International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 24-03-2020; Accepted: 26-04-2020; Published: 30-04-2020
www.medicalsciencejournal.com
Volume 6; Issue 4; 2020; Page No. 67-70

Glycemic impact on wound healing with basal bolus therapy versus Premix Insulin therapy – documented with FGM

Riyaz Mohammed[1*], Dilip Kumar Kandar[2]
[1] Department of Medicine, Endocrinology & Diabetes, Esani Diabetes and Multispeciality Centre, Hyderabad, Telangana, India
[2] Department of Medicine, Diabetes, Kandar Diabetes Centre, Hyderabad, Telangana, India

Abstract
Aim: To assess the impact of strict glycemic control on Wound healing in established type 2 diabetes mellitus patients using various combinations of Insulin. The glycemic control was assessed by Flash Glucose monitoring.
Material and Method: Inclusion criteria: know Diabetic Type 2 with wound (Grade 1 to 2), Exclusion criteria: Type 1 DM, Cardiac failure, hepatic failure, renal failure.
In the present study continuous glucose monitoring was done for 54 diabetic patients who presented with wound. The patients were put on Basal Bolus therapy plus Metformin 2gm/per day in Group 1 and in Group 2, patients were placed on Premix Insulin plus Metformin 2gm/per day. The response to glucose levels and healing was observed for a period of 15 days.
Results: In the present study it was observed that the mean overall glucose in group I was observed to be 155.3± 40.9 which was significantly lower than when compared to group II 237.7 ± 66.3 $p < 0.05$. estimated Hba1c was observed to be 7.05 ± 1.4 which was significantly better than when compared to group II 9.9 ± 2.3 $p < 0.05$.
Presence of variability was correlated with estimated hba1c, it was seen that patients who had shown variability in glucose levels had higher hba1c levels $r = 0.405$, $p < 0.05$.
In group I patients Low glucose levels and variability was correlated with targets observed in continuous glucose monitoring. It was seen that patients who had shown low glucose levels had significant positive correlation with percentage of times glucose level below the target $p < 0.05$. in patients who has shown minimal variability in glucose levels had higher percentage of times their glucose levels within target ($r = 0.652$, $p = 0.012$), in patients who had shown a higher variability in glucose levels had higher percentage of times their glucose levels above target ($r = -0.589$, $p = 0.024$). Linear regression analysis was done to assess the prediction of good wound healing in relation to average glucose levels above the target. it was seen that the overall average daily glucose goes down by 41.24 it would predict good wound healing with an odds of 1.11 times.
Conclusion: In our study it shows that offering the FGM technology to patients with type 2 diabetes mellitus with wound helps in identify the glycemic surges and peak glycemic levels, which can be promptly tackled with adjustment of insulin dosage eventually leading to strict and good glycemic control which can help in good wound healing and rapid recovery of patients. It has shown in our study that patient on Basal bolus therapy group of patients had better wound healing than the other group. The compliance was better in group 1 than compared to group 2. The risk of hypoglycaemia was seen in both the arm groups. In India as the cost of management plays an important role, it is pivotal to follow strict measures to get glycemic level under control or else it may lead to severe infection of wound and eventually may lead to amputation. Our study has confirmed that if strict glycemic levels are maintained it can get good results.

