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Original Research Article

A prospective, randomised, open label study to compare efficacy and safety of hydroxychloroquine and teneligliptin in patients of type 2 diabetes mellitus refractory to concomitant metformin and glimepiride

Manisha Anand, Gurpreet Kaur Randhawa, Surinder Kumar Salwan*

Department of Pharmacology, GMC Amritsar, Punjab, India

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***Correspondence:**
Dr. Surinder Kumar Salwan,
Email: surindersalwan05@gmail.com

ABSTRACT

Background: Diabetes mellitus is chronic, metabolic disease characterized by hyperglycemia, which over time causes both microvascular and macrovascular complications. If HbA_1c target is not achieved with dual therapy then 3rd drug is added. Aims of present study were to compare efficacy and safety of Hydroxychloroquine (HCQ) and Teneligliptin in patients of T2DM who are refractory to concomitant Metformin and Glimepiride.
Methods: It was interventional, randomized, prospective, parallel and open-label study. Patients were randomly divided into 2 groups either HCQ 400mg OD or Teneligliptin 20mg OD were added to their current treatment using Metformin 1gm BD and Glimepiride 4 mg OD as 3rd drug. Follow up was done every 15 days for 12 weeks and underwent assessment of glycaemic parameters (FBS, PPG, HbA_1c), LFT, RFT, CBC, ADRs and VAS in addition to anthropometric parameters.
Results: After 12 weeks of treatment, HCQ group showed statistically ($p<0.05$) better improvement in BMI than Teneligliptin group. Both groups showed comparable improvement ($p>0.05$) from baseline in FBS, HbA_1c, PPG and VAS score. In HCQ group there was significant number ($p<0.05$) of patients who achieved target glycaemic control ($HbA_1c \leq 7.5\%$) i.e., 56.6%, compared to 37% with Teneligliptin group. Both groups had comparable ($p>0.05$) safety profile with no serious adverse effects and no significant change ($p>0.05$) in hepatic, renal and complete blood profiles.
Conclusions: On the basis of effects of HCQ on the glycaemic parameters and BMI, HCQ may be preferred over Teneligliptin in patients of T2DM who are refractory to concomitant Metformin and Glimepiride.

Keywords: Oral hypoglycemic agents, Sulfonylurea, Fasting blood glucose, Visual analogue scale

INTRODUCTION

Diabetes mellitus is a chronic, metabolic disease characterized by elevated levels of blood glucose, which over time causes both microvascular and macrovascular complications. Diabetes occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.[1] Globally, the number of cases and the prevalence of diabetes have been slowly increasing over the past few decades especially in low-and middle-income countries and it became the leading causes of the death in the world and 1.6 million deaths are directly associated with diabetes.[2]

The aetiology of diabetes is multifactorial. Genetic and environmental factors such as obesity associated with rising living standards, steady urban migration, and lifestyle changes plays very important role in its aetiology. Over the last century, changes in human behaviour and lifestyle have resulted in a dramatic increase in the

incidence of diabetes worldwide.[3] The most effective management of T2DM includes both lifestyle modifications with diet and exercise and pharmacological therapies as necessary to meet individualized glycemic goals. Lifestyle modifications must be combined with oral hypoglycemic agents (OHA) for optimal glycemic control. American diabetes association suggests that each new class of oral hypoglycemic agents added to initial therapy generally lowers HbA_{1c}, approximately 0.7-1.0%. If the HbA_{1c} target is not achieved after approximately 3 months then start with dual therapy. If HbA_1C target is still not achieved after 3 months of dual therapy then proceed to the three drug combination and again, if HbA_{1c} target is not achieved after 3 months of triple therapy, then proceed to combination therapy with insulin.[4] After the diagnosis of T2DM, metformin is started as initial therapy. It is the first drug of choice in patients with T2DM.[5] Metformin is effective and safe, is cost effective and may decrease the risk of cardiovascular events and death. If we compare metformin with other OHAs, it has more beneficial effects on HbA_{1c}, weight, and cardiovascular mortality.

