ECRONICON OPEN ACCESS

EC ENDOCRINOLOGY AND METABOLIC RESEARCH

Case Report

Managing Uncontrolled Type 2 Diabetes: Role of Hydroxychloroquine in Therapy as AD on Antidiabetic Agent: A Case Study

Hiranmoy Paul*

Consultant Diabetologist, Siliguri, West Bengal, India

***Corresponding Author:** Hiranmoy Paul, Consultant Diabetologist, Kins Diabetes Speciality Centre, Siliguri, West Bengal, India.

Received: June 23, 2018; **Published:** July 02, 2018

Abstract

Newer therapy are emerging to control progression of type 2 diabetes. In recent past a large no of evidence confirms the blood glucose lowering ability of Hydroxychloroquine. Hydroxychloroquine (HCQ) can be a useful adjunctive therapy for patients with T2DM as it works through a novel mechanism. Here I report a case of 52 year Bengali male patients with uncontrolled type 2 diabetes with dyslipidemia who had achieved an optimal glycemic control when Hydroxychloroquine was added to the existing pharmacotherapy. There was a significant decrease in glycemic parameter over 24 weeks and the drug was well tolerated. There was a 4 kg reduction in weight after 24 week of treatment. The case highlights that Hydroxychloroquine 400 mg once a day is an effective add-on for achieving target glycemic control when appropriately used in type 2 diabetes mellitus patients who are inadequately controlled on other oral agents.

Keywords: *Hydroxychloroquine; Type 2 Diabetes; HbA1c; FBG; PPBG*

Introduction

Globally incidence of type 2 diabetes has increased by almost double in last few years and became most important public health challenges to most of the nations. The International Diabetes Federation (IDF) reported that, at present, approximately there are more than 415 million people worldwide who are suffering from Diabetes mellitus with the 8.8% global prevalence, and it is estimated that, with a prevalence of 10.4%, their number will grow up to 642 million in 2040 [1]. In India as per 2015 scenario, 69.1 million cases of diabetes were reported.

Hydroxychloroquine (HCQ) has shown its beneficial effects in diabetes and dyslipidemia management. HCQ showed improved glycaemic control in terms of reducing HbA1c, FPG and PPG in several clinical trial [2,3].

Although as monotherapy, all the oral antidiabetic agents are reasonably effective in improving glycaemic control but monotherapy is often associated with loss of efficacy and inadequate control of glycaemia over time due to progressive nature of type 2 diabetes mellitus [4]. Additive effects on glycaemic control can achieved by combining agents with different modes of action, this further allows the use of submaximal doses of the agents and thereby unwanted side effects can be avoided and have complementary benefits on cardiovascular and other risk factors. Therefore the need of adding additional oral antihyperglycemic agent is required when current medication do not achieved a HbA1C target.

Case Presentation

A 52 year old man with 5 year history of type 2 diabetes was presented to my clinic with symptoms indicating hyperglycemia. Patients was referred by his family physician to diabetes speciality clinic and present with recent weight gain, inadequate glycemic control and joint pain. Patients was diagnosed diabetes at late 2013 and at threw initial diagnosis he was advised for physical exercise and prescribed

metformin 500 mg at night. But no further action was taken and patients remain uncontrolled after 1 year. Patients was counselled for diet and exercise and 1mg glimepiride was added after breakfast along with additional metformin 500 mg. After that he was controlled for 3 years and was again presented with elevated glucose profile. He was then up titrated with 2 mg of glimepiride, but had stopped taking it because of dizziness, often accompanied by sweating and a feeling of discomfort, in the late afternoon. After that he was advised to take pioglitazone 30 mg along with glimepiride 1 mg but after few months he again become uncontrolled. He has increased his exercise for the past 6 months and been trying to lose weight but fails to achieve success. He was also prescribed sitagliptin 100 mg in place of glimepiride but patients express his anxiety regarding his cost of the drug, even he was refused to start insulin. His haemoglobin A1c (HbA1C) has never been < 8% as per the medical documents that patients brings to this appointment. I referred the patients to ophthalmologist and confirms that the patients doesn't had any retinopathy or of any grade including diabetic retinopathy, difficulty to examine optic disc, abnormal visual fields or evidence of retinal pigment epithelial abnormalities and patients with history or risk of macular edema.

