

Research Article



A Case Control Study on Evaluating the Antihyperglycemic Effect of Hydroxychloroquine along with other Oral Hypoglycemic agent among Type II Diabetes Mellitus Patient in Major Trauma Care Centre

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ABSTRACT

Hydroxychloroquine (HCQ) is an antimalarial and anti-inflammation drug recently approved in India for use in Diabetes. It acts by inhibiting the degradation of insulin and cause accumulation of insulin. In vitro studies have shown that it preserves islets cells and reduce inflammatory mediators. Treatment with higher dose of HCQ in obese subjects have shown improvement of insulin sensitivity and beta cell function. Acute trauma causes stress and inflammation and stress can cause new onset hyperglycemia and worsening of underlying diabetes mellitus. No study has used HCQ in post trauma setting. Current study has explored the use of HCQ in post trauma setting. The study is to evaluate the antihyperglycemic effect of Hydroxychloroquine along with other hypoglycemic agents among Type II Diabetes mellitus patient in major trauma care center. The objective of the present study was to evaluate the antihyperglycemic effect of the Hydroxychloroquine in Type II Diabetes mellitus patient and its adverse effects. It is prospective, interventional clinical study done in a major trauma care center. A total of 100 patient were included in the study. Hydroxychloroquine was introduced during hospital stay follow up was done after 3 and 6 months. Glycemic control was assessed by HbA1C and side effects were recorded. Out of 200 patients 62 completed the study at this time and 62 patients were included as control. The outcome is that mean baseline HbA1C from 10.68% was reduced to 7.25% in case and from 10.22% was reduced to 9.45% in control group. This shows that HCQ reduces 3.43% of HbA1c at first review in case whereas in control 0.77% of HbA1c was reduced. This study concludes that hydroxychloroquine can be an effective add on therapy to the subjects with uncontrolled Type II Diabetes Mellitus along with other Oral Hypoglycemic agents.

Keywords: Hydroxychloroquine, Type 2 Diabetes Mellitus, Oral hypoglycemic agent, HbA1c, Antimalarial.

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INTRODUCTION

The American Diabetes Association (ADA) defines Diabetes mellitus as a group of metabolic diseases characterized by inappropriate hyperglycemia resulting from defects in insulin secretion, insulin action or both. Symptoms of acute hyperglycemia include polyuria, polydipsia, polyphagia, weight loss, blurred vision fatigue, headache and poor wound healing. Chronic hyperglycemia can lead to damage and potentially failure of various organs including the eyes, heart, kidneys, blood vessels and nerves. The key management goals of type 2 diabetes mellitus are to achieve target glycemic control (HbA1c ≤ 7%) and prevention of long-term complications, whilst avoiding hypoglycemia. When treatment goals are not achieved with lifestyle modifications and strict dietary regimen, pharmacological treatment is advised. To optimize the management of type 2 DM, several oral

antihyperglycemic agents are available. Towards achieving good glycemic target, a combination of multiple oral antidiabetic drugs often are required even with an add on insulin among inadequately controlled Indian type 2 diabetes patients. In United States, the prevalence and incidence of diabetes have increased dramatically during past 2 decades in orthopedic patients. WHO estimates that Diabetes is the 7th leading cause of death. In 2017, an estimated 1.6 million deaths were directly caused by Diabetes which elevated to 2.2 million deaths in 2018. Hydroxychloroquine (HCQ), a commonly used antimalarial drug in rheumatic diseases is now 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 slows down insulin clearance. This is done possibly by stabilizing intracellular lysosomes and slowing the breakdown of internalized insulin-receptor complex and therefore inhibit cytosolic insulin metabolizing enzyme. Inflammation plays a crucial role in the progression of T2DM. Based on previous data, it is hypothesized that the addition of hydroxychloroquine in inadequately controlled T2DM patients under combinational (Oral hypoglycemic Agents) therapy will help to achieve better glycemic control in terms of HbA1c, FBS and RBS reduction with additional cardio and reno



protective benefits being continued with other medications.

METHODS AND MATERIALS

The prospective observational study was conducted for six-month time period, in the inpatients of Ganga Medical Care and Hospital Pvt (Ltd) Coimbatore, Tamil Nadu; 500-Bedded Tertiary Major Trauma Care Centre. The study was approved by the Institutional Ethics Committee and was conducted in accordance with good clinical practice (GCP) guidelines outlined in ICH guidelines (<https://ichgcp.net/>). The reports were collected by both active method (direct observation by clinical pharmacist) and passive methods (indirect observation by physician or other hospital staffs). The collected data were evaluated to gather information about the pattern with respect to the patient demographics, characteristics of the drugs involved, nature of the reactions and outcome of the reactions. The blood glucose level were analysed based upon the severity, preventability and reaction causality. In agreement with previous published research articles, age and sex of the patients were evaluated, total 200 patients were randomly classified as Inclusion Criteria, (Willing participants, Diabetic patients, Patients with FBS > 100 mg/dl, Patients with RBS >100 mg/dl, Patients with HbA1c >8, Patients on Rx with Oral Hypoglycemic Agents) and Exclusion Criteria (Pregnant women, Patients with severe cardiac disorders, High risk patients, Patients with FBS < 80mg/dl, Patients with RBS <80 mg/dl, Patients with HbA1c<8). Patients were grouped into age group of 20 years interval (0-20 years, 20- 40 years, 40-60 years, 60-80 years and >80years).

