Shimane J. Med. Sci., Vol.7, pp.67-73, 1983

Short Communication

GLYCOSYLATED HEMOGLOBIN IN IRON DEFICIENCY ANEMIA

(glycosylated hemoglobin/iron deficiency anemia)

Kazumi NOTSU*, Fumimaro OSEKO*, Shinya NOTE*, Jiro ENDO**, and Takeshi ENDO***

*Department of Internal Medicine, **Laboratory Medicine, Shimane Medical University, Izumo 693 and ***Daiwamura Health Insurance Clinic, Ohchi 696-07, Japan

(Received December 24, 1983)

Hb A_1 and Hb A_{1c} in cases with iron deficiency anemia (I.D.A.) and in controls were measured by high-performance liquid chromatography. The mean and S.D. levels of these in three hundred and sixty-seven normal subjects were 7.0 ± 0.8% and 4.7 ± 0.6%, respectively.

Hb A_1 in cases with I.D.A. (7.7%) was significantly higher than that in controls ($p<0.05$); however, in Hb Alc components, there was no difference between anemic patients and controls. Furthermore, there was no significant correlation between Hb A_1 and Hb A_{1c} in patients with I.D.A.. From these results, we suspected that other components excluding the Hb A_{1c} in Hb A_1 fraction, such as Hb A_{1a+b} and/or Hb F and so on, might relatively increase in patients with I.D.A..

Hb A_{1c} is a major part of Hb A_1 and comprises approximately 5% of the total hemoglobin in non-diabetic individuals. Rahbar first showed that this component increased two to three-fold in diabetics (1). Subsequently, it was shown that this hemoglobin is formed throughout the life-span of the red blood cell (2,3). Hb A_1 and Hb A_{1c} in cases with diabetes mellitus have been shown to reflect the integrated blood glucose levels during the previous 1-2 months (4-6). Furthermore, methods for measurement of glycosylated hemoglobin made remarkable progress (7,8). In a mass screening, we tried to measure this hemoglobin and it was

noticed that Hb A_1 in patients with iron deficiency anemia (I.D.A.) was significantly high.

SUBJECTS AND METHODS

In 1982, six hundred and twelve persons took part in a mass screening in Daiwa Village, Shimane. Medical history of diabetes mellitus, height and body weight, plasma glucose level and total hemoglobin concentration were studied in all participants. From the results, all subjects were classified into six groups; that is diabetes, borderline, obesity, emaciation, anemia and control groups. Patients included in the diabetes group had a past medical history of diabetes and/or high plasma glucose levels (fasting plasma glucose lebel: FBS 140 mg/dl or postprandial plasma glucose level: PBS 200 mg/dl) (9) in the present and in the previous mass screenings (10). The borderline group included cases with moderately elevated levels of plasma glucose (FBS: 110-140 mg/dl or PBS: 140-199 mg/dl). Participants with over + 20% standard body weight and with under - 20% were classified as the obesity and the emaciation group, respectively. Males with under 13.6 g/dl and females under 11.8 g/dl in total hemoglobin concentrations were included in the anemia group (11). The other participants were regarded as controls.

Serum iron, serum total iron binding capacity (TIBC) and serum ferritin levels were measured in severe anemic patients with under 11.0 g/dl in total hemoglobin concentrations.

Hb A_1 and Hb A_{1c} were measured by glycosylated hemoglobin autoanalyzer (Kyoto Daiichi Kagaku Co., LTD.) utilizing high-performance liquid chromatography. All samples were carried from Daiwa Village to our reserch institute and were measured within ten hours after blood collection.

RESULTS

Table I shows the number and the incidence of participants included in each group. The number of diabetics and of borderline subjects was 32 and 36, respectively. Sixty-three cases without high plasma glucose levels were obese and 16 subjects were thin. Eighty-nine patients were included in the anemic group; however, there were 5 patients with both anemia and obesity, and 4 anemic cases with emaciation. These cases were

Table I. NUMBER AND INCIDENCE OF CASES IN DIABETES, BORDERLINE, OBESITY, EMACIATION, ANEMIA AND CONTROL GROUPS

Group	Men	Women	Total	Incidence (%)
Diabetes	21	11	32	5.3
Borderline	21	15	36	6.0
Obesity	22	41	63	10.4
Emaciation	3	13	16	2.7
Anemia	57	32	89	14.8
Control	161	206	367	60.9
Total	285	318	603	100.1