Keywords: Premix, FGM, Glycemic, wound

Introduction
Type 2 diabetes mellitus is a progressive disease characterized by the coexistence of insulin action and insulin resistance, and accompanied by hyperglycemic microvascular complications and macrovascular complications [1]. Early initiation of Basal insulin treatment can prevent the complications; however, addition or changing insulin is necessary when the therapeutic goal is achieved. Many studies have shown benefits and advantages of both basal bolus therapy and premix insulin therapy, but it has been reported that with premix therapy there is increased risk of hypoglycaemia and bodyweight gain, when compared to basal bolus therapy. Thus, strengthening insulin therapy can increases the risk of hypoglycaemia, and eventually severe hypoglycaemia increases cardiovascular events and total mortality. It has also been reported that nocturnal unawareness of hypoglycaemia occurs at a higher frequency than what is thought, including in patients with favourable glycated hemoglobin (HbA1c) by insulin treatment [1-4].
Freestyle Libre Flash glucose monitoring system is a new approach to self-monitoring of glucose. We had used this FGM to record the effect of glycaemic control in these two groups (Basal bolus therapy group versus premix therapy) of patients. Basically a flash glucose monitor is a small sensor applied on your skin and with the help of adhesive it is firmed fixed to skin, without any needles. The sensor measures the amount of glucose in the fluid i.e. interstitial fluid. There is a small time delay when checking this fluid, especially after eating or if you're exercising. The sensor is commonly placed on the back of the upper arm for up to maximum 14 days and with the help of this device, it automatically stores glucose data every 15 min. The sensor is scanned by a separate reader, and real-time glucose levels can be obtained every minute. Data including the glucose trend; i.e., an arrow and a curve of glucose values for the

previous 8-h period are also displayed. This study was designed to assess the impact of this FGM system on treatment outcomes and diabetes control in patients with type 2 diabetes on MDI [5-6].

Material and Method

Inclusion criteria: 1) Age: men and women between age group 20 years to 70 years 2) uncontrolled FBS and PPBS 3) HbA1c between 7 to 10 % 4) Established Type 2 DM patients with poor glycemic control with wound (Grade 1 to 2 only).

Exclusion criteria: Type 1 DM, Cardiac failure, hepatic failure, renal failure, Patient with Grade 3 and above wound, COPD, Known Alcoholics.

In the present study Flash glucose monitoring was done for 54 diabetic patients who had presented with wound (grade1 –2). These patients were placed on Basal Bolus therapy plus Metformin 2gm/per day and they were categorised as Group 1. In Group 2, patients were placed on Premix Insulin plus Metformin 2gm/per day. The response to glucose levels and healing was observed for a period of 15 days.

Results

In the present study continuous glucose monitoring was done for 27 diabetic patients who presented with wound. The patients were put on Basal Bolus therapy plus Metformin 2gm/per day, in Group 1. In Group 2 patients were placed on Premix Insulin plus Metformin 2gm/per day. The response to glucose levels and healing was observed for a period of 15 days. Data obtained was measured with SPSS version 17 software. Present study comprised of 51.9% males and 48.1 % females of which 60 % males were in group I and 47.1% males were in group II. 40 % females were in group I and 52.9% females were in group II there was no statistically significant difference in the distribution of patients. P >0.05.

In the present study it was observed that the mean overall glucose in group I was observed to be 155.3± 40.9 which was significantly lower than when compared to group II 237.7 ± 66.3 p <0.05. estimated Hba1c was observed to be 7.05 ± 1.4 which was significantly better when compared to group II 9.9 ± 2.3 p <0.05.

In patients who had good response wound healing variability was observed in 42.1% cases compared to 57.9 % cases in group II. Presence of low glucose was observed in 72.7% cases in group I compared to 27.3% in group II.

The mean percentage of times level of glucose was seen to be in target for group I was observed to be 50.71% which was significantly more compared to group II where on an average the percentage time in target was observed to be 15.54 %. The average of percentage of times glucose level was below target was observed to be 8.5% which was significantly more compared to 2.69% in group II. The average percentage of times where the glucose level was above target was significantly more in group II patients 81.69% compared to 41.25% in group I p <0.05.

The mean of maximum glucose level observed in group I was 201.9 ± 52.3 which was significantly less than when compared to group II.

Presence of variability was correlated with estimated hba1c, it was seen that patients who had shown variability in glucose levels had higher hba1c levels r= 0.405, p <0.05.

In group I patients Low glucose levels and variability was correlated with targets observed in Flash glucose monitoring. It was seen that patients who had shown low glucose levels had significant positive correlation with percentage of times glucose level below the target p <0.05. in patients who has shown minimal variability in glucose levels had higher percentage age of times their glucose levels within target (r=0.652, p =0.012), in patients who had shown higher variability in glucose levels had higher percentage of times their glucose levels above target (r= -0.589, p = 0.024). In this group of patients the time below the target was significantly more than other group, but documentary hypoglycaemic episodes were not higher in both the arm groups.