Glimepiride is a long acting, third generation sulfonyl-urea with hypoglycemic activity. It is a very potent drug with longer duration of action.[6] In addition to the effects on pancreatic β-cell function, glimepiride also may enhance tissue sensitivity to insulin.[7] It is found to be a good option for glycemic control in T2DM. It decreases glucose level by stimulating insulin release from pancreatic β cells. Teneligliptin is a recently developed oral dipeptidyl peptidase 4 (DPP-4) inhibitor indicated for the treatment of T2DM in adults along with diet and exercise.[8] It inhibit the enzyme DPP-4 and prolong the action of glucagon-like peptide. This inhibits glucagon release, increases insulin secretion, and decreases gastric emptying thus decreasing blood glucose levels. Inflammation plays a crucial role in pathogenesis of diabetes and number of co-existing diseases. HCQ, a long-standing safe and inexpensive treatment for autoimmune disorders, may improve glucose tolerance and prevent diabetes. HCQ is an antimalarial drug with anti-inflammatory properties.[9] Use of HCQ for >4 years showed 77% reduction in the risk of diabetes. Some observational studies have suggested reductions in the incidence of diabetes in association with HCQ treatment in patients with rheumatic diseases. HCQ is derived from chloroquine, which has an insulin-sparing effect in T2DM and also improves glucose tolerance in T2DM.It has a new mechanism of action i.e., post receptor inhibition of insulin degradation for reducing blood glucose levels. It acts by inhibiting the insulin degrading enzyme and increasing the insulin concentration and decreasing glucose levels. Because of its anti-hyperglycemic potential, anti-inflammatory activity and pleiotropic effects such as lipid lowering action, antiplatelet action, antithrombotic action and nephroprotective action, it may emerge as a cost-effective therapeutic option for uncontrolled diabetes patients. HCQ would be an appealing option because it is generic, inexpensive, easy to administer and its safety profile has been known for decades. HCQ was selected for the study because it has a well-established safety profile and have multifaceted effects too. Considering its multifaceted effects, HCQ could slow down the progression from the prediabetes stage to diabetes and it can also improve the cardiovascular risk profile in patients of diabetes with its favorable actions on blood glucose, lipid profile, antithrombotic properties and anti-inflammatory properties, making it an attractive therapeutic choice for the treatment of T2DM patients.[10] Teneligliptin was selected for the study because it has longer plasma half-life, dual mode of elimination, cost effective in India when compared to other DPP-4 inhibitors, resulting in better compliance. Teneligliptan and metformin combination results in lowering of glycaemic and lipid profile with reduced side effects of hypoglycaemia and weight gain.

Aim and objectives

Aim and objectives of current study were; to evaluate the efficacy and safety of two drugs i.e., HCQ and Teneligliptin are compared in combination with Metformin and Glimepiride on glycaemic parameters and their effect on quality of life in patients of T2DM over a period of 3 months, to evaluates percentage of patients reaching treatment targets i.e., HbA_{1C} <7.5% and/or reduction in HbA_{1C} by 0.5% and/or 1%, FBS -126mg/dl and PPG- 180mg/dl and changes in BMI and to assess quality of life.

METHODS

This was a prospective, randomized, open label study conducted in department of pharmacology, Government medical college, Amritsar in collaboration with department of medicine, Guru Nanak Dev hospital attached to the Government medical college, Amritsar. A total of 60 patients suffering from T2DM visiting the outpatient department of medicine and fulfilling the inclusion criteria were recruited in the study after taking an informed consent.

Inclusion criteria

Inclusion criteria for current study were; patients diagnosed with T2DM and uncontrolled on a combination of metformin and glimepiride, patients of either sex aged between 18 and 65 years and patients with: HbA_{1C} between 7.5% and 13.0%, fasting blood sugar (FBS) >126 mg/dl (7mmol/l) (measured after at least 8 hours of fasting) and post-prandial blood glucose (PPG) >180mg/dl (10mmol/l) (measured at 2 hours post-lunch or first meal of the day) at screening visit for inclusion in the study.

Exclusion criteria

Exclusion criteria for current study were; patients receiving insulin therapy, or receiving immunosuppressive drugs or any other drug increasing the risk of myopathy were excluded. Patients with recent cardiovascular events,

active gastrointestinal or hematological disorders, diabetic ketoacidosis, hypoglycemia unawareness, abnormal renal or liver function or any other significant illness were not included in the study. Patients with a H/O any retinopathy including diabetic retinopathy requiring laser therapy, uncorrected visual acuity 20/100, abnormal visual fields, difficulty examining the optic disc, or evidence of retinal pigment, epithelial abnormalities. H/O myalgia, H/O psoriasis, porphyria, rash, scaling eczema and patients receiving any concomitant medication that may interact with the action of the study drug or evaluation parameters and pregnant or lactating women or women of child bearing potential not practicing contraception were also excluded.

