Original Research Article

Efficacy of continuous glucose monitoring in lowering HbA1c of patients with type 2 diabetes

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Abstract

HbA1c is a diagnostic indicator in determining the prognostic character of glycemic control in diabetes patients with less glycemic variability. It helps in assessment of the probability of vascular complications of diabetes mellitus. Continuous glucose monitoring is a newmodality that provides 24hours glucose values, direction of change and its rate of change. It displays the influence of day and night, lifestyle modifications like diet and exercise upon blood glucose levels,thereby helps clinicians in management of Type 2 diabetes mellitus. Despite of its numerous, unattainable merits in comparison to other diagnostic measures, acquaintance with the device is still at its initial stage. CGM reports are 24 hours based and their data give more clarity and accuracy in determining the personalised glycemic pattern, and thereby customising the treatment. This is a prospective study done to assess the efficacy of CGM using FREE STYLE LIBRE PRO device.

100 patients with Hba1C above 7.5 as entry value, were enrolled during the study period. CGM done in these patients has played a remarkable role in controlling nocturnal hypoglycaemia and to rectify the glycemic variability.
Key Words: Amala, CGM, DM, efficacy, libro pro.

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INTRODUCTION

The course of glucose monitoring has taken a pivot following introduction of continuous glucose monitoring device. It has considerable benefits starting from 24-hour updates on glucose trends and especially during sleep hours, alerting upon oncoming lows and highs, statistically showed to reduce 1% HbA1c, reporting how daily activities effect glucose levels, personalise drug therapy and attain a good glycemic control. Different glucose monitoring methods have proven its merits and demerits in their due course. SMBG estimate sugar levels directly from blood, limited number of test, involves multiple finger pricks, hardware-software dependent, with no notifications on oncoming high and lows that could endanger the patient, hence low reliability in regard with safeguard measures. Flash CGM share similar merits as CGM, excluding the fact that it doesn't provide 24 hours glucose trends and only flashes for the moment.Hence mere complexity shouldn't facade itsbeneficial aspects.

Studies of CGM inType 2 Diabetes mellitus: Recently,many studies have been done revolving around CGM. The juvenile Diabetes Research foundation continuous glucose monitoring study group cameup with a multi-centre clinical trial where adults and children receiving intensive insulin therapy took part who were categorised into a control group adhering to home monitoring with glucose meter and the test group on CGM.The outcome was determined after 26 weeks and found to have improved glycemic control in age group above 25 years and concluded that more research is in demand to give clarity upon its efficacy.

Studies showing efficacy and Hba1c reduction: Vigersky*et.al.*conducted a study focusing the short- and long-term effects ofreal time CGM in patients with T2DM.As per the study,a randomizedcontrolled trial done

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among 100 diabetic patients (Type 2 DM) who were noton prandial insulin.It compared the results of 12 weeks of intermittent RT-CGM with SMBG on glycemic control over a 40 week follow up.The testgroup showed mean unadjusted HbA1clower by 1.0 at 12 weeks(SBGM – 0.5),1.2 at 24 weeks (SBGM-0.5),0.8 at 38 weeks (SBGM-0.5) and 0.8at 52weeks(SBGM-0.2%).There is a significant depreciation in HbA1c valuesamong the test group in comparison to the control group after 3 months follow up($P<0.0001$).Fonda S J,*et.al*made another study to assess the cost effectiveness of real-timeCGM in T2DMusing randomized controlled trial method. It demonstratedthe decline of HbA1c values after 9 months of use of RT-CGM in diabetic(T2DM) patients not on prandial insulin.They highlight the life time effectiveness and economic benefit of CGM. It showed Life expectancy (LE) and Quality adjust life expectancy(QALE) were0.14 and 0.10 and cost perperson is $1312 over a lifetime and incremental cost effectiveness ratios as $9319 an$13.030 per LY and QALY gained and emphasise the cost effectiveness of CGM in lifetime of patients with Type 2 DM. Poolsup*et al* made a systemic review and meta-analysis 0f the effectiveness ofCGM on glucose control in both Type 1 and Type 2 Diabetes mellitus.It hasshown neither much effectiveness in T1DM nor thatretrospective CGM is superior to SMBG in sub group analysis.However, Real time CGMdemonstrated to have more effect in lowering HbA1c values in comparison with SBGM.Pepper at el conducted a study using Ipro device to assess the effect of shortterm Ipro CGM on HbA1c levels in clinical practiceusing blinding method.The study contained 50 males and 52 females who wereblinded for three days to check the improvement is glycemic control.It didn't show muchof a statistical difference from HbA1c levels before Blinded CGM testing and later.DIaMonD study examines the effectiveness of CGM in contrast to SMBG inType 1 DM on MDI insulin therapy.A randomized controlled trial of 158adults conducted over a period of 24 weeks using Dexcom G4 PLATINUMCGM system. It displayed a significant HbA1c reduction in MDI patients withCGM.

