Does G6PD-deficiency related oxidative stress and hemolysis affect erythroid response to erythropoietic stimulating agents (ESA) in Myelodysplastic patients?

Federica Pilo[1], Valeria Santini[2], Anna Angela DiTucci[1], Valentina Serreli[1] and Giorgio La Nasa[1]

[1] Hematology and Bone marrow Transplant Unit, A. Businco Hospital, Cagliari, Italy [2] MDS Unit, Hematology, AOU Careggi, Firenze, Italy

Background

Anemia is the most frequent cytopenia in Myelodysplastic Syndrome (MDS) . ESA have been investigated in several studies as useful to treat anemia in this category of patients. Available pre-clinical data support oxidative stress and hemolysis contributing to ESA resistance but not clinical data is today available. G6PD deficiency is an X-linked condition characterized by a markedly reduced capability to protect red blood cells from oxidative stress. In the island of Sardinia the prevalence of G6PD deficiency is reported to be as high as 12%.

Design

We retrospectively analyzed all MDS patients who had received ESA in our Center in the last 10 years. Diagnosis of MDS was made according to WHO criteria. Patients were stratified based on International Prognostic Scoring System (IPSS). At diagnosis baseline EPO level and G6PD quantitative estimation were detected. G6PD deficiency was defined as an enzyme dosage of less than 0.96 UI/g of Hb in the peripheral blood. Erythroid hematologic improvement (HI-E) was evaluated according to the International Working Group (IWG) response criteria (Cheson JCO 2006).

Materials & Methods

Forty-two patients met the above specified criteria. Of them 13 were G6PD-defiecient and 29 had normal G6PD level values. Median age was 71 years (range 51-96). Thirty-four patients were IPSS low- risk and 8 Intermediate I. At baseline serum EPO level was less then 200 IU/L in all patients before starting ESA treatments.

Patient's characteristics

	G6PD deficient patients	G6PD normal patients
Number	13	29
Sex	5 F ; 8 M	13 F ; 16M
Age (years)	70 (62-93)	70,5 (51-96)
Diagnosis	5 AR; 5 RARS; 3 RCMD	19AR; 7 RARS; 3 RCMD
G6PD level (UI/g Hb)	Median 0,4 (range 0,04-0,89)	Median 1,19 (range 1,02-1,44)
ESA type	9α-epo, 2β-epo, 2 DAR	24α-epo, 4β-epo, 1 DAR
Serum EPO level < 200 UI/L	13	29
RBC requirement before treatment	13 no, 0 yes	13 no, 16 yes

Results

Twenty-eight (80%) achieved an HI-E (16 major and 12 minor). In the G6PD-deficient group HI-E was observed in 13 over 13 patients (major in 7 and minor in 6). In the control group HI-E was observed in 23 over 29 patients (major in 13 minor in 10). (P= 0.29).

Discussion

We evaluated 42 MDS low- risk and Intermediate I IPSS patients who received ESA in the last 10 years in our centre. Despite the common belief that oxidative stress and hemolysis may contribute to ESA resistance, no statistically significant difference to potentially resistance to ESA treatment in G6PD deficiency have been observed. We conclude that G6PD-deficiency does not contraindicate the use of ESA in this setting of patients.