EFFECT OF CHLOROQUINE ON BLOOD GLUCOSE LEVELS IN PATIENTS WITH NON INSULIN DEPENDENT DIABETES MELLITUS

H. Mostafavi

Department of Internal Medicine, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract - Thirty six patients with non insulin dependent diabetes mellitus, whose blood sugar was not controlled with maximal doses of oral hypoglycemic agents and did not accept insulin treatment, were selected for this study. The patients were randomly divided into two groups, the treatment group and the control group. The treatment group received oral hypoglycemic agent and chloroquine (150 mg twice daily) and the control group received oral hypoglycemic agent and placebo for a period of six months. The fasting blood sugar (FBS) and Hb A1C were recorded before and after treatment. The age, sex, weight and duration of disease were similar in both groups (P>0.05). The blood sugar level, was significantly lower after 3-6 months of chloroquine therapy (P ≤ 0.001). Serious drug reactions were not noticed, except for gastrointestinal upset in three patients and hypoglycemia in another two cases. In conclusion we believe that the combination of chloroquine and oral hypoglycemic agents can be useful for the control of blood sugar levels in some resistant cases of non insulin dependent diabetes mellitus.
Acta Medica Iranica 36 (2): 109 - 112: 1998

Key words: Non insulin dependent diabetes mellitus, insulin, oral hypoglycemic agents, chloroquine

INTRODUCTION

Over the past 40 years chloroquine has been used for the treatment and prophylaxis of malaria . Previous studies (1, 2, 3) have revealed that it is a potent hypoglycemic agent in malaria patients and can dramatically decrease the insulin requirement of patients with severe insulin resistant syndromes. Animal studies (6) have shown that chloroquine inhibits the hepatic degradation of insulin via its lysosomotropic effects. This study was carried out to evaluate the effects of this agent on the blood sugar levels of patients with resistant forms of non insulin dependent diabetes mellitus (NIDDM).

MATERIALS AND METHODS

During a period of six months, 36 patients with NIDDM, whose blood sugar was not adequately controlled with maximal doses of oral hypoglycemic agents were studied in Shiraz University hospital clinics.

There were 12 males and 24 females with an age range of 42 - 70 years. They were randomly divided in to two groups , namely the treatment and control groups. An informed written consent was obtained from all participants and cases were informed of the possible side effects of the drug.

All cases were checked for the absence of diabetic complications and presence of a normal serum glucose-6-phosphate dehydrogenase level. The treatment group received their usual daily dose of oral hypoglycemic agent plus chloroquine 150mg twice daily and the second group received oral hypoglycemic plus placebo. The fasting blood sugar (FBS) and HbA1C were checked prior to and 3 and 6 months after the initiation of therapy in both groups. HbA1C was measured by gel electrophoresis method. The results were analyzed by Mann-Withney test, and a $P < 0.05$ was considered to be significant.

RESULTS

There were no significant differences between the two groups as far as the age, sex, body weight, diet, duration of disease and baseline HbA1C were concerned (Table 1).

There was however a significant difference in the baseline FBS levels among the two groups ($P < 0.01$)

(Table 1).

A significant improvement in the blood sugar (Fig. 1) and HbA1C levels (Fig. 2) were noted in the treated group after 3 and 6 months of therapy ($P < 0.001$) (Table 2). Drug associated complications were uncommon, however three cases of gastrointestinal upset and two cases of hypoglycemia were noted. There were no ophthalmic complications.

Table 1. The baseline data of the treatment and placebo groups

	GROUP			
	Treated(n=18)		Placebo(n-18)	
Characteristics	Mean	S.D	Mean	S.D
Age	54.6	10.6	54.1	9.9
Weight	65.6	8.4	65.3	8.4
Disease duration	32.11	20.5	32.6	22.3
Baseline FBS(0)	215.5	29.8	184.0	23.0
Baseline HbA1C(0)	9.9	1.2	9.8	10
FBS after 3 months(1)	176.2	35.8	183.0	20.0
HbA1C after 3 months (1)	8.2	1.8	9.1	1.1
FBS after 3 months (2)	175.8	26.0	1915	32.3
HbAIC after 6 months (2)	8.7	1.3	9.2	1.2

Table 2. Comparison of FBS and HbA1C changes,after 3 and 6 months of therapy in treatment and placebo groups.

	Treated Group		Placebo		
Charal	Mean	S.D	Mean	S.D	P-Value
FBS(1)-FBS(0)	-39.3	27.5	-1.0	16.5	<0.001
FBS(2)-FBS(0)	-39.7	31.3	7.5	39.5	<0.01
HbA1C(1)-HbA1C(0)	-1.7	1.0	-0.7	0.6	<0.001
HbA1C(2)-HbA1C(0)	-1.8	0.7	-0.6	1.1	<0.001

(0)=Baseline blood sugar and HbA1C.