A physical examination reveals the following:

- **Weight:** 79 KG; Height: 5'8'', Body Mass Index: 26.5 kg/m^2
- **Blood pressure:** Lying, right arm 131/85 mmHg; sitting, right arm 126/80 mmHg; Lungs: clear to auscultation, Heart: Rate and rhythm regular, no murmurs or gallops.
- **Neurological assessment:** Diminished vibratory sense to the forefoot, absent ankle reflexes, monofilament (5.07 Semmes-Weinstein) felt only above the ankle.

Lab Results reveals the following:

Fasting Blood Glucose: 182 mg/dl; Post Prandial Blood Glucose: 318 mg/dl; haemoglobin A1c: 9.6%; Urea: 27.5 mg/dl; Creatinine: 0.8 mg/dl; Sodium: 143 mg/dl; Potassium: 4.4 mg/dl Total Cholesterol: 193 mg/dl, HDL: 61.7 mg/dl, LDL: 103.8 mg/dl, VLDL: 27.5 mg/dl, Triglyceride: 169.7 mg/dl, Cholesterol: HDL: 3.18 mg/dl. Urine micro albumin: 45 mg; AST (SGOT): 18 IU/L; ALT (SGPT): 23 IU/L.

Ongoing medication: He was in combination treatment of metformin 1000 mg, Sitagliptin 100 mg, Pioglitazone 30mg as an antidiabetic treatment. He was also on Rosuvastatin 10 mg, Perindopril 4 mg and 1.25 mg indapamide.

Diagnosis: Patients need an inexpensive antidiabetic medication which will help him to achieve target glycemic goal. Moreover he needs to reduce his obesity and get rid of joint pain. His lipid profile and BP is under control.

Change in treatment regimen: To achieve targeted HbA1c level, patients was advised to take Metformin 1000 mg, Pioglitazone 30 mg and Hydroxychloroquine 400 mg. Rosuvastatin 10mg, Perindopril 4 mg and 1.25 mg indapamide was continued.

Treatment Outcome

There was a drop in HbA1c by almost 1.8% in his first visit which is after 12 weeks, along with significant decrease in FBG and PPBG. Patients was delighted as his weight is reduced after long time which inspire him for further lifestyle modification and strict exercise regimen. After 24 weeks, her fasting blood glucose was 118 mg/dL, postprandial glucose was 165 mg/dL and her HbA1c was 6.8%. Even with strict diet and exercise there was further 2 kg weight reduction as compare to his last visit. His quality of life has significantly improved as his joint pains has come down drastically and he feels better than before.

Characteristic	Baseline	3 months	6 months	Decrease from baseline
Weight (Kg)	79	77	75	-4
FPG (mg/dL)	182	145	118	-64
PPG (mg/dL)	318	196	165	-153
HbA1c (%)	9.6	7.8	6.8	-2.8
Creatinine (md/dl)	0.8	0.8	0.8	0

Table 1: *Changes in blood parameters at baseline, 12 week and at 24 week.*

Patients was advice to check his fasting (before breakfast) and post prandial (2 hour after breakfast) at home and keep the record. FBG and PPBG was performed at 12th week and 24th week at laboratory. There was a systemic reduction of FBG and PPBG after addition of Hydroxychloroquine 400 mg. The details has demonstrated in figure 1.

