Role of Hydroxycholoroquine in Type 2DM/ LADA/ Type 1 DM

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ABSTRACT

Introduction: Hydroxychloroquine is an effective drug in the treatment of inflammatory disorders such as rheumatoid arthritis and systemic lupus erythromatosis. Recent evidences have focused its major role in glucose hemostasis in hyperglycemic patients. The present study was conducted to assess the role of Hydroxycholoroquine in Type 2DM/ LADA/ Type 1 DM.

Material and methods: The present study was conducted to assess role of Hydroxycholoroquine in Type 2DM/ LADA/ Type 1 DM patients at KIMS, BBSR PG dept of Medicine over a period of 1 year. Information for this study, which include antidiabetic medications, demographic data was collected by using a predesigned structured proforma. Those Patients on Insulin were put to Basal Insulin and Hydroxy Choloquine, and patients already on 2 to 3 OHA, Hydroxy Choloroquine was added. Lab investigations were done. The recorded data was compiled and data analysis was done.

Results: The present study showed that the gradual reduction of both FBS and PPBS. Reduction of FBS and PPBS occur in both group but more reduction occur in group 2. Attainment of normal blood sugar occur in 7 months to 1 year.

Conclusion: It was observed that those patients with history of chicken pox, herpes or rheumatoid arthritis or other autoimmune diseases like vitiligo responded well with Hydroxycholoroquine.

Keywords: FBS, PPBS, Glycemic Control, Hydroxychloroquine, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes mellitus is the fourth leading cause of death worldwide, following cancer, cerebrovascular disease, and heart disease. It is triggered by hyperglycemia and other metabolic disorders. In India type 2 Diabetes consider as a major health problem and no of uncontrolled patients are increasing day by day. As per 2015 International Diabetes Federation (IDF) report India is 2nd largest diabetic population which is second to china.[1] Hydroxychloroquine is an antimalarial drug that also acts as a disease-modifying agent in rheumatoid arthritis and lupus erythematosus.[2,3] Hydroxycholoroquine use is associated with reduced DM incidence, reduction in HbA1c, blood glucose levels and improved lipid profile.[4-8] Hydroxycholoroquine most likely acts by reducing the lysosomal degradation of internalised insulin-insulin receptor complex.[5,9,10] Hydroxychloroquine is approved by DCGI (Drug Controller General of India) in 2014 as a third line add on treatment in T2DM patient uncontrolled on metformin and sulfonylurea. Hydroxychloroquine has a unique mode of action which is different from other antidiabetic drugs. It causes inhibition of insulin degradation in cells thus enhancing the metabolic effects of the hormone and has also shown to improve insulin sensitivity in nondiabetic obese individuals.[11] The present study was conducted to assess the role of Hydroxycholoroquine in Type 2DM/ LADA/ Type 1 DM.

MATERIAL AND METHODS

The present study was conducted to assess role of Hydroxycholoroquine in Type 2DM/ LADA/ Type 1 DM patients at KIMS, BBSR PG dept of Medicine over a period of 1 year. Before the commencement of the study ethical approval was taken from the Ethical Committee of the institute and written consent was taken from the patient after explaining the study. Information for this study, which include antidiabetic medications, demographic data was collected by using a predesigned structured proforma.

Inclusion Criteria

- All Type 1 DM cases
- Young Type 2 cases/ LADA
- Type 2 cases associated with autoimmune diseases
- Type 2 DM with recent H/O chickenpox, herpes zoster, mumps

Exclusion criteria

- Patients allergic to Hydroxycholoroquine
- Patient with Blood Dyscriasis
- Patient with G6PD deficiencies
- Cardiac conduction disorders
- Chronic liver disease
- H/O DM>10yrs (Both Type 1 &Type 2 DM)
- Patient with Type 2 DM > 10yrs on insulin

Patients who were on various type of Insulin (Regular, 30:70 , Long Acting Insulin) were put on Basal Insulin and Hydroxychloroquine, and those patients who are on 2 or 3 OHA Hydroxychloroquine was added (Young diabetics with 100 mg Hydroxycholoroquine and older diabetics with 200mg Hydroxycholoroquine daily). Lab investigations were done such as to find antibodies to insulin, LFT, USG abdomen for R/O spleenomeglly, CBC, Hb electrophoresis, Plasma insulin level/ C protein level, RA factor, ESR, CRP.

