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Superoxide Dismutase Activity in Hydroxyurea-treated $E\beta$ Thalassaemia

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Abstract : The aim of the present study was to examine the activity of superoxide dismutase (SOD) and the level of fetal hemoglobin (HbF) in hydroxyurea (HU) -treated $E\beta$ thalassaemia. We measured SOD level, HbF, mean corpuscular volume (MCV), packed cell volume (PCV) and hemoglobin (Hb) in $E\beta$ thalassaemia patients treated with HU (dose 30 mg/kg/day) for 90 consecutive days. There was an increase in HbF synthesis without any increase in Hb in HU-treated patients. The decreased SOD level in long-term HU therapy in $E\beta$ thalassaemic patients suggests that HU plays some role in inhibiting the superoxide radical generation in thalassaemic erythrocytes. HU may act as an inhibitor of oxidative damage of red cells in $E\beta$ thalassaemia.

Key words : superoxide dismutase (SOD), hydroxyurea (HU), $E\beta$ thalassaemia, fetal hemoglobin (HbF)

Introduction

The chronic use of hydroxyurea may improve the clinical phenotype of sickle cell disease¹⁾. HU augments fetal hemoglobin levels and improves ineffective erythropoiesis in β thalassaemia/HbE patients²⁾. Rodgers²⁾ stated that the thalassaemic patients who are transfused before or during the course of HU therapy may have a delayed response. Superoxide dismutase (SOD), an essential enzyme for biological defense, catalyzes the dismutation of two superoxide radicals ($O_2 \cdot^-$) into O_2 and H_2O_2 . In β thalassaemia, hemoglobin E and hemoglobin H diseases, the SOD activities are significantly higher than normal³⁾.

The objective of this study was to investigate the activity of Cu, Zn, SOD in erythrocytes in non-transfused $E\beta$ thalassaemia after 90 days of consecutive HU therapy and to study the effect of HU on the correction of production of SOD in $E\beta$ thalassaemia.

Materials and Methods

The study enrolled non-transfused $E\beta$ thalassaemia patients (n=20) diagnosed by clinical hematological and mutational study. HU was administered at a dose of 30 mg/kg/day for 90 consecutive days, after informed consent had been obtained by all patients.

Venous blood was collected in EDTA for the study of PCV, MCV, hemoglobin, HbF and in acid-citrate-dextrose solution for the assay of SOD at baseline and 90 days of HU therapy in non-transfused $E\beta$ thalassaemia. Permission to administer HU drug in $E\beta$ thalassaemia

Table 1. SOD, HbF, MCV, PCV, Hb of E β thalassaemia on day 0 and 90 of HU therapy (dose 30 mg/kg/day)

Variable	Day 0	Day 90
Age yr	15.19	15.49
Hb g/dl	5.85 $\pm$ 0.08	6.00 $\pm$ 0.17 *
MCVfl	71.21 $\pm$ 1.99	70.41 $\pm$ 2.10 *
PCV %	19.79 $\pm$ 0.69	21.49 $\pm$ 0.21 *
HbF %	16.68 $\pm$ 2.59	27.80 $\pm$ 4.4 **
SOD Unit/mg protein	27.40 $\pm$ 0.71	5.24 $\pm$ 0.46 ***

Values are expressed as mean $\pm$ SE

(n=20)

* Non significant (o value), ** p<0.05, *** p<0.005

was obtained from the ethical committee of Vivekananda Institute of Medical Sciences, Calcutta. The drug has been extensively used in clinical practice. Neodrea used as therapy for the patients was procured from VHB Pharmaceuticals Private Limited, Dadar (E), Mumbai. SOD was measured by xanthine and xanthine oxidase method⁴⁾ and purification of SOD was done by Tsuchihashi fractionation⁴⁾. HbF was measured by its resistance to alkali denaturation⁵⁾. Hb, PCV and MCV were analyzed by cell counter (Sysmex, K, 1000, Japan).

Results and Discussion

There was substantial increase of HbF synthesis in HU-treated E β thalassaemia patients after 90 days of HU therapy, with no increase in Hb, PCV and MCV, and a decrease in SOD activity (Table 1). The lack of an increase in total Hb despite a substantial increase in HbF during HU therapy is hard to explain. It is assumed that the elevation of HbF without any change of Hb in E β thalassaemia after prolonged HU therapy may be due to the lack of change in HbA level. The increased SOD activity in thalassaemia is a response to (O₂ ·) generated in greater amounts because of accumulation of excessive globin chains and iron in red cells³⁾. The decreased level of SOD in long-term and low-dose HU therapy in E β thalassaemics may inhibit superoxide radical formation of erythrocytes initiated by Fenton-reaction generated OH · radicals. HU therapy may prove useful in the augmentation of fetal hemoglobin in β hemoglobinopathesis¹⁾ and sickle cell patients²⁾. However, no report to date has examined the effect of HU therapy in E β thalassaemia. The present results need to be extended with further studies of oxidative damage in red cells in HU-treated E β thalassaemia. Studies of HU-mediated protection of RBC from lipid peroxidation⁶⁾ suggest that the decreased SOD level in long-term HU therapy in E β thalassaemic patients may reflect a role for HU in inhibiting the superoxide radical generation in thalassamic erythrocytes.

Acknowledgment

The research was supported by the Indian Council of Medical Research. We thank our secretary, Ramakrishna Mission Seva Pratisthan, Dean, VIMS and N. Das.

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[Received August 15, 2001 : Accepted December 26, 2001]