Studies on Hypoglycemia: PazosCouselo made an observational study in1521 spanish people,who werenormoglycemic. He excluded pregnant,affected with kidney disease or liverdisease and those on drugs that caneffectglycemic levels.The study aimed to evaluate how early CGM monitoring could make a predignosis of dysglycemiain people.As per his study,he found that CGM showed a mean relativedifference of 6.9% against fingerstick tests.73% of the normoglycemic had events of blood glucose level above impaired glucose tolerance and 5% of themshowed above the threshold for Diabetes.Hence it concludes that CGM is agood way of detecting dysglycemia early.Zick*et al* conductednon-randomised study, where CGM monitoring was done to assess the efficacy to reduce the incidence of daytime hypoglycaemia and nocturnal hypoglycaemia against Finger prick test.The results show similar reduction during day hours but profound reduction in nocturnal hypoglycaemia in group under CGM monitoring. Klimontov and Myakina conducted a blind CGM study among 83 insulin treated patients,65-80 years old to assess the predictability for CGM in reduction of nocturnal hypoglycaemic events during a period of 176 nights. Daytime mean glucose, standard deviation, 2hr continuous overlapping net glycemic action and mean absolute glucose, pre-midnight mean glucose, SD and MAG, 24 hours mean amplitude of glucose excursions were scrutinised and concluded that CGM- obtained data has the potential to reduce the nocturnal hypoglycaemic events in insulin treated-type 2 diabetes patients.

Glycemic Variability: Glycemic variability demonstratesblood glucose levels during a 24 hours period,that includes short falls and ascends in them, could clinically imply in treatingcomplications and prevent from their forthcoming,also could lower the rate ofhypoglycaemic events in Type 1 and Type 2 Diabetes patients.Initially SMBGwas used to provide the variability results,nevertheless CGM monitoring, nextfrontier, has shown better results later.As per VARIATION STUDY,a cohort study, done to determine theglucosevariability and hypoglycaemic incidence in diabetic patient on combination ofGLP-1Receptor Agonist and Basal Insulin, CGM was used as the tool to record the data.Itproduced better results than SMBG.160 patients, 18-80 years,$\leq$ 45kg/m^2BMI on stable insulin regimen for atleast 6 months,stable A1c value $\leq$7.5% before studytook part in it using blind CGM. It was observed that a combination of GLP-1 receptor agonist and basal insulin gives lowest glucose variability and hypoglycaemic rate depreciation in Type 2 Diabetes. Eli lilly and Company conducted clinical trials to determine the therapeuticbenefit when insulin-GLP-1 agonist (exanatide) combined together. It is an 8month study where middle aged and old age with risk factors are trialed. As per the study, participants are initiated with long acting insulin, meal time insulin and metformin. RFT levels monitored. After 2months run-up, Half of them given a new drug, Byetta instead of meal time insulin and blood sugars will be assessed at the end of next 6 months, using DexCom, a continuous bloodglucose monitoring system.It is a randomized control study. Thomas Haak and Hanaire did an open label randomized controlled studyfocusing of patients with Type 2 DM. It is a comparative study between FLASH CGM and SMBG. At the end if initial 6 months,

no remarkable difference was showed in HbA1c levels between intervention and control,but later wasdetected in age group <65 years. Rate of hypoglycaemic incidence loweredreduced by 0.47±0.13 h/day and <3.1 mmol/L reduced by 0.22±0.07h/day.Hence it concludes that FLASH CGM is a better surveillance and control check for hypoglycaemia.

