Enhanced Gylcosylation of Haemoglobin in AIDS

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We previously documented supernormal glycohaemoglobin concerntrations in about 40% of patients with AIDS [1]. Our findings were later confirmed in another study [2]. In both these studies, fasting plasma glucose concentrations were not elevated. However, it is unclear whether enhanced glycosylation in the presence of normal glycaemia occurs in all patients with AIDS or only in a certain population. Therefore, this study was undertaken to assess the degree of glycosylation of haemoglobin in patients with AIDS in comparison to the process in normal subjects.

METHODS

One hundred and one consecutive patients with AIDS, 100 men and one woman with a mean age of 45 ± 7 years attending AIDS clinic at VAMC Phoenix, Az during a six month period participated in the study.One hundred and twenty three, age-matched normal volunteers, 106 men and 17 women (mean age, 50 ± 8 years) were used as a control population. Six ml blood was withdrawn from the antecubital vein after an overnight fast in each participant. Three ml blood collected in a heparinized tube, was immediately centrifuged and plasma was extracted for determination of glucose level on the same day. The remaining 3 ml whole blood was collected in the tube containing an EDTA anticoagulant and refrigerated for later determination of glycohaemoglobin within 7 days. None of the subjects with AIDS had previous diagnosis of diabetes mellitus. Neither were any of the volunteers previously diagnosed as having diabetes mellitus or impaired glucose tolerance. Fasting plasma glucose level was determined by Parallel Analyzer (AM Diagnostic Inc. Indianapolis, Indiana) and glycohaemoglobin levels wsere estimated by a commercial kit (REP glyco-30 System, Helena Laboratories, Beaumont, Texas) using agar gel electrophoresis. The comparisons for both parameters between AIDS subjects and normal volunteers were performed by Student's t- test. Furthermore, linear regressions were determined between the same two parameters separately for each group and compared. All data are reported as mean ± SEM.

RESULTS

The subjects in both groups, i.e., AIDS patients and normal volunteers were divided into four sub groups according to their fasting plaslma glucose concentrations (Table 1). For each range of fasting plasma glucose levels, the glycohaemoglobin concentration was significantly higher in AIDS patients in comparison to normal subjects (Table 1). Furthermore, the slope of the linear regression curve between fasting plasma glucose and glycohaemoglobin levels (0-033) in AIDS subjects was markedly steeper as compared with the curve (0.015) obtained in normal volunteers (Fig. 1). Finally, supernormal glycohaemoglobin levels (> 8.2%) were documented in 28 subjects with AIDS.

Table 1

Mean fasting plasma glucose (FPG) levels and glycohaemoglobin (HbA_1) concentrations in 101 patients with AIDS and 123 normal volunteers. Both groups are divided into further subgroups according to fasting plasma glucose concentrations.

		Normal Subjects		AIDS	
Groups	Glucose Range	FPG mM/I	HbA_1 %	FPG mM/I	HbA_1 %
A	< 4.8	4.6±0.05(17)*	6.52±0.14	4.3±0.07(26)	7.71±0.29
B	4.8-5.3	5.1±0.05(41)	6.71±0.20	5.0±0.05(33)	7.94±0.33
C	5.4-5.9	5.6±0.05(48)	6.81±0.17	5.5±0.03(28)	8.42±0.41
D	6.0-6.5	6.0±0.04(17)	6.92±0.22	6.1±0.06(14)	8.76±0.49+

* - No. of subjects in each subgroup in parenthesis.
+ - P < 0.001 vs. normal subjects in the same group.

DISCUSSION

This study demonstrates that enhanced glycosylation of haemoglobin occurs in all patients with AIDS and may result in supernormal glycohaemoglobin concentrations in many of them as noted in previous studies [1, 2] . However, the mechanism of the enhanced glycosylation of haemoglobin in AIDS is unclear. A recent study [2] demonstrated a close relationship between plasma ferritin and glycohaemoglobin concentrations suggesting a role of increased iron stores in enhancing the affinity of haemoglobin to circulating normal glucose. However, other well documented causes of enhanced glycosylation i.e., hypoxia, chronic renal failure, acute alcoholism, lack of vitamin E or C, may also be responsible and require evaluation [3-8]. Moreover, it also remains to be seen if the enhanced glycosylation

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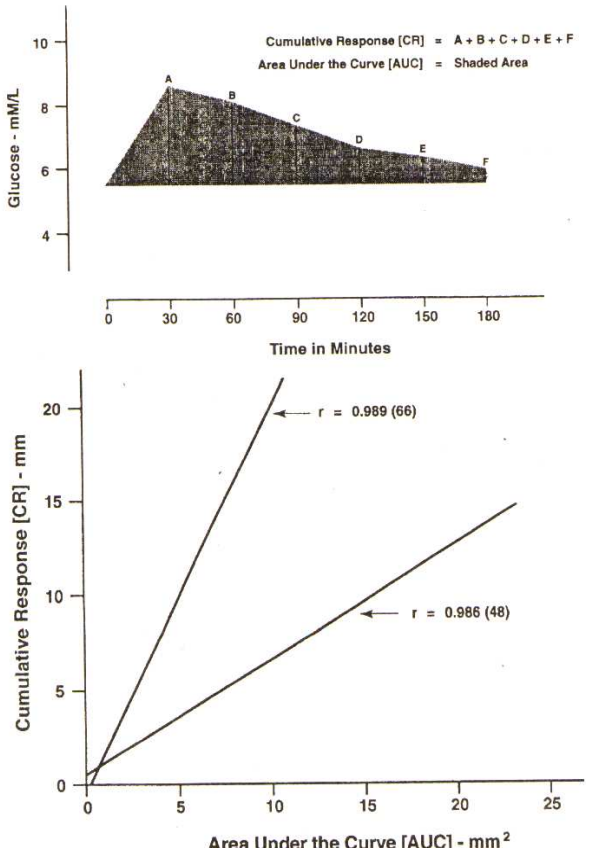

Fig 1. : Linear regression curves between fasting plasma glucose and glycohaemoglobin levels derived independently in subjects with AIDS and normal subjects.

involves exclusively haemoglobin or it is an universal phenomenon involving other plasma proteins, a finding well documented in uncontrolled diabetes mellitus [9] . Finally, if a role of this enhanced glycosylation of haemoglobin and probably other proteins in the grave rapidly progressive course of this disease is established, therapeutic strategies like Vitamin E supplementation to reduce glycosylation of proteins may be important in total management of this disorder.

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