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Group	Treatment alloted
Group 1 (120 patients)	Metformin (2000 mg), Glimepiride (2 mg), Teneligliptin (20 mg)
Group 2 (120 patients)	Metformin (2000 mg), Glimepiride (2 mg), Hydroxychloroquine (200 mg)

Table-1:

Patients Characteristic	Group 1 Mean± SD	Group 2 Mean± SD	p-Value
FBS			
Baseline	170.12± 40.44	174.43±40.56	<0.005
Change from baseline to 6 months	137.23±41.29	129.21±9.56	
Change from baseline to 7-12 months	131.13	127.67	
PPBS			
Baseline	264.68±60.43	266.44±58.61	<0.005
Change from baseline to 6 months	196.34 ± 53.23	193.65 ± 55.65	
Change from baseline to 7-12 months	193.51 ± 67.56	191.78 ± 68.45	

Table-2: Clinical characteristics of the study participants at baseline.

The recorded data was compiled and data analysis was done.

RESULTS

In the present study total sample was 240 patients who were divided into 2 groups. In group 1 patients only OHA was given and in group 2 patients OHA and hydrocholoroquine was given. The result showed that the gradual reduction of both FBS and PPBS. Reduction of FBS and PPBS occur in both group but more reduction occurs in group 2. Attainment of normal blood sugar occurs in 7months to 1 year.

DISCUSSION

Diabetic patients require multiple drugs to control blood sugar levels and to minimize long-term complications which are associated with diabetes. The association between hyperglycemia, inflammatLon, and vascular complications in diabetes is now well established. Since metabolic dysregulation itself induces inflammation, elective antidiabetes treatments may alleviate inflammatLon by virtue of improving the metabolic state.[12]

Hydroxychloroquine has been found to be an effective antihyperglycemic in patients with type 2 diabetes. An RCT of adults with poorly controlled type 2 diabetes found that the addition of hydroxychloroquine to standard sulfonylurea treatment reduced HbA1c by 1.02% (95% CI 0.24%, 1.81%) more than placebo at 18 months of follow-up.[13] In patients with type 2 diabetes on insulin therapy, hydroxychloroquine was also found to significantly reduce HbA1c compared to placebo at 6 months of follow-up.[14]

In the present study total sample was 240 patients who were divided into 2 groups. In group 1 patients only OHA was given and in group 2 patients OHA and hydrocholoroquine was given. The result showed that the gradual reduction of both FBS and PPBS. Reduction of FBS and PPBS occur in both group but more reduction occurs in group 2. Attainment of normal blood sugar occurs in 7months to 1 year.

Some studies show that treatment with hydroxychloroquine for a period of 6 months can effectively decrease blood glucose and also hemoglobin A1c probably due to increase insulin production and secretion from B cells,[15] or to decrease insulin clearance.[15] In fact, this drug can reduce insulin post receptor clearance and facilitate glucose transfer by insulin.[15] Moreover, hydroxychloroquine can inhibit inflammatory biomarkers as well as regulate the level of lipid profile, leading to a reduced risk of diabetes mellitus.[15,16]

Severe hypoglycemia has been reported in patient with insulin dependence and T2DM within 2 weeks of starting Hydroxycholoroquine at a dose of 400 mg daily for his polyarthritis. The patient had a subsequent decrease in his insulin requirements by 37%.[17]

Since Hydroxycholoroquine is an immunomodulatory drug (has an inhibitory and an immunomodulatory effect on T cells and interleukin 1 and interleukin 6) and type 1 diabetes is an autoimmune disease, a possible reduction in islet-cell autoimmunity by Hydroxycholoroquine could be the underlying mechanism since our patient has longstanding type 1 diabetes with no insulin reserve and an effect on insulin resistance is less likely to be the underlying mechanism that led to the improvement in glycemic control.[18]

CONCLUSION

It was observed that those patients with history of chicken pox, herpes or rheumatoid arthritis or other autoimmune diseases like vitiligo responded well with Hydroxycholoroquine.

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