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Original Research Article

HCQ: A Promising Frontier in Diabetes Care and its benefits in diabetic rat model

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Abstract:

Background: The study is done to evaluate the efficacy of different interventional drugs in treating diabetes and their impact on the kidney and liver changes using a rat model.

Methods: For this study 6 groups of 6 Wistar Rats were used. Out of which 3 groups were treated with hydroxychloroquine (HCQ), alpha-lipoic acid (ALA), and chromium picolinate (CrP), and their kidney with renal profile and SGPT were analyzed.

Results: The results showed that administration of HCQ for 42 days improved SGPT, creatinine, and urea levels in diabetic rats. When compared with the normal group and metformin, HCQ values were closer to those of the normal group than to metformin, and it also exhibited protective properties against liver and kidney damage.

Conclusion: HCQ showed a promising result to be used therapeutic agent for diabetes management, particularly due to its improving effects on liver and renal profiles. On comparing with ALA and CrP, HCQ showed better improvement in renal profiles and also exhibited hepatoprotective properties.

Keywords: Diabetes Mellitus, Renal Profile, SGPT, Hydroxychloroquine, Therapeutics, HCQ.

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Introduction

Diabetes Mellitus is a condition of elevated blood glucose levels due to inadequate insulin secretion by pancreas. It increases the risk of microvascular damage leading to retinopathy, nephropathy and neuropathy [1]. It is linked to lower quality life, increased morbidity rates and shorter life expectancy. When left unnoticed or untreated, the microvascular damages may escalate to macrovascular complications which may even lead to heart attacks and kidney failure [2]. As per the IDF Atlas 2021, around 537 million adults globally have been diagnosed with diabetes. In 2022, 62% of the diabetes cases were detected in people aged 20 years and above. India itself contributes to 49% of the global diabetes burden and is predicted to increase in upcoming years [3]. Many risk factors contribute in developing Diabetes in young age which includes sleep deprivation, drug induced metabolic changes, Environmental pollutants, low birth weight, fetal malnutrition etc. [4-6].

In diabetes, liver and kidney disorders are considered as major risk factors altering renal and liver profiles. Diabetes is associated with liver diseases such as non-alcoholic fatty liver, abnormal liver enzymes, and hepatocellular carcinoma, which can lead to liver failure [7]. Similarly, complication such as diabetic kidney disease usually progresses towards end-stage renal disease, leading to life-threatening situations [13]. With proper laboratory diagnosis and adequate treatment, these comorbid conditions are highly preventable. Treatments can be done using interventional drugs such as Metformin, and other oral hypoglycemic agents. These drugs help to overcome insulin resistance, increases glucose absorption, has antiplatelet, antithrombotic and lipid-lowering properties [6-9]. Therefore, this study was done to explore the therapeutic effects of drugs like HCQ, ALA, CrP and metformin on liver and kidney in diabetic rat model. This study further helped in understanding the management and co-morbidities of diabetes in the rat model.

Materials and Methods

Place of study: Department of Pharmacology and Biochemistry at Rajendra Institute of Medical Sciences, Ranchi.

Type of study: Experimental

Duration of Study: 42 Days

The experiments were conducted in accordance with ethical norms approved by Institutional Animal Ethics Committee (IAEC) Guidelines (Memo

no: - 162, IAEC Rims Ranchi, dated on 26/02/2021).

Methodology:

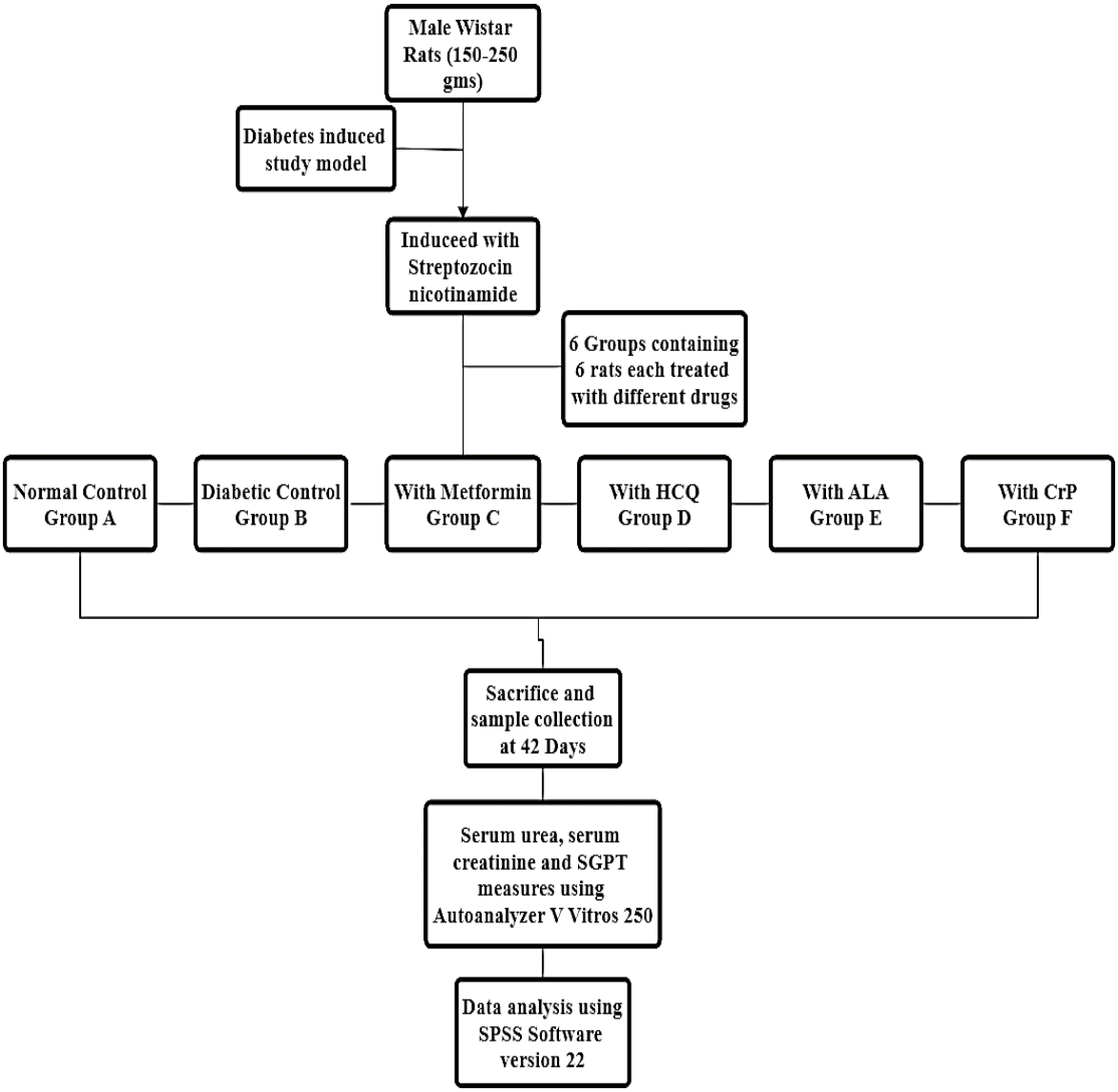

Figure 1:

Results

In this study, 6 groups of rats were used which were induced with different drugs. Table No. 1 shows the no. of rat groups, drugs they were induces with and their respective doses.

Table 1: Different rat groups treated with different drugs

	Rats	Drugs	Dose
A. Normal Control	6	Vehicle Gum acacia 1%	10 ml/kgbody wt
B. Diabetic control	6	Vehicle Gum acacia 1%	10 ml/kgBody wt
C. Diabetic Controlwith metformin	6	Metformin	500 mg/70kg
D. Diabetic control withhydroxychloroquine (HCQ)	6	Hydroxychloroquine	400 mg/70kg
E. Diabetic control withalpha lipoic acid (ALA)	6	Alpha Lipoic Acid	600 mg/70kg
F. Diabetic control withChromium picolinate (CrP)	6	Chromium Picolinate	600 mcg/70kg

