ORIGINAL RESEARCH ARTICLE

Efficacy of Addition of Remogliflozin to Type-2 Diabetic Patients, Uncontrolled with Dual Drug Treatment with Metformin and Glimeperide, an Observational Study

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A B S T R A C T

Introduction: Type-2 diabetes is a significant health problem with different management protocols and newer therapeutic options are need of the hour. The present study evaluated the efficacy of remogliflozine (100 mg BD) as add on to T2DM patients with inadequate control with metformin and glimeperide.

Material and methods: A single centre study evaluated efficacy and safety of addition of new SGLT -2 inhibitor, remoglliflozin, 100 mg BD, in to type -2 diabetes patients, inadequately controlled with metformin and glimeperide. Overall, 50 patients were prescribed remoglifozin in addition to dual drug treatment with metformin and glimeperide.

Results: And the end of the study, a statistically significant reduction in the pre and post treatment measures of HbA1c, body weight, blood pressure, FBS and PPBS levels was seen. Creatinine levels did not show significant changes following the treatment.

Conclusion: Remogliflozin has shown significant efficacy when used as add on drug to dual drug treatment with metformin and glimeperide in T2DM patients with inadequate glycaemic control.

Keywords: Remogliflozin, Type-2 Diabetic, Dual Drug Treatment, Metformin, Glimeperide

INTRODUCTION

Diabetes is a major health problem affecting the whole world. It has been estimated by the IDF that by the year 2030, more than 700 Million all over the world will suffer from this malady. Once the disease of the affluent class, now even people in the poorer starta of the society are getting affected. More worrisome is the fact that the working class of people are being predominantly affected. WHO has projected this disease to be the seventh leading case of death by 2030.[1]

Hence there is an urgent need to get newer therapies, which will be helpful in managing this condition and help in attaining not only the optimal glycaemic control, but also have pleotropic effects, which can reduce the long term complications while at the same time not increasing the incidence of hypoglycemia. Moreover the therapies should be affordable and have beneficial effect on co-morbidities – mostly atherosclerotic cardio-vascular disease and renal complications.

In this background, SGLT-2 inhibitus (the gliflozines) are now occupying central place in the treatment algorithm in the management of Diabetes. These drugs were initially introduced as hypoglycaemic agents, by their ability to lower blood sugar by inhibiting glucose re-absorption at the level of proximal convulted tubules and thereby attaining glycaemic control.[2] However, with the disclosure of the results of the long term CVOT trials with agents like Empagliflozine, Dapagliflozine and Conagliflozine, newer facets of their pharmaceutical effects emerged. The use of these agents were found to have not only significant benefits in cardiovascular and renal complications, but also a highly statistical reduction in mortality.[3,4,5]

However, one drawback with these agents are cost. Recently, another agent in this class, Remogliflozine was introduced, which was expected to be less expensive. This drug is expected to be used as monotherapy as well as combination therapy with other drugs. This drug is commonly used in a daily dose of 100mg. two times daily. By its glycocuric, uricosuric and natriuretic effect, it is expected to be of significant help in diabetic patients.

Limited studies are available regarding the efficacy of remogliflozine as add on to dual drug therapy with metformine and glimeperide. The present study evaluated the efficacy of remogliflozine (100 mg BD) as add on to T2DM patients with inadequate control with metformin and glimeperide.

MATERIAL AND METHODS

The prospective observational study included subjects of T2DM, inadequately controlled with metformin and glimeperide (HbA1c > 7.5) enrolled in a clinical setting from

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June 2019 to December 2019. Informed consent was taken from all the participants. The inclusion criteria considered were: subjects aged between 30-70 years, and glycated haemoglobin > 75%. Patients with significant co-morbidity like significant osmotic symptoms, acute myocardial infarction, CVA, UTI, and pneumonia were excluded. The demographic details of the study subjecs such as age, gender, and BMI were recorded and they received remogliflizine 100mg. BD along with existing treatment with metformin and glimiperide for three months. The following clinical and anthropomatric parameters were measured at baseline and three months after the treatment: weight, blood pressures, serum urea, creatine, HbA1c, FBS and PPBS levels.

STATISTICAL ANALYSIS

Data with normal distribution were represented as mean ± SD, without normal distribution as median (range) and categorical data as counts. Comparison of pre and post treatment, anthropometic and laboratory parameters were performed using pared t-test for normal data and wilcoxon paired test for data without normal distribution. P-value <0.05 was considered as statistically significant. Delta analysis was performed for comparing pre and post data and to quantify the data as: increased, decreased and stable (remained unchanged). All the statistical analysis were performed with medicala software version 14.8.1 (Medcalc, software, Ostend, Belgium).

RESULTS

The study included 50 patients with inadequately controlled T2DM. The descriptive details of the study participants are given in Table-1. The mean (SD) age noted as 60 (46-68) with a male to female ratio of 1:0.78. The medium (range) of BMI was 23.78 (19.20 – 38) kg/m^2.