Table II. LABORATORY DATA IN CASES WITH IRON DEFICIENCY ANEMIA

No.	Age	Sex	t-Hb* (g/dl)	s-Iron (ug/dl)	s-TIBC (ug/dl)	s-Fer. (ng/dl)	FBS (mg/dl)	Hb A1 (%)	Hb A1c (%)
1.	37	M	7.6	23	340	1.1	66	6.8	3.7
2.	40	F	9.5	30	-	1.2	78	6.3	4.2
3.	50	F	9.5	29	397	1.3	82	9.0	4.4
4.	57	F	10.0	32	422	2.5	85	7.6	4.6
5.	53	M	10.1	40	435	4.0	94	8.2	5.5
6.	49	F	10.5	33	433	1.8	78	8.6	4.4
7.	52	F	10.5	42	393	2.4	86	6.8	4.2
8.	46	F	10.6	52	385	1.5	101	8.1	5.9
9.	47	F	10.8	70	373	2.3	86	8.9	4.0
10.	42	F	10.9	32	461	1.8	80	6.3	4.2
11.	47	F	11.0	42	427	2.0	81	8.0	5.3

t-Hb*; total hemoglobin concentrations

Table III. GLYCOSYLATED HEMOGLOBIN LEVELS IN CASES WITH IRON DEFICIENCY ANEMIA AND IN CONTROLS

	Hb A_1 (%) mean ± S.D.		Hb A_{1c} (%) mean ± S.D.	
Cases with IDA* (n=11)	7.7 ± 1.0	$p<0.05$	4.6 ± 0.7	n.s.**
Controls (n=367)	7.0 ± 0.7		4.7 ± 0.5	

IDA*; Iron Deficiency Anemia
n.s.**; not significant

excluded from statistical analysis in this study. The other subjects, or 367 cases, had none of those abnormal data in this survey and were classified as the control group. On the other hand, 23 cases out of 89 anemic patients had severe anemia with under 11.0 g/dl in total hemoglobin levels; furthermore, 11 patients among the severe anemic patients had low levels of serum iron and serum ferritin, and had high concentrations of serum TIBC (Table II). The normal ranges of serum iron and serum TIBC

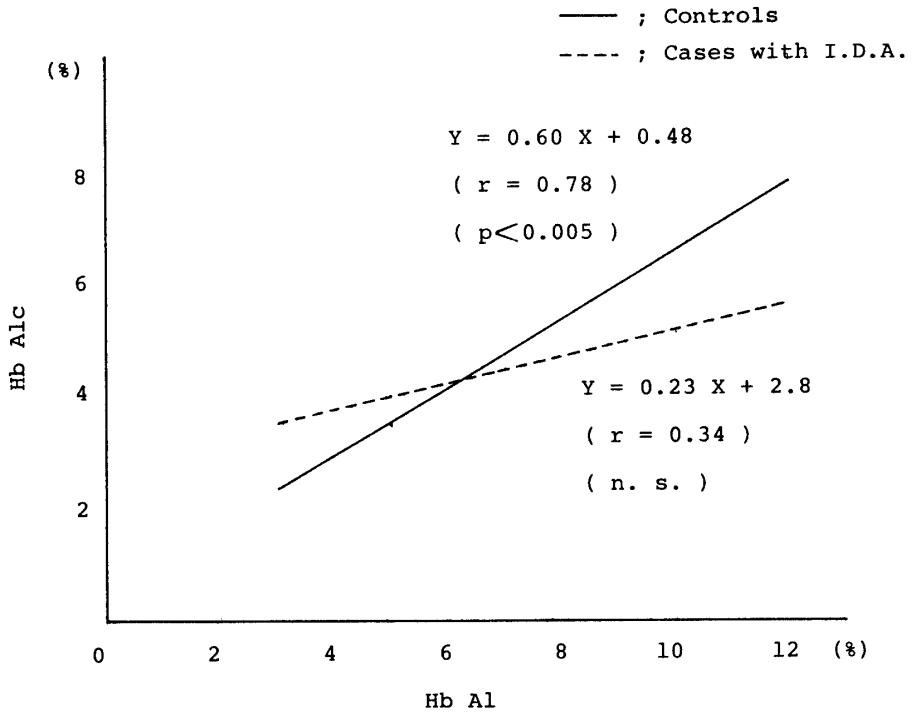

Fig. 1. Correlation coefficient between Hb A_1 and Hb A_{1c} in cases with iron deficiency anemia and in controls.

in our institute is 70-150 ug/dl and 290-355 ug/dl, respectively. In our previous paper (12), we reported that the normal range of serum ferritin was 28.1-230 ng/ml in men and 5.1-130 ng/ml in women. None of the 11 patients had normal levels according to these data and we regarded them as patients with typical I.D.A.. Table III shows the glycosylated hemoglobin levels (Hb A_1 and Hb A_{1c}) in cases with I.D.A. and in controls. The mean level of Hb A_1 in anemic patients and in normal participants was 7.7% and 7.0%, respectively. Hb A_1 in cases with I.D.A. was significantly high ($p<0.05$). On the other hand, Hb A_{1c} in anemic patients and in normal subjects was much the same. Subsequently, we studied the correlation coefficient between Hb A_1 and Hb A_{1c} in these two groups (Fig. 1). That in controls was 0.78 and there was statistical signifiacance between Hb A_1 and Hb A_{1c} ($p<0.005$). On the other hand, there was no significant correlation ($r=0.34$) in patients with I.D.A..

Hb A_1 and Hb A_{1c} in diabetics were 8.8% and 6.4%, and those in borderline cases were 7.8% and 5.3%, respectively. Both Hb A_1

and Hb A_{1c} in these two groups were significantly higher than those in controls ($p < 0.01$).