Data analysis

The data collected was evaluated and entered into Microsoft excel spreadsheet. Analysis was performed by using Paired-t-test. The categorical data were presented in the form of frequency and percentage. Results are presented in the form of tables, figures and texts.

RESULTS AND DISCUSSION

In this study, total 200 patients enrolled out of which 76 subjects were excluded due to the severity of their condition (36 patients) and complications (40 patients). This case-control study randomized 124 Type II diabetes patients out of which 62 (50%) were case (with HCQ) and 62 (50%) were control (without HCQ) subjects. It was found that the number of males (72.58%) was higher than the number of females (27.42%) among patients with HCQ. Among patients without HCQ, the number of males (62.90%) was higher than the number of females (37.10%). This study demonstrated that the higher number of subjects was found between the age group of 41-60 years in subjects with HCQ as well as in those subjects without HCQ. From this study reports, we found that there was no significant association between social habits such as alcohol-smoking-tobacco in patients with HCQ and those patients without HCQ. The study reported that the highest number of subjects among the normal range of BMI (18.6-

22.9) was higher in patients with HCQ as well as those without HCQ. In the present study, the increased HbA1C levels was seen in the range of 9.1-10% for subjects with HCQ and 8-9% for subjects without HCQ (Table.1). From the (Figure.1) it was observed that among the co-morbidities occurrence of hypertension was higher compared to other co-morbidities. Most of the subjects in this study were also presented without any co-morbidities. Table.2 demonstrated that higher number of subjects i.e., nearly 32.25% of the subjects were having the fasting blood sugar (FBS) level of range 151-200mg/dl in case (with HCQ) and 30.64% of those having 100-150mg/dl in control (without HCQ). Table.3 demonstrated that the highest number of subjects whose RBS ranges from 151-200mg/dl and >300mg/dl in case (29.04%) and 201-250mg/dl in control (22.58%). In the study (Table.4) showed the higher usage of oral hypoglycemic agents to treat Type II DM in both subjects with HCQ and without HCQ. There were also subjects who were not on OHA in both case and control. It was found that nearly 29.03% of patients in case and 33.87% of patients in control were known to be diabetic since 6-10 years (Table.4). Figure.2 reveals that more number of were under prior medications(OHA) in case whereas none of the patients were taking any prior medications in control. The study shows the antihyperglycemic effect of HCQ in uncontrolled Type II DM patients in which it reduces approximately 3.43% of HbA1C level and 40.45mg/dl of FBS level after 3 months.

Table 1: Distribution of subjects based on hba1c in case and control

HbA1C	Case (N)	Case (%)	Control (N)	Control (%)
8-9%	12	19.35	16	25.81
9.1-10%	15	24.19	18	29.03
10.1-11%	11	17.74	08	12.90
11.1-12%	11	17.74	07	11.29
12.1-13%	07	11.29	04	06.45
13.1-14%	02	03.23	06	09.68
>14%	04	06.46	03	04.84
TOTAL	62	100	62	100

Table 2: Distribution of Subjects Based Fasting Blood Sugar (FBS) Level in Case and Control on Admission

FBS	Case(N)	Case(%)	Control(N)	Control(%)
<100	04	06.45	05	08.06
100-150	15	24.19	19	30.64
151-200	20	32.25	18	29.03
201-250	13	20.97	10	16.13
251-300	05	08.07	05	08.07
>300	05	08.07	05	08.07
TOTAL	62	100	62	100



Table 3: Distribution of Subjects Based Random Blood Sugar(RBS) Level in Case and Control on Admission

RBS	Case(N)	Case(%)	Control(N)	Control(%)
<100	01	01.61	03	04.84
100-150	08	12.90	10	16.13
151-200	18	29.04	12	19.35
201-250	10	16.12	14	22.58
251-300	07	11.29	11	17.74
>300	18	29.04	12	19.36
TOTAL	62	100	62	100

Table 4: Distribution of Subjects Based on Length of Years With Type II DM

DM Duration (YEARS)	Case(N)	Case(%)	Control(N)	Control(%)
1-11 Months	11	17.74	12	19.36
1-5 Years	16	25.80	11	17.74
6-10 Years	18	29.03	21	33.87
11-15 Years	06	09.68	09	14.51
16-20 Years	06	09.68	05	08.07
>20 Years	05	08.07	04	06.45
TOTAL	62	100	62	100