Patients were randomly divided into 2 groups; A and B consisting of 30 patients each. Randomisation was carried out with the help of random numbers generated by computer software programmer (Random number generator). Group A received HCQ 400mg OD, Metformin 1 gm BD and Glimepiride 4 mg OD for 90 days. Group B received Teneligliptin 20mg OD, Metformin 1gm BD and Glimepiride 4 mg OD for 90 days. Follow up was done every 15 days for 90 days for assessment of anthropometric parameters, fasting blood sugar (FBS), Post prandial glucose (PPG), HbA_{1c}, Complete blood count (CBC), Liver function test (LFT), Renal function test (RFT), Adverse drug reactions (ADRs) and Visual analogue scale (VAS). All the parameters were recorded, tabulated and analysed using 't' test; paired `t`-test for intragroup comparison and unpaired `t` test for intergroup comparison.

RESULTS

In this present study we have analyzed a data of 60 patients. 45% were males and 55% were females out of the entire patient population. Baseline population and clinical characteristics of the study participants was comparable and shown in (Table 1). At the end of 90 days, Group A (1.2±0.91) had shown statistically better ($p<0.005$) effect in improving the BMI as compared to Group B (1.0±0.95). A highly significant ($p<0.01$) reduction was seen over 90 days in both the groups in Glycaemic parameters i.e., FBS, PPG and HbA_1c (Table 2-3). The intergroup difference was non-significant ($p>0.05$) (Figure 1). It has been noted that in HCQ treated group there was a significant number ($p<0.05$) of patients who achieved target glycaemic control ($HbA_1c \leq 7.5\%$). 56.6% of patients have achieved $HbA_1c \leq 7.5\%$ in group A, compared to 37% with the group B. No significant changes in CBC, LFT and RFT were found in patients in both the groups. The incidence of adverse drug reactions in both the groups were similar and these ADRs were not serious and did not require hospitalisation or discontinuation of therapy. There was no incidence of hypoglycemia in either group. There was highly significant improvement ($p<0.001$) in VAS scale indicating improvement in quality of life in Group A and B over a period of 90 days (Table 5). But the intergroup difference was non-significant ($p>0.05$).

The intergroup difference between Group A and B over a period of 90 days of treatment for mean % change of glycaemic parameters was statistically non-significant ($p>0.05$). Both groups had comparable effect on glycaemic parameters.

Table 1: Intergroup comparison of various parameters at day '0'.

Parameters	Group A (Mean±SD)	Group B (Mean±SD)	P value
Age	55.2±9.4	55.1±10.0	0.989
BMI (kg/m^2)	23.0±2.2	25.03±2.5	0.437
FBS (mg/dl)	193±22.7	189.5±23.0	0.556
PPG (mg/dl)	235.3±15.5	241.5±15.6	0.130
HbA_1c (%)	9±0.85	8.8±0.86	0.561
Hb (g/dl)	10.9±1.1	10.8±1.2	0.915
TLC (/cmm)	7093.3±1484.1	7026.6±1421.2	0.860
Monocytes (%)	4.6±2.4	4.2±2.4	0.565
Eosinophils (%)	3.4±1.4	3.1±1.6	0.371
Lymphocytes (%)	29.3±5.8	28.2±5.5	0.475
Platelets count ($x10^9$/l)	300.1±60.2	281.5±58.1	0.229
S. Bilirubin (mg/dl)	0.33±0.23	0.25±0.22	0.164
SGOT (U/l)	24.0±6.5	22.6±8.5	0.470
SGPT (U/l)	24.1±6.9	24.5±6.5	0.849
S. Albumin (g/dl)	4.0±0.18	4.0±0.21	0.747
Alk_Phosp (IU/l)	196.2±56.0	171.1±73.5	0.143
B.urea (mg/dl)	18.0±2.2	18.0±2.7	1.0
S. Creatinine (mg/dl)	0.85±0.17	0.84± 0.17	0.826
VAS	48.5±6.6	45.5±6.6	0.234

p>0.05: Not significant *p<0.05: significant **p<0.001: highly significant (p value: Unpaired t test).