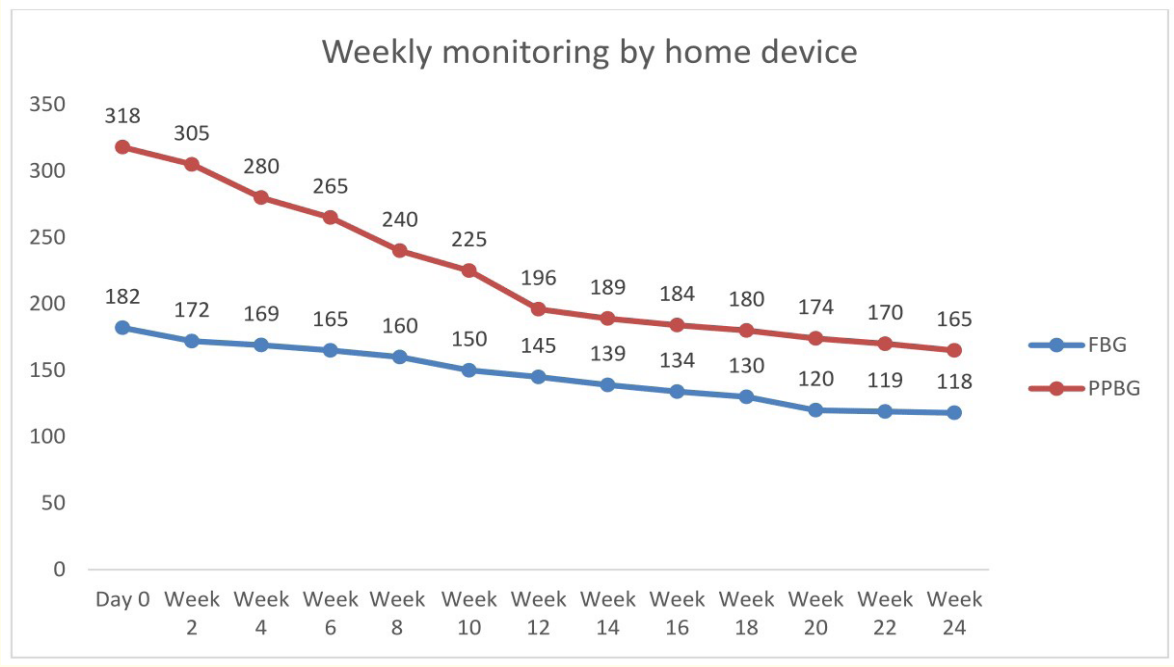

Figure 1: *Weekly report of FBG and PPBG levels.*

Discussion

Insulin clearance defect is an integral part of pathogenesis of T2DM [4]. Subjects with insulin resistance as well as diabetic patients exhibit an increased rate of intercellular insulin degradation [5]. It has been proposed that in the degradation process of the Insulin, the dissociation of insulin from its receptor appears to be the rate limiting step. HCQ affects the insulin metabolism as suggested by several scientific evidences. Direct interaction of HCQ with the insulin receptor reduces the rate of dissociation of insulin from its receptor. It has been postulated that, this may increase the biological half-life of the receptor insulin complex and consequently prolong the action

of insulin [6]. In a recent Indian clinical trial [7], HCQ was evaluated against one of the DPP4i teneligliptin and it has observed that HCQ significantly reduced HbA1c, FPG and PPG as compare to teneligliptin based treatment. Moreover 61% patients has achieve HbA1c > 7%. In an another Indian trial [8], it has seen that that hydroxychloroquine 400 mg can be an effective alternative to DPP-4 inhibitor like vildagliptin for add on therapy to the patients who are inadequately controlled with metformin and glimepiride combination therapy. In a recent conducted Indian Clinical trial by Surendra Prasad Singh., *et al*. [9], were hydroxychloroquine was compared with sitagliptin in patients who were inadequately controlled on combination with metformin and gliclazide, it has been observed that at 24 weeks, there was a statistically significant difference in the mean HbA1c reduction in hydroxychloroquine group (0.92%) as compared to sitagliptin group (0.80%) (P = 0.001).