Professional use CGM: CGM consist of three parts:the sensor,the transmitter and the receiver.Thesensor uses the same enzyme to measure glucose levels as a test strip-glucose oxidase.The transmitter hooks into the sensor and streams glucose informationover radio waves to the receiver.The receiverhas a screen where one can checkcurrent glucose level, look into historical data,and get trends about whetherglucose is likely to go up or down and how fast.CGM helps people to livebetween the lines.Professional CGM gives an insight on the trending pattern of glucoselevels in human body.It identifies insulin action and additional management required to control post prandial glucose.It helps to regulate the meal timings andinsulin administration.It provides continuous data for overnight basal testingand assessment of nocturnal hypoglycaemia.It allows for efficient and effective therapeutic management for patient's target goal by identifying the clinical challenges. It promotes patient to use personal CGM.Professional CGM is more appropriate for those candidates who are on uncontrolled Type 1 and Type 2DM,those who are new to this and wants todetermine if their management plan is effective,those unaware ofhypoglycaemia,pregnant women and patients planning to choose personal CGM.Eugene E Wrightand James R Gavin have made observational studies on theclinical use of professional Continuous Glucose Monitoring. As per the study, itwas very well understood that the retrospective data and the informationprovides more accuracy upon glycemic trends over a period of time comparingto SMBG.It discards the disadvantage of "point-in time" measures in glucose,as produced in fasting blood sugar and post prandial blood sugar values.Itoverrules the inadequacy of A1c to provide continuous, day-today lucose variability.Iteliminates the short falls of SMBG such as inability toprovide continuous 24 hr information regarding glucose levelswith minimalintervention and notinvasive.Ambulatory Glucose Profile(AGP) is a single page,standardised report forinterpreting a patient's daily glucoseand insulin patterns.It providesgraphical as well as quantitative picture about daily glucose patterns.It is consistent and regardless of device.It enables in assesment of glycemicvariation and manage accordingly.It has become an important tool in glycemiccontrol and being implemented in many diabetic centres.It is organised andeasy to interpret. Itcreates a better communication and understanding between clinicians and patients upon the associative factors, current glycemic status and its further management. Professional CGM means Continuous glucose monitoring for healthcare providers.It access unaltered glucose patterns to make appropriate therapeuticadjustments.It displays blinded and unblended glucose values. DexCom G4and Medtronic Ipro2 are the professional Use CGM. DexCom G4 lasts for 6months and need not be charged and works with receiver, iphone,Tslim and Animas pumps. Medtronic Enlite lasts 12 months, needs to be charged 20mins every 2-3 days and works with Medtronic pump.

Personal use CGM: The personal continuous glucose monitoring system is another variant of CGM moreapplicable for patients. It gives 24 hour glucose level feed-back and can be uploaded and shared with the physician.The sensor needs to be charged. The painless scan provides real time glucose readings for insulin dosing.Retrospective CGM is pertinent among adults and children with DiabetesMellitus.It has shown less improvement in adults with Type 1 DM.It is recommended for those adults who are unaware of their "hypo", occurrence of hypoglycaemia atleast once in a year, pregnant women,extreme fear ofhypoglycaemia and those with HbA1c level ≥75mmols/mol. It can be indicatedin those children who are not able to communicate their symptoms due to developmental or neurological disability,frequent incidence of hypoglycaemia,especially under school age,on steroids and have high blood sugar levels inspite of vigorous insulin and OHAsupport.Dexcom G6 continuous glucose monitoring system is an innovator in Diabetestechnology.They invented world's first CGMsystem to be approved for Nonadjunctive use. They also improvised the system by linking to smartphonesand battery life of 7 days.G6 CGM system has a 10 day wear sensor, an easy touse applicator and no need for calibration which makes its less complex forusers.It has no acetaminophen contraindication.It provides MARD 9.0%.The FDA has approved Senseonics Eversense CGM, the first implantableCGM in US. It provides lifespan of 3 months via an implantable sensor, therebyeliminates the need for weekly sensor insertion and maintenance. They haveMARD of 8.5%.It has connectivity tosmart phones, tablets and laptops via apps.