Table 2: Intragroup comparison of glycemic parameters in Group 'A' over '90' days of treatment.

Parameters	Baseline	90 days	% Change	P value
FBS (mg/dl)	193±22.7	166.2±24.1	26.7±6.4	<0.001**
PPG (mg/dl)	235.3±15.5	192.9±16.1	42.4 ±7.6	<0.001**
HbA_{1c} (%)	9±0.85	7.98±0.91	1.01±0.24	<0.001**

p>0.05: Not significant *p<0.05: significant **p<0.001: highly significant (p value: Unpaired t test).

Table 3: Intragroup comparison of glycemic parameters in Group 'B' over '90' days of treatment.

Parameters	Baseline	90 days	% Change	P value
FBS (mg/dl)	189.5±23.0	169.1±23.1	20.4±4.7	<0.001**
PPG (mg/dl)	241.5±15.6	200.7±20.5	40.8±7.4	<0.001**
HbA_{1c} (%)	8.8±0.86	8.1±0.86	0.77±0.18	<0.001**

p>0.05: Not significant *p<0.05: significant **p<0.001: highly significant (p value: Unpaired t test).

Table 4: Comparison of adverse effect profile of patients in group 'A' and 'B' over '90' days of treatment.

Adverse effect	Group A		Group B	
	N	%	N	%
Tiredness	10	33	-	-
Dizziness	-	-	3	10
Headache	8	26.6	7	23.3
Bloating	-	-	9	30
Abdominal pain	5	16.7	-	-
Constipation	-	-	5	16.7
Total number	23	-	23	-

Table 5: Intragroup comparison of VAS of patients in group 'A' & 'B' over '90' days of treatment.

Time	Group A			Group B			P value
	Mean±SD	Mean change from Day '0'	P value	Mean±SD	Mean change from Day '0'	P value	
At 0 day	45.50±6.61	-	-	45.50±6.61	-	-	
At 90 day	78.50±11.24	33.0±10.58	<0.001**	75.50±10.77	30.0±10.82	<0.001**	>0.05

p>0.05: Not significant *p<0.05: significant **p<0.001: highly significant (p value: Unpaired t test).

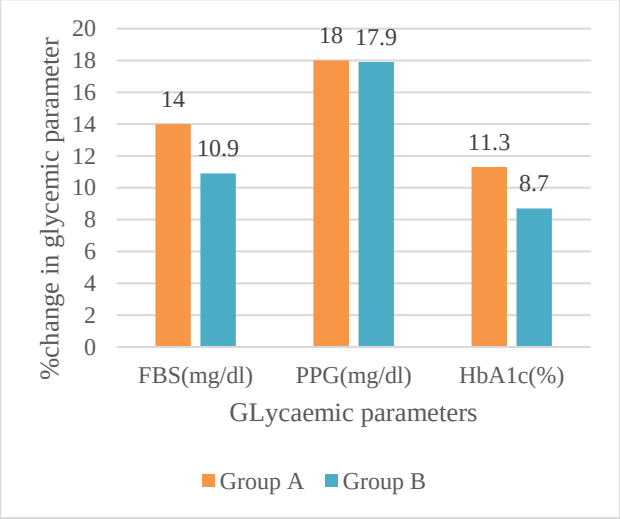

Figure 1: Intergroup comparison between group A and B of glycaemic parameters over '90' days.

DISCUSSION

The present study was carried out to evaluate the hypoglycemic potential of HCQ in comparison with Teneligliptin in patients inadequately controlled on a combination of Glimepiride with Metformin.