In group II patients It was seen that patients who had shown low glucose levels had significant positive correlation with percentage of times glucose level below the target p <0.05. there was no significant correlation between variability and time with in target, time below target and time above target in group II patients p >0.05.

Linear regression analysis was done to assess the prediction of good wound healing in relation to average glucose levels above the target. it was seen that the overall average daily glucose in the groups has shown upto 41.24, it would predict good wound healing with an odds of 1.11 times.

Table 1: Comparison of variables in between groups

Parameter	Group 1	Group II	p value
Average Glucose			
Day1	199.43	262.62	0.053
Day2	158.57	237.15	0.006
Day3	156.57	244.62	0.003
Day4	163.29	254.15	0.001
Day5	152.86	227.77	0.006
Day6	152.57	231.38	0.003
Day7	153.38	233.69	0.003
Day8	166.62	250	0.012
Day9	155.18	227.62	0.01
Day10	142.91	222.25	0.004
Day11	141.3	237.42	<0.001
Day12	138.11	235.08	0.003
Day13	129.14	242.45	0.008
Day14	114.5	188.13	0.113
Day15	129.6	146.67	0.581
Over all			
Glucose	155.29	237.77	0.001
Estimated Hba1c	7.03	9.9	0.001
Time Below Target	8.5	2.69	<0.001
Time In Target	50.71	15.54	0.028
Time Above Target	41.25	81.69231	<0.001

Table 2: Gender

	Sex	
	Male	Female
Group 1	6	8
Group II	4	9
Total	10	17

Table 3: Correlations

			Time in target overall	Time below target overall	Time above target overall
Group II	Low glucose	r value	0.046	-0.589*	0.104
		p value	0.880	0.034	0.736
	Variability	r value	0.044	-0.233	0.022
		p value	0.887	0.443	0.944
Group I	Low glucose	r value	-0.246	-0.769	0.443
		p value	0.396	0.001	0.112
	Variability	r value	.652*	0.206	-0.599
		p value	0.012	0.479	0.024