The details of comparison of pre and post treatment clinical and laboratory parameters are given in Table-2. Statistical significant different between the pre and post treatment levels of weight, systolic BP, diastolic BP, Urea, FBS, PPBS, and HbA1c was noted. However, creatinine values were not significantly different.

The results of data analysis, performed for pre and post treatment clinical and laboratory parameters are given in Table-3. Pre and post treatment weight showed increase in 13 patients, decrease in 24 patients and stable in 13 patients. Systolic BP increased in 6 Patients, decreased in 40 patients and was stable in 4 patients. Diastolic BP increased in 4 patients and decreased in 46 patients. Decrease in urea levels were noted in 36 patients, while it was increased in 10 patients and was stable in 4 patients. Creatine was increased in 18 patients, decrease in 20 patients and remained unchanged in 12 patients. There was an overall decreased in the post treatment FBS, PPBS and HbA1c level.

Parameters	Values*
Age (Years)	60 (46-68)
Gender (M/F)	28 / 22
BMI	23.78 (19.20 – 38)
(Descriptive statistics for demographic and anthropometric variables of the subjects). (* Data without normal distribution as median (range) and categorical data as counts).	

Table-1:

Parameters	Increase	Decrease	Stable
Pre- and Post-treatment			
Weight	13	24	13
Systolic BP	06	40	04
Diastolic BP	04	46	01
Urea	36	10	04
Creatinine	18	20	12
Baseline and after 3 months			
FBS	0	50	0
PPBS	0	50	0
HbA1c	1	47	2

Table-3: Delta Difference between Pre- and Post-Treatment Levels of Anthropometric and Laboratory Parameters.

DISCUSSION

Remogloflozine is one of the newer SGLT-2 inhibitors, introduced to improve not only glycemic control but also to exploit a battery of its other pleotropic effects. SGLT-2 facilitates the reabsorption of filtered glucose from the proximal convulated tubules by around 90%. Therefore, the treatment by these agents, significantly reduces the reabsorption of the filtered glucose load, thereby increasing the renal excretion of glucose. Accumulating evidence has demonstrated the efficacy of the drug as mono and add on therapy in T2DM.

Sykes et all (2014), in a randomized, double blind, placebo controlled trial, observed a statically significant reduction in HbA1C from baseline.[6] In a study of 6 months duration, which was fashioned in the form of a double blind, double dummy, active controlled, three-arm parallel group, multicentre, phase

Parameters	Pre-treatment / Baseline*	Post-treatment / After 3 months *	P Value
Weight (n=50)	64.63 ± 7.44	64.01 ± 7.22	0.0032
Systolic BP (n=50)	136 (110-190)	134 (108-154)	< 0.0001
Diastolic BP (n=50)	82 (64-98)	80 (60-90)	< 0.0001
Urea (n=50)	27.23 ± 6.49	25.25 ± 5.94	< 0.0001
Creatinine (n=50)	1 (0.6-1.3)	0.9 (0.4-3.5)	0.6154
FBS (n=50)	154 (94-204)	121.5 (84-170)	< 0.0001
PPBS (n=50)	284 (184-360)	175 (144-310)	< 0.0001
HbA1c (n=50)	8.10 (7.40-9.60)	7.0 (6.50-9.10)	< 0.0001

Table-2: Comparison between Pre and Post treatment Levels of Anthropometric and Laboratory Parameters in the Subjects.

III study, Mala Dharmalingam et all, demonstrated the non-inferiority of remogliflozin compared with dapagliflozin.[7] V. Mohan et all in a study, published recently, have found clinically meaningful glycaemic control with remogliflozin.[8] In a paper presented at the AACE 29th Annual Scientific and Clinical Congress (Embrace 2020) Rajiv Chawla and colleagues demonstrated a 0.94% reduction in HbA1C.[9] Dobins et all also reported a significant reduction in plasma glucose in their patients treated with remogliflozin.[10]

As reported in the literature for most of the studies with SGLT-2 inhibitors, including the present one, there was significant loss of body weight and the proposed mechanism underlying this effect includes loss of calorie vide glycosuria, reduced total body adiposity or improvement in weight related quality of life.[11] In most of the studies with SGLT-2 inhibitors, both the systolic and diastolic blood pressure were found to be reduced. Same observation was also noted in the present study

The present finding are significant as the study is first of its kind reporting the efficacy of remoglflozin as an add on therapy to dual drug combination of metformin and glimiperide in T2DM patients with inadequate glycaemic control.

The limitation of this study includes small sample size, single centre based and non-randomized study design. The present study has also not evaluated the safety of the drug as add on to the dual drug therapy. The study warrants prospective cohort studies, involving larger sample size to find out the long term efficacy of this drug combination on disparate population to corroborate the present study findings.

CONCLUSION

The present study suggests remogliflozin as an effective add on oral therapeutic option T2DM patients, not adequately controlled with dual therapy, with metformin and glimipride. The drug can provide adequate glycaemic control with a battery of other pleotrophic benefits.

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