BMI

In the present study, it was observed that Group A had shown statistically better effect in improving the BMI as compared to Group B i.e., 1.2±0.91 vs 1.0±0.95 (p<0.005) respectively. The results are similar to a multicentric study of 12 weeks conducted by Pareek et al which showed significant reduction (p<0.05) in weight after addition of HCQ (400 mg) with Metformin (1000mg) and Glimepiride (4 mg).[11] Similar results were seen in another randomised study conducted by Chakravarti et al (n=304) at Kolkata, in which patients were divided into three groups and three different doses of HCQ (200,300,400 mg) per day were

given to patients. Results of this study also showed reductions in body weight (-0.7 to -2.1 kg at week 12) in all HCQ groups.[12] On the contrary, an observational study (n=180) conducted at 2 diabetic centres of Patna city by Kumar et al (October 2017 to May 2018) showed no statistically significant reduction in mean weight with HCQ (400 mg/day) and Teneligliptin (20 mg/day) over a period of 12 weeks.[13] Similarly another multicentric study conducted by Baidya et al from October, 2017 to March, 2018 in India proved that there was no obvious change in the BMI observed after 6 months of HCQ (400 mg/day) treatment.[14]

Diabetic parameters

In the present study, highly significant reductions were seen in glycaemic parameters in both the treatment groups. Mean percentage change in FBS with both Groups A and B respectively i.e., 14.0±3.7 mg/dl ($p<0.001^{**}$); 10.9±2.8 mg/dl ($p<0.001^{**}$). Mean percentage change in PPG in both Groups A and B was respectively i.e., 18.0± 3.2 mg/dl ($p<0.001^{**}$); 17.9±3.6 mg/dl ($p<0.001^{**}$). Mean percentage change in HbA_1c in both Groups A and B was respectively i.e., 11.3±2.8 ($p<0.001^{**}$); 8.7±2.2 ($p<0.001$). The intergroup difference for the mean change in FBS, PPG and HbA_1c at Day '90' in the present study was non-significant ($p>0.05$). Hence both the drugs were similar in decreasing glycaemic parameters. It has been noted that in group A there was a significant number ($p<0.05$) of patients who achieved target glycaemic control ($HbA_1c \leq 7.5\%$). 56.6% of patients have achieved $HbA_1c \leq 7.5\%$ in group A, compared to 37% with the group B. These findings are in concordance with a multicentric study of 24 weeks (n=200) conducted by Jagnani et al at tertiary care clinics of Ranchi, Jharkhand and Kolkata, West Bengal, India. This study observed significant mean reduction in FBS (46±25 mg/dl), PPG (78±37 mg/dl) and HbA_1c (1.8±1.1) in HCQ (400 mg/day) group ($p<0.001$). Similarly mean reduction in FBS (40±31 mg/dl), PPG (72±32 mg/dl) and HbA_1c (1.6±1.1) ($p<0.001$) was observed in Teneligliptin (20 mg/day) group.[10] Similarly, there was a significant number ($p<0.05$) of patients who achieved target glycaemic control (≤7.5%). 60%of patients have achieved $HbA_1c \leq 7.5\%$ in group A, compared to 40% with the group B. Another multicentric study of 12 weeks conducted by Pareek et al (n=267) across India between December 2009 and July 2013, also showed highly significant reduction ($p<0.0001$) in glycemic parameters with addition of the third drug HCQ (400 mg/day) to Metformin (1000 mg/day) and Glimepiride (4 mg/day).[11] Similar findings were seen in another multicentric study conducted by Singh et al from August 2017 to March 2018, which compared the efficacy and safety of Teneligliptin (20mg/day) with HCQ (400 mg/day).[15] Results of this study showed that there were significant reduction in FBS (-29.87±8.9 mg/dl), PPG (-56.89±9.2 mg/dl) and HbA_1c (-1.1±0.17%; p=0.001) values from the baseline to 12 weeks, which is in agreement with the present study. Another observational study (n=180) was conducted by Amit Kumar et al (2019) at 2 diabetic centres of Patna city (from October 2017 to May 2018). They observed that at the end of 24 weeks there was statistically significant reduction in mean FBS (48±17 mg/dl, $p<0.001$), PPG (71±18 mg/dl, $p<0.001$) and HbA_1c (1.1±0.3, $p\leq0.001$) was observed in the HCQ (400 mg/day) group. Similarly, the mean change in FBS 50±15 mg/dl ($p<0.001$), PPG was -78±20 mg/dl ($p<0.005$) and HbA_1c (0.82±0.3, $p\leq0.001$) was observed in Teneligliptin (20mg/day) group, which is in agreement with the present study. But in contrast to present study the intergroup difference for the mean change in FBS, PPG and HbA_1c from baseline to 24 weeks between HCQ and Teneligliptin groups was also statistically significant ($p\leq0.001$), which indicated the superiority of HCQ in reducing glycaemic parameters.[13] Above mentioned studies showed that there was significant reduction in FBS, PPG and HbA_1c with the addition of HCQ (400 mg OD)/Teneligliptin (20 mg OD) along with their standard treatment, but the intergroup difference for the mean change in glycaemic parameters at Day '90' in the present study was non-significant ($p>0.05$). Hence both the drugs were similar in decreasing glycemic parameters over a period of 90 days.