MATERIALS AND METHODS

It is a prospective study conducted at Amala Institute of Medical Sciences,Thrissur.The study was done among 100 patients with Type 2 DM after taking consent. US FDA approved Freestyle LIBRE PRO CGM, professional

use CGM was used in this particular. Patients were explained in detail about the method of study, merits and demerits,purpose of study and very rare complications.Patients were observed over a period of 2 weeks. All the patients were monitored for glycemic fluctuations with the sensor. After completion of two weeks of CGM, the reports are analyzed using AGP (ambulatory glucose profile).Criteria includesType diabetic patients with HbA1c value above 7.5 as entry value. After careful analysis of the report, required changes are made in the treatment which includes, titrating the dose of insulin, adding or removing oha etc. Then, all the patients are monitored with CGM sensor again to assess the response of the change in treatment made.

OBSERVATION AND RESULTS

Patterns observed are

a. Nocuturnal hypoglycemia
b. Dawn phenomenon
c. Somogyi phenomenon
d. Inter meal variability
e. Stress induced hyperglycemia
f. Hypoglycemia unawareness

HbA1C was checked three months after completion of second monitoring, Minimum change observed – 0.8%Maximum change observed – 1.3%, Observation - 79% of the patients achieved target hba1c which is less than 7%.21% of the patients who failed to attain the target had erratic diet patterns or poor compliance or other reasons due to which HbA1c was kept on higher range.

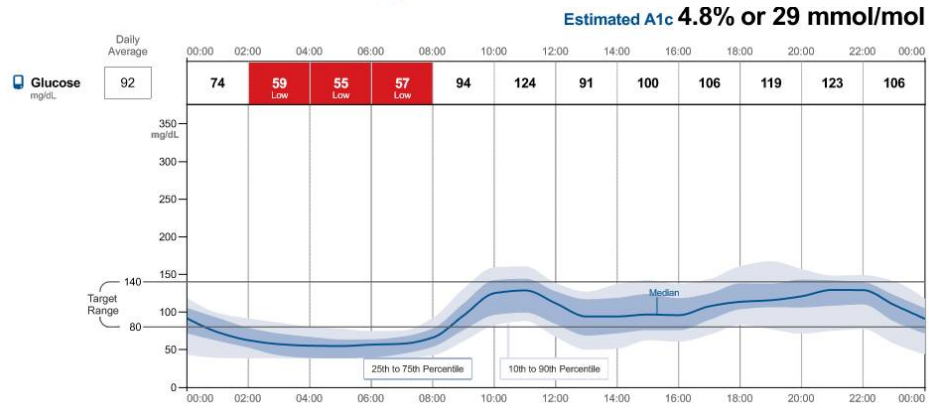

Figure 1:

DISCUSSION

CGMData Interpretation: CGM is a softwarebased system. It is vital to follow the preparatory partbefore commencing to use the system for better results.The data interpretationneeds reliable informationfor the authentication of the results.The clockshould be set and need to make sure the calibration is standardised andverified that enough calibrations were performed. The emotional and physical conditions need to be mentioned to correlate the results.The finger prick testsare used to evaluate the standardisation of CGM system against SMBG.The graphical representation helps in assessing the magnitude ofPPBS,effectiveness of Insulin therapy and the additional support,to quantify the correction factor,to determine that the insulin dosage is effective or in needof personalisation,effectiveness in association withlifestyle routine,to measurethe duration of insulin action curve and have better awareness of hypoglycaemia.The data interpretation has its own limits due to less acceptance from the patients. Hence more research is required for better professional and personal consumption.

CONCLUSION

CGM with AGP is an important tool in achieving the target hbA1C, especially in patients who have controlled fasting and post prandial blood sugars but uncontrolled hbA1c. Also, it is a must have device to detect nocturnal hypoglycemia and hypoglycemia unawareness. To determine the glycemic fluctuations or variability is a very important factor in attaining euglycemia round the clock.

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