Transfusional Iron Overload and Iron Chelation Therapy in Thalassemia Major and Sickle Cell Disease

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KEYWORDS

• Thalassemia major • Sickle cell disease • Iron overload • Iron chelation
• Deferoxamine • Deferiprone • Deferasirox

KEY POINTS

- Thalassemia major is caused by defects in the synthesis of one or more of the globin subunits of hemoglobin, resulting in variable phenotypes.
- The yearly incidence of symptomatic individuals is estimated at 1 in 100,000 people throughout the world (22,989 new births) and 1 in 10,000 people in the European Union.
- Patients with thalassemia, being transfusion-dependent and having a hyperactive marrow, accumulate iron in tissues.
- The worldwide birth rate of individuals with symptomatic sickle cell disease (SCD) is approximately 2.2 per 1000 births. However, the disease incidence varies between ethnic groups.
- Blood transfusions may be required in both acute and chronic complications of SCD.
- SCD and thalassemia major differ in iron-loading patterns and in the prevalence of iron-induced organ damage.

Video demonstrating a schedule of administration of iron chelators accompanies this article at http://www.hemonc.theclinics.com/

INTRODUCTION

The natural history of both thalassemia major (TM) and sickle cell disease (SCD) has been completely transformed in industrialized countries by the introduction of modern blood transfusions (filtered red cell concentrates that carry an extremely low residual

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risk of pathogen transmission) and iron chelation. The life expectancy in TM has changed from a few years to 5 or 6 decades and it may soon equal that of the nonthalassemic population. Mortality continues to decrease, mainly because of a reduction in cardiac deaths (**Fig. 1**).

Despite the difficulties they still encounter, patients with SCD have also experienced great improvement in quality of life thanks to the introduction of transfusions and hydroxyurea for the prevention and treatment of several complications.[1–4]

BLOOD TRANSFUSIONS

TM

The anemia of TM becomes symptomatic between 6 months and 2 years of age, requiring the institution of a regular transfusion program. As a consequence of continuous anemia, erythropoiesis, although inefficient, can be intense; the bone marrow undergoes an enormous expansion with consequent distortion of facial features, and the plasma volume increases. In addition, hepatosplenomegaly develops. A regimen maintaining a minimum hemoglobin concentration of 9.5 to 10.5 g/dL prevents all the above complications and fosters normal growth at least until puberty.

SCD

Red blood cell transfusions are a mainstay in the treatment of both acute and chronic SCD complications.[5,6] Most patients receive at least one transfusion in their lifetime, usually for acute complications. Blood transfusions increase arterial oxygen pressure and hemoglobin oxygen-affinity, thereby reducing red cell sickling, and they also improve microvascular perfusion.[7,8] Regular blood transfusion regimens additionally suppress endogenous erythropoiesis and therefore the production of red cells containing sickle hemoglobin.

Common indications for both acute and chronic transfusions are shown in **Box 1**.[9]

Erythrocytapheresis in SCD

In SCD, erythrocytapheresis or manual exchange transfusions are alternatives to long-term simple transfusions. Automated erythrocytapheresis is the most accurate method for achieving a target hemoglobin S, but it is also expensive, invasive, and not available in all centers. Manual partial exchange transfusion can be used as an alternative. Both methods slow or prevent further accumulation of transfusional iron.[26]

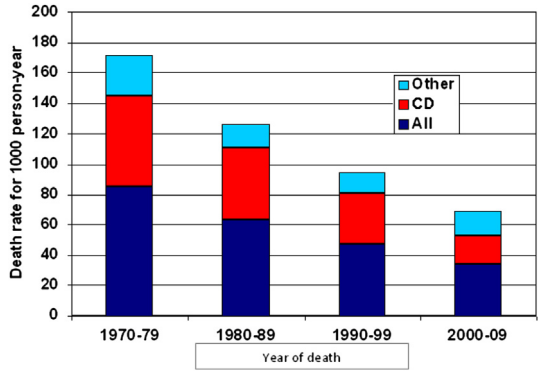

Fig. 1. Death rate of patients with TM observed in Italy according to cause and year of death. CD, cardiac disease.