Complete blood count

In the present study, there was no worsening or improvement of haematological profile. But we also observed that mean change in Hb, TLC, DLC and platelets count was statistically non-significant ($p>0.05$). In rare cases HCQ can lead to bone marrow depression and cause leucopenia and thrombocytopenia but these findings were not seen in present study. We could not find a similar study comparing the effects of concomitant therapies on haematological profile as assessed in the present study.

Hepatic parameters

In the present study there was no worsening or improvement of hepatic profile (i.e., Serum bilirubin, SGOT, SGPT, Alkaline phosphatase, S. Albumin) which was in agreement with a randomised controlled trial of 12 weeks conducted by Hsia. Results of this study also showed that there was no worsening or improvement of hepatic parameters with use of HCQ (400 mg/day) ($p>0.05$).[16] Another multi centric prospective, parallel-group, randomized study of 6 months conducted by Baidya et al (from October, 2017 to March, 2018) also showed that there was no significant difference in hepatic parameters with HCQ (400 mg/day). There was no incidence of renal and hepatic toxicity with HCQ (400 mg/day) and Teneligliptin (20 mg/day).[17]

Renal profile

In the present study, there was no worsening of renal profile i.e., blood urea and serum creatinine levels. Change in blood urea (from 18.7±2.5 to 18.9±2.6 mg/dl, p=0.805) and S. creatinine (from 0.84±0.16 to 0.89±0.14 mg/dl, p= 0.216) was statistically non-significant ($p>0.05$). A multicentric study conducted by Singh et al (from August

2017 to March 2018) (n=500) also showed that there was no worsening of renal profile with HCQ (400 mg/day) and Teneligliptin (20 mg/day) over a period of 12 weeks. Change in blood urea (from 28.54±0.60 mg/dl to 28.37±0.61 mg/dl) and S. creatinine (from 0.97±0.03 to 0.97±0.01 mg/dl, p=0.967) was statistically non-significant (p>0.05) with HCQ. It was also observed that after switch from Teneligliptin to HCQ there was no change in serum creatinine and eGFR.[15] Similarly another studies conducted by Baidya et al and Kumar at Patna, showed that there was no worsening of renal profile with HCQ (400 mg/day) (p>0.05) over a period of 6 months.[18,19] These studies showed that there was no incidence of renal and hepatic toxicity with HCQ (400 mg/day) and Teneligliptin (20 mg/day).

Safety profile

On analysis of adverse effects in the present study, both the groups had comparable safety profile. None of the groups had shown any serious/ unexpected adverse effect or the need to discontinue the treatment. A multicentric study of 12 weeks conducted by Pareek et al (n=267) across India between December 2009 and July 2013 have mentioned about the adverse effects of HCQ. [11]

Visual analogue scale (VAS)

The improvement in mean VAS score for Group A was 33.0±10.58 (p<0.001) and for Group B it was 30.0±10.82 (p<0.001) with no statistical difference between the two groups (p=0.234). Quality of life was improved in both groups A and B over a period of 12 weeks. We could not find a similar study comparing the effects of concomitant therapies on quality of life as assessed in the present study. Hence, both Group A and B showed improvement in the Glycaemic parameter, BMI and VAS (quality of life) over a period of 90 days. Group A has better effect on BMI. While both groups showed equivalent and beneficial effect on diabetic parameters and VAS. Overall assessment of safety demonstrated that both HCQ and Teneligliptin were well tolerated in this study.

Strengths and limitations

Effect of these drugs on safety profile and quality of life were also studied which is the strength of current study. Limitations of current study are small sample size (n=60) and time constraint (3 months). Larger sample size and studies of long-term duration are desirable.