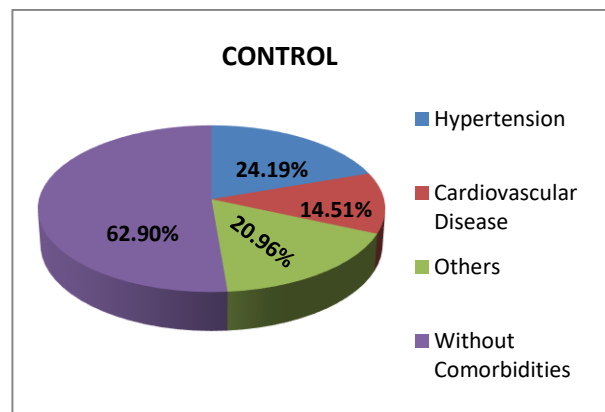
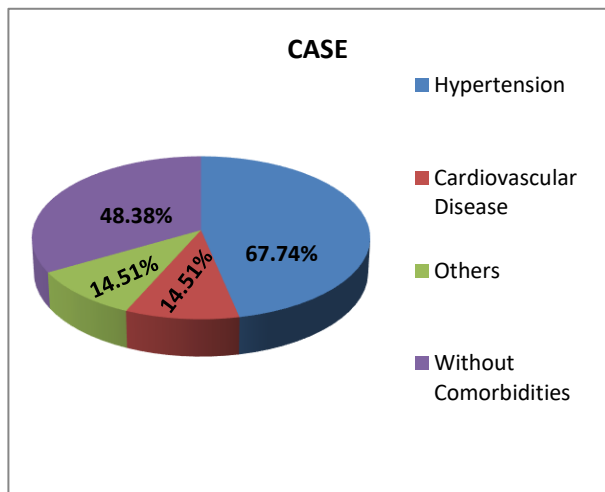


Figure 1: Distribution of Subjects with and without Comorbidities In Case and Control

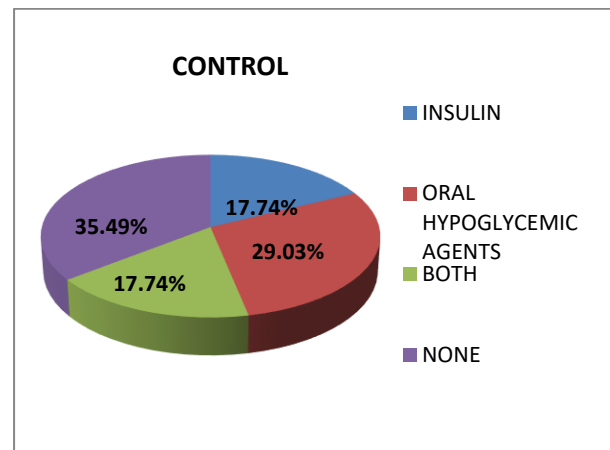
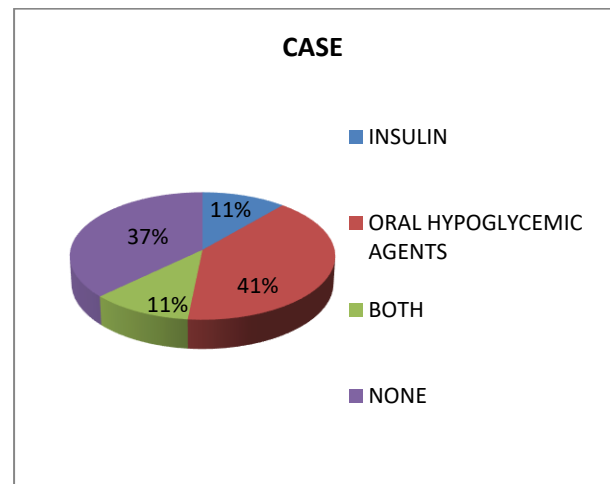


Figure 2: Distribution of Subjects Based on their Prior Medication in Case and Control

Limitations

In this study follow up was unable to do properly due to the subjects in cooperation. Unwillingness of the subjects to take the drug (HCQ). For a few subjects they refused and showed less interest to take HbA1C test. Since this study was done in a major trauma care centre, a few subjects refused to come for review once their condition gets better. A stronger conclusion was unable to achieve in this study since the duration of the study was short.

CONCLUSION

Out of 124 patients 104 completed the study at this time. The outcome is that mean baseline HbA1C from 10.68% was reduced to 7.25% in case and from 10.22% was reduced to 8.44% in control group. This shows that HCQ reduces 3.43% of HbA1C at first review in case whereas in control 1.78% of HbA1C was reduced, respectively. This study concludes that hydroxychloroquine can be an effective add on therapy to the subjects with uncontrolled Type II Diabetes Mellitus along with other Oral Hypoglycemic agents.

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Conflict of Interest: None declared.

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