(2)=Blood sugar and HbA1C after 3 months.

(3)=Blood suger and HbA1C after 6 months.

DISCUSSION

Diabetes mellitus is the most common chronic metabolic disorder. This disease is characterized by metabolic abnormalities and causes long term complications involving eyes, kidneys, nerves and vessels. Type 2 diabetes is defined as non-ketotic non-insulin dependent diabetes mellitus in patients over 40 years (7) of age. Many patients are obese and most of them are old. The disease is frequently associated with cardiovascular complications and their deleterious effects. The aim of treatment of type 2 diabetics is to achieve near normal blood glucose values, so as to prevent diabetic symptoms and possibly, the development of diabetic complications. Only 20% of these cases, however, can successfully be treated with diet alone, emphasizing the limitation of this mode of treatment in man (8). On the other hand, weight reduction is associated with improved glucose tolerance (9) but ideal weight is rarely achieved and maintained.

Since the introduction of sulfonylureas in 1950s, these drugs have represented the mainstay of oral antidiabetic therapy, however treatment failure is commonly seen, and it has been suggested that about 40% of type 2 diabetics are not satisfactorily controlled with oral antidiabetic agents (10, 11). Treatment failure can be primary or secondary. The term secondary failure has been used to characterize patients in whom, after an initial successful control of blood sugar for at least one month, the drugs gradually become ineffective (12, 13). The mechanisms underlying true secondary drug failure are still uncertain although deterioration of insulin secretion has been suggested as a causative factor (11, 14).

Resistance to insulin is one of the main distinguishing features of non-insulin dependent diabetes mellitus (15). In most cases it is thought to be caused by a combination of a reduction in the number of receptors and the presence of a post receptor defect.

The liver is the major target organ for insulin metabolism, removing up to half of the available circulating insulin (4). This hepatic uptake is mediated by insulin receptors. Once the insulin-receptor complex has been internalized, the hormone undergoes rapid degradation and clearance from the liver (5). In the rat chloroquine cause hepatic retention of insulin, an effect which has been ascribed to its lysosomotropic action. In our study, chloroquine - treated cases had a significant reduction ($p=<0.001$) in their blood sugar levels both at 3 and 6 months intervals, without having much of any drug associated side effects.

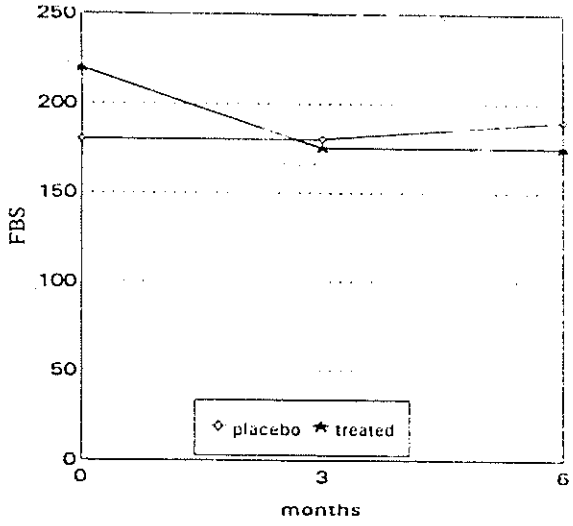

Fig 1. FBS changes 3 and 6 months later in placebo and treatment groups

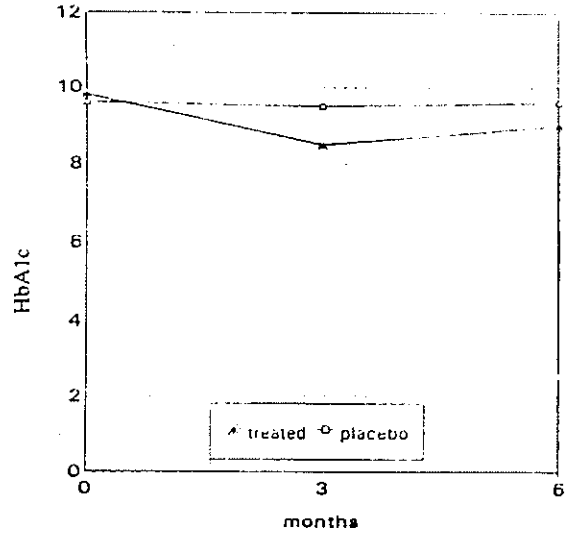

Fig 2. The HbA1C changes 3 and 6 months later in placebo and treatment groups

This significant effect on glycemic control confirms the short-term beneficial effects of this agent which mayopen a new horizon in diabetes control. Further longterm studies are recommended for a more concrete solid conclusion.

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