CONCLUSION

From these observations it can be concluded that Group A was statistically better than group B in reducing BMI. Both the groups showed comparable improvement in FBS, PPG, HbA_1c, safety and VAS score. It has been noted that in group A there was a significant number (p<0.05) of patients who achieved target glycaemic control (HbA_1c ≤7.5%) i.e., 56.6%, compared to 37% with the group B. Hence, on the basis of effects of HCQ on the glycaemic parameters and BMI, HCQ may be preferred over Teneligliptin in patients of T2DM who are refractory to concomitant Metformin and Glimepiride.

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REFERENCES

1. Diabetes. Available at: https://www.who.int/news-room/fact-sheets/detail/diabetes. Accessed on 10 June 2021.
2. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017;128:40-50.
3. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414(6865):782-7.
4. Ramachandran A. Know the signs and symptoms of diabetes. Indian J Med Res. 2014;140(5):579-81.
5. Ganesan K, Sultan S. Oral hypoglycemic medications. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2019.
6. Gottschalk M, Danne T, Vlajnic A, Cara JF. Glimepiride Versus Metformin as Monotherapy in Pediatric Patients With Type 2 Diabetes: A randomized, single-blind comparative study. Diabetes Care. 2007;30(4):790-4.
7. Sharma SK, Panneerselvam A, Singh KP, Parmar G, Gadge P, Swami OC. Teneligliptin in management of type 2 diabetes mellitus. Diabetes Metab Syndr Obes. 2016;9:251-60.
8. Deogaonkar N. Hydroxychloroquine: a therapeutic choice in diabetes mellitus. J Diabetes Res. 2020;2020:5214751.
9. Jagnani VK, Bhattacharya NR, Satpathy SC, Hasda GC, Chakraborty S. Effect of hydroxychloroquine on type 2 diabetes mellitus unresponsive to more than two oral antidiabetic agents. J Diab Metab. 2017;8(10):1-6.
10. Pareek A, Chandurkar N, Thomas N, Viswanathan V, Deshpande A, Gupta OP, et al. Efficacy and safety of hydroxychloroquine in the treatment of type 2 diabetes mellitus: a double blind, randomized comparison with pioglitazone. Curr Med Res Opin. 2014;30(7):1257-66.
11. Chakravarti HN, Nag A. Efficacy and safety of hydroxychloroquine as add-on therapy in uncontrolled type 2 diabetes patients who were using two oral antidiabetic drugs. J Endocrinol Invest. 2021;44(3):481-92.
12. Kumar A, Prakash AS. Effectiveness and Safety of Hydroxychloroquine compared to Teneligliptin in uncontrolled T2DM patients as add-on Therapy. J Asian Fed Endocr Soc. 2019;34(1):87-91.

13. Baidya A, Kumar M, Pathak SK, Ahmed R. Study of comparative effect of hydroxychloroquine and vildagliptin on glycaemic efficacy and HbA_1c in type 2 diabetes patients who were inadequately controlled with metformin and glimepiride dual therapy. JMSCR. 2018;6(4):409-15.
14. Singh UP, Baidya A, Singla M, Jain S, Kumar S, Sarogi RK, et al. Efficacy and safety of substituting teneligliptin with hydroxychloroquine in inadequately controlled type 2 diabetes subjects with combination therapy of teneligliptin, metformin and glimepiride with or without other antidiabetic therapy. Clin Diabetol. 2018;7(5):209-14.
15. Hsia SH, Duran P, Lee ML, Davidson MB. Randomized controlled trial comparing hydroxychloroquine with pioglitazone as third-line agents in type 2 diabetic patients failing metformin plus a sulfonylurea: A pilot study. J Diabetes. 2020;12(1):91-4.
16. Diabetes. Available at: http://jmscr.igm.org/6-i4/68%20jmscr.pdf. Accessed on 20 November 2022.
17. Baidya A, Ahmed R. Effect of early addition of hydroxychloroquine in type 2 diabetic patients inadequately controlled on metformin and sulfonylurea combination therapy. Int J Res Med Sci. 2018;6(8):2626.
18. Kumar V, Singh MP, Singh AP, Pandey MS, Kumar S, Kumar S. Efficacy and safety of hydroxychloroquine when added to stable insulin therapy in combination with metformin and glimepiride in patients with type 2 diabetes compare to sitagliptin. Int J Basic Clin Pharmacol. 2018;7(10):1959-64.

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