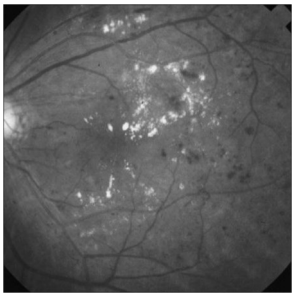
ORIGINAL
(CLINICAL PRACTICE ARTICLE)
PROF-820

DIABETES MELLITUS;
INTERFERON-β INVOLVEMENT IN THE ONSET



MR. NASIR MAHMOOD
M.Sc, M.Phil, PGD (CS), PhD
School of Biological Sciences,
Quaid-e-Azam Campus, University of the Punjab,
Lahore, Pakistan.

DR. NASEER AHMAD,
MBBS, MS (Public Health)
Program Director,
District Health Development Center (DHDC),
Health Department, Jhelum.

DR. MUZAFFAR JALAL KHAN NIAZI,
MBBS
Professor of Anatomy (Retd)
K E Medical College, Lahore

ABSTRACT ... nasir_lhr@yahoo.com A number of cytokines have been shown to alter the function of pancreatic β-cells and thus might be involved in the development of type I diabetes. **Objectives:** To study whether interferon IFN- alters -cellfunction in vivo and leads to diabetes. **Patients & Methods:** We have studied three groups of patients (group I, 20-35, group II, 35-50 and group III, 50-70 years age) taking β-interferon after chronic liver infection due to hepatitis. **Results:** 80 % patients in group II and 90 % group III patients particularly showed higher level of blood glucose. However, only 30 % patients in group I exhibited abnormal level of blood glucose. 20 % patients of group I and 30 % patients in group II also represented higher level of alanine amino transferase (ALT). **Conclusions:** These results suggest that IFN-β may be involved in the onset of type 1 diabetes and elevated serum alanine amino transferase (ALT) level.

INTRODUCTION

Despite an immense research effort, the etiology of type 1 diabetes has not been elucidated. It has been proposed that type 1diabetes is caused by nongenetic factors, probably environmental, operating in a genetically susceptible host to initiate a β-cell destructive immune process[1]. These environmental factors, such as viral infections, may operate over a limited period to induce the immune process[2]. Thereafter, there is a long prodrome before the onset of clinical diabetes during which clinical, immunulogic, and metabolic changes can be detected in the β-cells[3]. During the prediabetic period, a decline in the insulin secretion as well as impaired glucose tolerance can be detected several years before the clinical onset of type I diabetes[4]. Thus, alterations in β-cell function might be a previous step to the development of diabetes mellitus.

Cytokines are hormone-like peptides mainly used by

immune system cells to control local and systemic events of immune and inflammatory responses[5,6]. Studies in vitro have demonstrated that certain cytokines, such as IL-1,[1] tumor necrosis factor-, or IFN can be cytotoxic to pancreatic cells, inhibiting insulin secretion[7]. Furthermore, when combined, these cytokines can destroy cells[8]. Moreover, studies in mice showed that these cytokines have been found in the pancreatic insulitis lesion and may thus be considered mediators of cell damage in type I diabetes[9]. Type I interferons (IFNs) are pleiotropic cytokines involved in host defenses against viral infections that can be produced by most cell types in response to a virus[10]. There are three families of type I IFNs, and these are closely related structurally. These IFNs also bind to a common receptor and have potent antiviral activities[11]. Several studies have implicated IFN in the development of type I diabetes[12]. However, little is known about the role of IFN in the development of type I diabetes. Here we studied whether IFN may lead to elevated serum ALT level in blood and type I diabetes in patients having chronic liver hepatitis.

MATERIALS AND METHODS

Samples collection:

The blood samples were collected from Lahore, Faisalabad and other areas of the country. These samples were categorized under three groups containing 10 samples each. Group I contains blood samples of patients 20-35 years age administering b-interferon after chronic liver infection of hepatitis. The group II patient's age was 35-50 years while group III patients have age range of 50-70 years.

Hematology

a. Blood glucose

The blood glucose concentration was measured enzymatically (Glucoquant^{R}, Boehringer Mannheim). Glucose levels were also determined in blood by using a Glucometer^{R} analyzer (Bayer, Germany). Blood samples were obtained from patients of six hours fasting condition.

b. Serum ALT concentration

The alanine aminotransferase (ALT) level in blood serum was determined by using the diagnostic kit (Bio Lab, Merck, Germany). The diagnostic kit was used in the automotive analyzer for quantitative estimation of ALT.

c. SDS-PAGE

The blood serum proteins isolated from all the groups of patients were subjected to SDS-PAGE in order to compare the banding patterns specific to diabetic patients.

RESULTS AND DISCUSSION

The patients having chronic liver infection due to hepatitis are usually subjected to intensive beta interferon therapy. The results (Table) indicated that high percentage of blood glucose i.e, 90 % is most prevalent in group III patients of age 50-70 years while least percentage of elevated blood glucose level (30 %) was detected in group I patients of age 20-35 years. The 80 % patients of group II exhibited abnormal elevated level of blood glucose after two months intensive beta interferon therapy. These results are in agreement with[13,14,15] who reported that interferon therapy induces type I diabetics and hence elevated level of blood glucose.

The elevated blood ALT level is an indicator of liver disorder. 40 % patients of group III exhibited maximum blood ALT level however only 20% patients of group I showed elevated blood ALT level. The high ALT blood level despite administration of gamma and beta interferon is due to the reason that beta and gamma interferon prevents viral proliferation largely by inhibiting protein synthesis in infected cells and thus prevent further damage to lymphocytes as well as liver tissue. The liver tissue which has already been damaged by hepatitis infection resulted in elevated blood ALT level. This observation was also supported by Dawson et al[16] who also reported increased blood ALT level of patients affected with chronic liver infection by hepatitis.

Interferons are effective anti viral agents in concentrations as low as $3*10^{-14}$ M and prevent further viral damage of tissue(Novick[10], Sen GC[11]). The occurrence of diabetics was also confirmed by subjecting

serum proteins to SDS-PAGE. The percentage of samples which exhibited characteristic banding patterns of diabetics patients as same as samples having elevated blood glucose level (Table).

This research work describes that beta interferon therapy of patients affected by acute liver infection of hepatitis induces diabetic mellitus represented by specific banding patterns and elevated blood glucose levels. The elevated serum ALT level in blood of patients also recommends early treatment so that further liver damage could be prevented.

Table-I. Effect of IFN on blood glucose and ALT level in patients with chronic liver infection due to hepatitis.

Group	Total no. of samples	Samples having normal blood glucose	Samples having elevated level of blood glucose	Samples having elevated level of blood glucose (%)	No. of samples having normal ALT level	No. Of samples having elevated level of ALT	Samples having elevated ALT level (%)	No. Of samples (+) to SDS-PAGE
I	10	7	3	30	8	2	20	3
II	10	2	8	80	7	3	30	8
III	10	1	9	90	6	4	40	9

Note : Group I= 20-35 years age, Group II= 35-50 years age, Group III= 50-70 years age.

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Failures are like skinned knees – painful but superficial

Ross Perot