting and post prandial sugars.

Initially, 32.4% (35) patients were only on oral agents, 36.11% (39) patients were on Basal and OHAs, 17.6% (19) patients were on Basal Bolus plus OHAs therapy, 11 (10.18%) patients

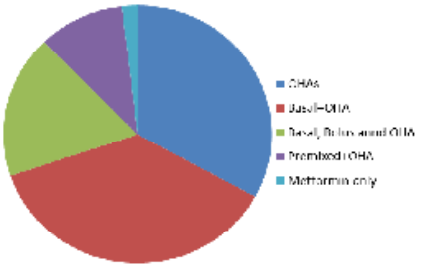

Fig. 4: Distribution of treatment regimens amongst the subject patients. OHA – 35, Basal+OHA - 39, Basal-Bolus+OHA – 19, Pre-mixed+OHA – 11, Metformin only-2

were on premixed insulin regimes plus OHAs and 2 (1.85%) patients were on metformin alone (Figure 4).

Out of the 35 patients on oral agents, 28 patients were on sulfonylureas alongwith other OHAs. The rest were on medications other than sulfonylureas. Most frequently taken sulfonylurea was Glimeperide, others used were gliclazide, glibenclamide, glipizide.

Most commonly used sulfonylurea with Insulin was found to be Glipizide (n=48) followed by Gliclazide (n=17).

On the first visit, 4 of the 11 patients on premixed insulin were shifted to basal bolus regime due to persistent nocturnal asymptomatic hypoglycemia (<70mg/dl). 8 of the 35 patients only on OHAs had to be started with basal insulin due to persistently high blood glucose levels. The second visit showed multiple treatment changes in the form of further shifts from premixed insulin to basal plus OHAs, Basal insulin doses were reduced, OHAs were reduced (sulfonylureas were stopped in 37 (35.57%) patients). Other OHAs were started in patients with metformin alone. The third visit showed few minor titrating changes in the patients' insulin and OHA doses. The diet therapy was reinforced and modified further according to the patients' individual requirement. The final visit showed the overall 14 day improvement in the patients' glycemic variability.

The most frequent change observed was increase in insulin doses; many subjects also had their treatment regimens changed with respect to oral medications, diet and exercise.

Discussion

The study results support the previous studies that HbA1c may not be an appropriate indicator of glycemic variability.[3] The glycemic variability observed can thus be a good judge for subsequent treatment decisions.

The study helped in identifying the mismatch between HbA1c and the patient's complete glycemic profile. It also helped in visually categorizing the patient's glucose levels versus the target range and easily correlated with the patient's individual dietary pattern. After the various changes made in the medications on day 7 and day 11, the graphical changes helped to monitor the changes that occurred in the glycemia, thus making it easier to adjust OHA and/or insulin doses.

Furthermore it acts an educational tool for the patients themselves to be able to see and determine the causes and results of their diabetes self management.

Analysing Glucose Variability

SMBG is an important tool that empowers the patient to judge their own glucose levels, thus making it more educative and comprehensive than an HbA1c level. However, due to its episodic nature it may miss the in between hypo or hyperglycemias. For SMBG to adequately show a true representation of glycemic variability, it would take 7-10 capillary glucose measurements per day.[6]

On conducting a CGM, data reflects significant hypoglycemias and meal time hyperglycemic excursions that are missed in SMBG. Studies show a lower HbA1c level with CGM than patients who use SMBG.[7] However, alongwith CGM, AGP can make HbA1c potentially more useful in clinical practice. Different patients with the same or similar HbA1c values have markedly different rates of hypo and hyperglycemias throughout the day and overnight, as well as different rates of hypoglycemia.[3,4]

In a study, review of serial AGPs obtained for sequential 2-wk periods for 23 non-pregnant individuals with type I diabetes and 10 women with gestational diabetes revealed changes in AGP corresponding to alterations in regimen.[8] In a study by Roger Mazze et al, Blood glucose levels showed that HbA1c levels were not consistent with the individual's glycemic variability. AGPs provided a visual representation of improved glucose responses to exenatide once weekly showing that results of treatment alterations can be best visualized graphically by the AGP.[9]

The role of AGP in diabetes management is not only useful for the health professional but also provides an actual insight to the patients about their glucose control. AGP serves as an educational tool in categorizing the patient as having optimal glycemic control not only in terms of their HbA1c levels but also by their glycemic variability pattern.

As was recently shown in the ICMR - INDIAB study, less than a third of patients in India are able to achieve A1C values <7%.[10] AGP provides a systematic method of presenting an SMBG data, i.e. the complete glycemic profile of the patient. It reflects the glycemic control of a typical day. The data can thus be used for individualizing patient care and diabetes management in relation to control, complications, impact of therapeutic management and adjustment of insulin doses.

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