In the present study there was a significant decrease in overall glycemic levels, which makes patients satisfied and inspire to maintain good glycemic levels. Cost of sitagliptin is one of the main reason to discontinuation of the drug. In this case also there is a sudden rise in blood glucose may because patients is not regularly taking his current medication. On counselling patients even admit that irregularities of sitagliptin mainly because of its higher cost. Thus there was a need of Hydroxychloroquine which not only exhibit a potent glycemic effect but also available in economical price. Diabetes with joint pain has triggered the thinking of adding hydroxychloroquine to this patients and which turned beneficial from day one.

There was significant change in body weight. The potential of weight gain with sulfonylureas or any other medication may be neutralized by the weight loss properties of metformin and Hydroxychloroquine. This finding was in accordance with the previous study conducted by Parekh., *et al* [10]. Initial weight loss has motivate the patients to perform further regular exercise.

Taken together, these case study showed that the addition of hydroxychloroquine 400 mg could help lower the levels of HbA1c and blood glucose in patients with type 2 diabetes who were inadequately controlled with any oral medication.

Conclusion

The case highlights that Hydroxychloroquine 400 mg once a day significantly improves glycemic parameters in Indian T2DM patients when prescribed as add-on to one or more antidiabetic drugs.

Acknowledgments

Author acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The author is also grateful to authors/editors/publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

Disclosure

The author report no conflicts of interest in this work.

Bibliography

1. International Diabetes Federation. IDF Diabetes Atlas, 7th edition. Brussels, Belgium: International Diabetes Federation (2015).

2. Jagnani VK., *et al*. "Effect of hydroxychloroquine on type 2 diabetes mellitus unresponsive to more than two oral antidiabetic agents". *Journal of Diabetes and Metabolism* 8.10 (2017): 771.

3. Baidya A., *et al*. "Efficacy of maximum and optimum doses of hydroxychloroquine added to patients with poorly controlled type 2 diabetes on stable insulin therapy along with glimepiride and metformin: association of high-sensitive c-reactive protein (hs-crp) and glycosylated haemoglobin (hba1c)". *Endocrinology and Metabolic Syndrome* 7 (2018): 283-287.

4. Mudaliar S. "New frontiers in the management of type 2 diabetes". *Indian Journal of Medical Research* 125.3 (2007): 275-296.

5. Duckworth WC., *et al*. "Insulin Degradation: Progress and Potential". *Endocrine Reviews* 19.5 (1998): 608-624.

6. Farris W., *et al*. "Insulin-degrading enzyme regulates the levels of insulin, amyloid β-protein, and the β-amyloid precursor protein intracellular domain in vivo". *Proceedings of the National Academy of Sciences of the United States of America* 100.7 (2003): 4162-4167.

7. Jagnani VK., *et al*. "Effect of Hydroxychloroquine on Type 2 Diabetes Mellitus Unresponsive to More Than Two Oral Antidiabetic Agents". *Journal of Diabetes and Metabolism* 18.10 (2017).

8. Baidya A., *et al*. "Study of comparative effect of hydroxychloroquine and vildagliptin on glycaemic efficacy and HbA1c in type 2 diabetes patients who were inadequately controlled with metformin and glimepiride dual therapy". *Journal of Medical Science and Clinical Research* 6.4 (2018).

9. Surendra Prasad Singh., *et al*. "Comparative Study to Evaluate Effect of Hydroxychloroquine Versus Sitagliptin as Add on Therapy in Patients with Type 2 Diabetes Inadequately Controlled on Combination with Metformin and Gliclazide: A Multicenter, Observational Trial". *Scholars Journal of Applied Medical Sciences* 6.5 (2018): 2150-2156.

10. Pareek A., *et al*. "Efficacy and safety of hydroxychloroquine in the treatment of type 2 diabetes mellitus: a double blind, randomized comparison with pioglitazone". *Current Medical Research and Opinion* 30.7 (2014): 1257-1266.

Volume 3 Issue 2 July 2018