On comparing urea, creatinine and SGPT from Day 0 to Day 42, it was observed that after 42 days of treatment, HCQ lowered urea, creatinine and SGPT levels compared to that of the rest interventional groups. Therefore, it can be assumed that HCQ has renoprotective and hepatoprotective properties [Fig. 1]

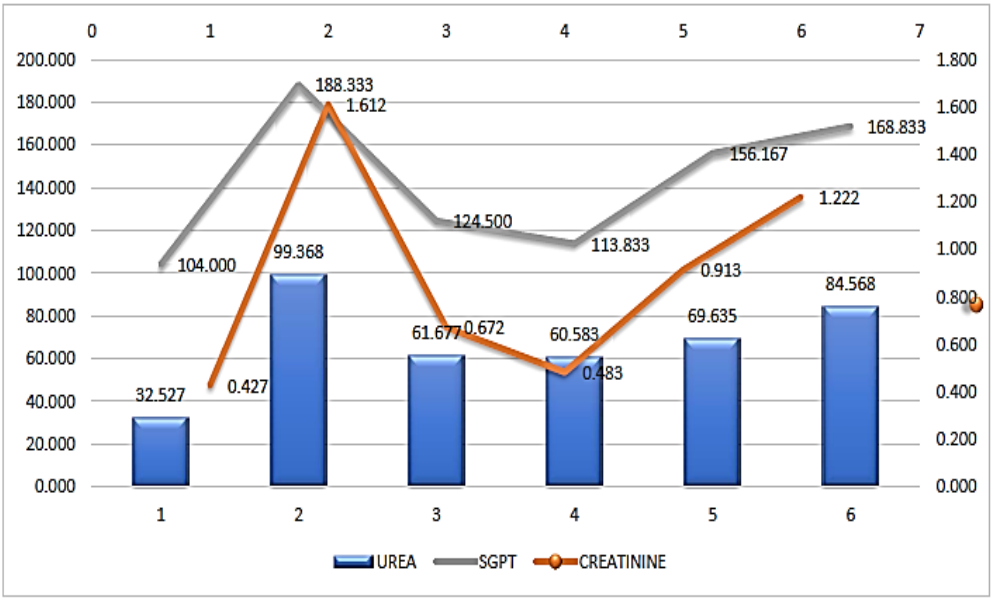

Figure 2: Comparison of urea, creatinine and SGPT in all groups from Day 0 to Day 42

Comparison of all groups in relation to SGPT: Out of all the groups, HCQ group showed more significant findings (P<0.01) than metformin and all other groups. In comparison with control group, HCQ showed more significance and had close values to the normal group.

Comparison of all groups in relation to Urea and Creatinine (renal profile): Here also, HCQ showed significant reduction in urea as well as creatinine levels. Metformin, ALA and CrP gave non-significant finding with p>0.05. However, in comparison to ALA and Crp, metformin showed better reduction in creatinine levels.

Table No. 2 displays the comparison of all administered interventions with the normal group. Among all the drugs, the values of HCQ were closer to those of the normal group, indicating its better efficacy on renal and kidney profiles.

Table 2: Comparison of drugs with the normal group

Group		Metformin	HCQ	ALA	CrP
		C	D	E	F
SGPT	Mean Difference	-20.50000*	-9.83333	-52.16667*	-64.83
	Std. Error	6.12765	6.12765	6.12765	6.12765
	p Value	0.025	0.602	0	0
CREATININE	Mean Difference	-29.15000*	-28.05667*	-37.10833*	-52.04167*
	Std. Error	1.77531	1.77531	1.77531	1.77531
	P Value	0	0	0	0
UREA	Mean Difference	-.24500*	-0.05667	-.48667*	-.79500*
	Std. Error	0.06837	0.06837	0.06837	0.06837
	p Value	0	0	0	0

Table No. 3 shows comparison of all interventions with Diabetic control and Metformin while Table No. 4 shows comparison of interventions with Metformin treated group.