DISCUSSION

Brooks and their colleagues showed that glycosylated hemoglobin A_1 in patients with I.D.A. was high and decreased with improvement in the anemia condition, and it was suspected that diabetic patients with I.D.A. might have severe complications through the glycosylation of several organs such as retina and blood vessels (13). In our survey, Hb A_1 level in cases with I.D.A. was significantly higher than that in controls; however, Hb A_{1c} was much the same in the two groups. Furthermore, we noticed that there was no significant correlation between Hb A_1 and Hb A_{1c} in anemic patients with poor storage of iron. Brooks et al. reported nothing about Hb A_{1c} in their paper. Therefore, it was suspected that Hb A_1 might be high because of the increment of other components excluding the Hb A_{1c} in Hb A_1 fraction, such as Hb A_{1a+b} and/or Hb F. From this speculation, it was concluded that none of the diabetics with I.D.A. had severe complication through the glycosylation of several organs.

Oimomi et al. suggested that determination of Hb A_1 components should be carried out in various pathophysiological conditions from a different standpoint (14). Hb A_{1c} is well correlated with Hb A_1 and measurment of Hb A_1 is easier than that of Hb A_{1c}; however, as our results and Oimomi et al. show, measurement of Hb A_{1c} is necessary for distinguishing non-diabetic individuals from diabetics.

Though levels of glycosylasted hemoglobin were not shown in the obesity or in the emaciation group, there was no difference between these two groups and the control group (15).

ACKNOWLEDGMENT

I woule like to thank H. Tanaka and K. Sonoyama for their kind co-operation.

REFERENCES

1) Rahbar, S. (1968) An abnormal hemoglobin in red cells of diabetes. Clin. Chim. Acta, 22, 296-298

2) Koenig, R. J., Peterson, C.M., Jones, R.L., Saudek, C., Lehman, M., and Cerami, A. (1976) Correlation of glucose regulation and hemoglobin Alc in diabetes mellitus. N. Engl. J. Med., 295, 417-420
3) Bunn, H. F., Haney, D. N., Kamin, S., Gabbay, K. H., and Gallop, P. M. (1976) The byosynthesis of human hemoglobin Alc. J. Clin. Invest., 57, 1652-1659
4) Gabbay, K. H., Hasty, K., Breslow, J. L., Ellison, R. C., Bunn, H. F., and Gallop, P. M. (1977) Glycosylated haemoglobins and long-term blood glucose control in diabetes mellitus. J. Clin. Endocrinol. Metab., 44, 859-864
5) Gonen, B., Rubenstein, A. H., Rochman, H., Tanega, S., and Horwitz, D. L. (1977) Haemoglobin Al : An indicator of the metabolid control of diabetic patients. Lancet, 2, 734-737
6) Ditzel, J. and Kjaergaard, J.-J. (1978) Haemoglobin Alc concentrations after initial insulin treatment for newly discovered diabetes. Br. Med. J., 6115, 741-742
7) Kynoch, P. A. M. and Lehmann, H. (1977) Rapid estimation ($2\frac{1}{2}$ hours) of glycosylated hemoglobin for routine purposes. Lancet, 2, 16
8) Welch, S. G. and Boucher, B.J. (1978) A rapid micro-scale method for measurement of hemoglobin Al (a+b+c). Diabetologia, 14, 209-211
9) National Diabetes Data Group (1979) Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes, 28, 1039-1057
10) Note, S., Notsu, K., Hirata, M., Yaita, A., Nakamura, T., Nabeya, N., Kuno, S., and Sakurami, T. (1983) Diabetes mellitus in one population (1) : The incidence of I.C.A. Tonyobyo, 26, 879-884 (Eng. Abstr.)
11) Hibino, S., Kawabata, K., and Okita, A. (1963) Normal human blood.: In Nippon Ketsuekigaku Zensho, (Nippon Ketsuekigakkai ed.) pp.93-138 Maruzen, Tokyo, (in Japanese)
12) Notsu, K., Sonoyama, K., Umaki, I., Sato, T., Hara, H., Watanabe, M., Hirata, M., Sakurami, T., Note, S., Notsu, Y., Kunishi, H., and Endo, J. (1982) Serum ferritin levels in one population. Igaku to Yakugaku, 8, 857-862 (in Japanese)
13) Brooks, A. P., Metcalfe, J., Day, J. L., and Edwards, M. S. (1980) Iron deficiency and glycosylated hemoglobin Al. Lancet, 2, 141
14) Oimoi, M., Ishikawa, K., Kawasaki, T., Kubota, S., Takagi,

K., Tanke, G., Yoshimura, Y., and Baba, S. (1981) Clinical significance of the determination of Hb A1 components. Tonyobyo, 24, 989-994 (in Japanese)

15) Notsu, K., Sato, T., Oseko, F., Note, S., Endo, J., Goto Y., and Sakurami T. (1983) Glycosylated hemoglobin in a mass screening of diabetes mellitus. Tonyobyo, 26, 358 (in Japanese)