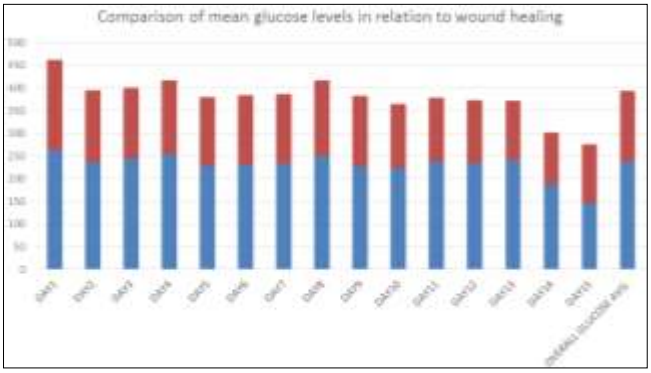

Fig 1

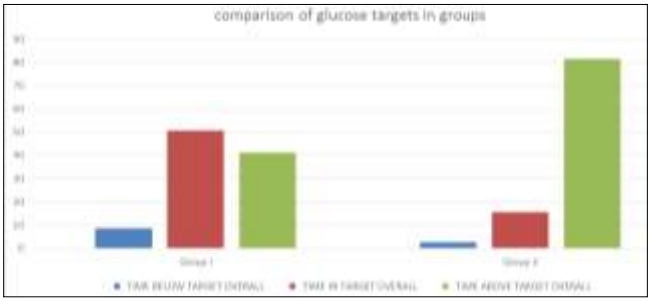

Fig 2

Discussion

The major issue in Type 2 Diabetes mellitus is progressive deterioration of pancreatic β-cell function which necessitates the advancement of treatment over time for most patients. The dysglycemia is a hallmark of diabetes, includes two components: sustained chronic hyperglycemia and blood glucose fluctuations [7]. For patients in whom oral antihyperglycaemic agents (OHAs) has failed to help in achieving the glycemic control, basal insulin is often initiated [8-10]. When glycemic control can no longer be achieved or maintained with this therapy, then prandial insulin is added. Potential options for advancement of insulin therapy to include prandial insulin are prandial premixed therapy or basal bolus therapy. Basal bolus therapy is the recommended regimen for insulin intensification. However, prandial premixed therapy is a more convenient regimen that has the potential to work as effectively as basal bolus therapy. Basal bolus therapy is the recommended regimen for insulin intensification. However, Premix therapy is a more convenient regimen that has the potential to work as effectively as Basal Bolus Therapy [11-17].

In our study it was observed that group I patients had Low glucose levels and variability was correlated with targets observed in Flash glucose monitoring. It was seen that patients who had shown low glucose levels had significant positive correlation with percentage of times glucose level below the target p <0.05. in patients who has shown minimal variability in glucose levels had higher percentage of times their glucose levels within target (r=0.652, p =0.012), in patients who had shown higher variability in glucose levels had higher percentage of times their glucose levels above target (r= -0.589, p = 0.024). In group II patients It was seen that patients who had shown low glucose levels had significant positive correlation with percentage of times glucose level below the target p <0.05. there was no significant correlation between variability and time with in target, time below target and time above target in group II patients p >0.05.

Robbins *et al*. (2006) 24-week study compared overall glycemic control with lispro mix 50/50 three times daily (plus metformin) to once a daily basal insulin - glargine (plus metformin) in type 2 diabetic patients. The end point mean A1C for the lispro mix 50/50 group was 7.1, respectively. However, it should also be noted that the Robbins et.al. Study had a lead-in period of 6 wks in which patients received twice a daily lispro mix 75/25 and metformin, which may have resulted in a lower baseline A1C of 7.8% [18].

Herman *et al*. (2005) compared Basal Bolus Therapy (glargine/lispro) to a continuous subcutaneous insulin infusion using insulin lispro in older adults with type 2 diabetes. That study demonstrated a good glycemic control with both the type of regimen [19].

Julio et.al 2008, Compared Both insulin regimens demonstrated a clinically meaningful ability to improve glycemic control, although, based on the prespecified margin, noninferiority of Premix insulin Therapy compared with Basal Bolus Therapy was not demonstrated [20]. Basal Bolus Therapy was associated with a greater reduction in A1C from baseline and a larger proportion of patients who achieved A1C targets of <7.0 and ≤6.5%. However, both Premix insulin Therapy and Basal Bolus Therapy (in combination with OHAs) can effectively lower A1C levels to <7% in patients with type 2 diabetes who have previously been treated with insulin glargine plus OHAs with is similar to our study.

Conclusion

In our study it shows that offering the FGM technology to patients with type 2 diabetes mellitus with wound helps in identify the glycemic surges and peak glycemic levels, which can be promptly tackled with adjustment of insulin dosage eventually leading to strict and good glycemic control which can help in good wound healing and rapid recovery of patients. It has shown in our study that patient on Basal bolus therapy group of patients had better wound healing than the other group. The compliance was better in group 1 than compared to group 2. The risk of hypoglycaemia was seen in both the arm groups.

In India as the cost of therapy plays an important role due to multiple reasons. It is pivotal to follow strict measures to get glycemic levels under control or else it may lead to severe infection of wound and eventually may lead to amputation. Our study has confirmed that if strict glycemic levels are maintained it can get good results.

Limitation of study was short duration of study, and sample size of patient was less. Large randomized control trail are required.