Table 3: Comparison of drugs with the control group

Group		Metformin	HCQ	ALA	CrP
		C	D	E	F
SGPT	Mean Difference	63.83333*	74.50000*	32.16667*	19.50000*
	Std. Error	5.78657	5.78657	5.78657	5.78657
	p Value	0.000	0.000	0.000	0.019
Creatinine	Mean Difference	0.94000*	1.12833*	0.69833*	0.39000*
	Std. Error	0.07277	0.07277	0.07277	0.07277
	P value	0.000	0.000	0.000	0.000
UREA	Mean Difference	37.69167*	38.78500*	29.73333*	14.80000*
	Std. Error	1.86439	1.86439	1.86439	1.86439
	p Value	0.000	0.000	0.000	0.000

Table 4: Comparison of drugs with the metformin group

Group		HCQ	ALA	CrP
		D	E	F
SGPT	Mean Difference	10.66667	-31.66667	-44.3333
	Std. Error	5.78657	5.78657	5.78657
	p Value	0.372	0.000	0.000
CREATININE	Mean Difference	0.18833	-0.24167	-0.55000
	Std. Error	0.07277	0.07277	0.07277
	p Value	0.103	0.021	0.000
UREA	Mean Difference	1.09333	-7.95833*	-22.89167*
	Std. Error	1.86493	1.86493	1.86493
	p Value	0.976	0.002	0.000

Therefore, Group D (HCQ) showed overall improvement in renal and liver parameters. Hence, the sequence of effectiveness of our experimental drugs in controlling all parameters is HCQ >ALA>CrP.

Discussion

In this study, streptozocin-nicotinamide induced diabetes rat model was used for the screening of anti-diabetic drugs. This study utilizes the parameter such as SGPT and renal profile of the experimental animal model. Diabetic patients are often associated with abnormal liver and renal profiles. The liver helps in metabolizing and maintaining normal blood glucose levels, but in the case of diabetic patients, this function is impaired, leading to abnormal increases in liver enzymes, which in turn contribute to hepatotoxic effects [10]. Ewing DJ et.al, 1980 concluded that diabetes leads to macrovascular as well as microvascular complications such as neuropathy, nephropathy, ketoacidosis, and retinopathy [11,14].

This study results revealed that HCQ lowers kidney parameters including urea and creatinine levels. When HCQ was compared to metformin, it significantly increased LFT and KFT. Additionally, it was observed that HCQ protected the kidneys from harm in diabetic nephropathy. Khushwaha JS et.al., 2018, conducted a controlled non-randomized trial where they showed that HCQ can be used on patients at early stage of Diabetic Kidney Disease to prevent it from progressing towards Diabetic nephropathy as glomerular filtration rate was improved post administration of HCQ [12].

HCQ possesses anti-inflammatory properties and prevents from conditions such as diabetic nephropathy. And our study showed low serum creatinine and urea levels post the use of HCQ for 42 days. Also, both metformin and HCQ showed promising results in reducing the level of SGPT while ALA and CrP showed no effects. HCQ exhibited comparable values to the control group, indicating its better impact on correcting SGPT levels in diabetic patients. ALA supplementation has been proven to prevent the progression of diabetic nephropathy in patients by controlling and maintaining creatinine, urea levels, and other blood profile factors [16].However, in this study, other drugs such as CrP and ALA showed very little to no improvement in the renal and kidney profile of these diabetic rats. Therefore, these controversial results warrant further research to obtain a clearer understanding.

Therefore, this present study indicates that hydroxychloroquine has promising antidiabetic properties and human trials can help in obtaining more experimental data for further benefits.

Conclusion

This study provided insights into the use of various interventional drugs to treat diabetes and their effects on the renal and kidney profile of a rat model. Among all the administered drugs, HCQ proved to offer the most benefits by controlling renal and liver profile parameters and slowing down the progression from the pre-diabetic stage to diabetes. In contrast, ALA and CrP failed to provide any improvements in the parameters studied.

Considering the potential of HCQ to retard the progression of diabetes from the prediabetic stage and its positive effects on liver and renal profiles, HCQ holds promise as a multifaceted therapeutic agent.

A few drawbacks of this study include the failure to collect blood at the start of the study for liver and renal profile analysis, as well as the absence of brain and other organ samples for histopathological examination. For further understanding and enhanced research to confirm the efficacy and safety of these drugs, investigations involving animals and human subjects are recommended. Such experimental findings will enhance the outcome of the results.

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