References

1. Fowler MJ. Microvascular and macrovascular complications of diabetes. Clin Diabetes. 2008; 26:77–82.
2. Holman RR, Farmer AJ, Davies MJ, *et al*. Three-year efficacy of complex insulin regimens in type 2 diabetes. N Engl J Med. 2009; 361:1736–1747.
3. Miller ME, Williamson JD, Gerstein HC, *et al*. Effects of randomization to intensive glucose control on adverse events, cardiovascular disease, and mortality in older versus younger adults in the ACCORD Trial. Diabetes Care. 2014; 37:634–643.
4. Veneman T, Mitrakou A, Mokan M, *et al*. Induction of hypoglycemia unawareness by asymptomatic nocturnal hypoglycemia. Diabetes. 1993; 42:1233–1237.
5. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kröger J, Weitgasser R. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. Lancet. 2016; 388:2254–2263.
6. Haak T, Hanaire H, Ajjan R, Hermanns N, Riveline JP, Rayman G. Flash glucose-sensing technology as a replacement for blood glucose monitoring for the management of insulin-treated type 2 diabetes: a multicenter, open-label randomized controlled trial. Diabetes Ther. 2017; 8:55–73.
7. Brown JB, Nichols GA, Perry A. The burden of treatment failure in type 2 diabetes. Diabetes Care. 2004; 27:1535–1540.
8. Matthews DR, Cull CA, Stratton IM, Holman RR, Turner RC. UKPDS26: sulphonylurea failure in non-insulin-dependent diabetic patients over six years: UK prospective diabetes study (UKPDS) group. Diabet Med. 1998; 15:297–303.
9. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). JAMA, 281, 2005–2012.
10. Monnier L, Colette C, Owens DR. Glycemic variability: the third component of the dysglycemia in diabetes. Is it important? How to measure it? J Diabetes Sci Technol. 2008; 2:1094-1100.
11. Riddle MC. Evening insulin strategy. Diabetes Care. 1990; 13:676–686.
12. Rosenstock J. Basal insulin supplementation in type 2 diabetes: refining the tactics. Am J Med. 2004; 116:10S–16S.
13. Hermansen K, Davies M, Derezinski T, Martinez Ravn G, Clauson P, Home P. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naive people with type 2 diabetes. Diabetes Care. 2006; 29:1269–1274.
14. Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R, *et al*. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetelogia. 2006; 49:1711–1721.
15. Garber AJ, Wahlen J, Wahl T, Bressler P, Braceras R, Allen E, *et al*. Attainment of glycaemic goals in type 2 diabetes with once-, twice-, or thrice-daily dosing with biphasic insulin aspart 70/30 (the 1-2-3 Study). Diabetes Obes Metab. 2006; 8:58–66.
16. Jacober SL, Scism-Bacon JL, Zagar AJ. The IONW Study Investigators: A comparison of intensive mixture therapy with basal insulin therapy in insulin-naïve patients with type 2 diabetes receiving oral antidiabetes agents. Diabetes Obes Metab. 2006; 8:448–455.
17. Kazda C, Hulstrunk H, Helsberg K, Langer F, Forst T, Hanefeld M. Prandial insulin substitution with insulin lispro or insulin lispro mid mixture vs. basal therapy with insulin glargine: a randomized controlled trial in patients with type 2 diabetes beginning insulin therapy. J Diabetes Complications. 2006; 20:145–152.
18. Robbins DC, Beisswenger PJ, Ceriello A, Sarwat S, Jones CA, Tan MH. Thrice-daily lispro mid mixture (MM) plus metformin (Met) improved glycemic control better than glargine (G) plus met in patients with type 2 diabetes (T2D) (Abstract). Diabetes. 2006; 55(Suppl. 1):A132.
19. Herman WH, Ilag LL, Johnson SL, Martin CL, Sinding J, Harthi AA, *et al*. A clinical trial of continuous subcutaneous insulin infusion versus multiple daily injections in older adults with type 2 diabetes. Diabetes Care. 2005; 28:1568–1573.
20. Julio Rosenstock, Andrew J, *et al*. "Advancing Insulin Therapy in Type 2 Diabetes Previously Treated With Glargine Plus Oral Agents", Diabetes Care. 2008; 31(1):20-25.