health technology assessment

EXECUTIVE SUMMARY

MANAGEMENT OF THALASSAEMIA

HEALTH TECHNOLOGY ASSESSMENT UNIT
MEDICAL DEVELOPMENT DIVISION
MINISTRY OF HEALTH
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EXECUTIVE SUMMARY

1. BACKGROUND

Thalassaemias and Sickle cell disorders, are the commonest human inherited haemoglobin disorders that can be treated effectively, and also prevented at community level. Haemoglobin disorders occur in most countries of the world due to global migration, and are emerging as health problems in developing countries.

Thalassaemia is the commonest single gene disorder in Malaysia and a paradigm of monogenetic diseases. In 1995, it was estimated that about 8,000 persons were afflicted with HbE beta Thalassaemia, and 8,000 with Homozygous beta-Thalassaemia, about 40% of whom were dependent on regular blood transfusions for survival (Kaur, 1995). In addition, the carrier rate for beta Thalassaemia and HbE is estimated to be 3-5%, with about 120-350 new patients born each year. Each year there are an estimated 46 births of beta-Thalassaemia major. Sabah appears to have a higher incidence of Thalassaemia major, with 676 cases registered with the Thalassaemia Association of Sabah.

Besides blood transfusion, another curative option is the use of haemopoietic stem cell transplantation. The first patient with Thalassaemia was successfully transplanted with allergenic marrow in Seattle in 1981. In Pesaro, Italy, of the 800 bone marrow transplants carried out over the last 20 years, a survival rate of 95 % has been reported in patients with no hepatomegaly, minimal liver fibrosis and a good history of previous iron chelation. (Lucarelli, 1999). In Malaysia, it is currently being offered to potential patients with suitable donors at two centres, namely, University Malaya Medical Centre and the Paediatrics Institute, Kuala Lumpur Hospital.

2 OBJECTIVE

To determine the safety, effectiveness, cost implications as well as ethical, legal and social implications of management of Thalassaemia

3. SCOPE

This assessment does not include diagnosis of Thalasaemia, as well as antenatal screening for Thalassaemia that has already been assessed previously under antenatal screening.

4. RESULTS

There is sufficient evidence that a screening and prevention programme is effective for the control of β-thalassaemia trait. The options for effective screening include screening of 15-16 year old school students, pre-marital screening, and screening of relatives of known carriers. Screening tests include MCH and osmotic fragility test.

The complications of Thalassaemia include Hepatitis B and Hepatitis C, cardiac complications like heart failure, short stature, pubertal delay, and osteoporosis. Other less common complications include diabetes mellitus.

With respect to blood transfusion, there is sufficient evidence to conclude that leukocyte reduced red cells, produced either in the blood bank or using bed-side filters, are effective in reducing transfusions reactions, the better the filter, the greater the reduction in transfusion reactions. The use of neocytes for transfusion can decrease blood requirement, but is costly. The pre-transfusion Hb level should be not less than 9g/dL and more than 10 g/dL, so as to ensure adequate suppression of erythropoiesis (and its complications). This will reduce blood consumption and iron loading, thus ensuring a better quality of life. The transfusion interval ranges from 2-4 weeks. There is evidence that group and cross matching for ABO, Rh (CDE) and Kell antigen will

reduce the incidence of red cell alloimmunisation to a very low level compared to only routine ABO and RH (D) screening. This is especially so with patients who start transfusion much later in life (> 3 years old).
For the treatment of Thalassaemia by chelation therapy, that there is sufficient evidence that Deferoxamine is effective in preventing or improving serious complications of the disease. Deferiprone is a safe and effective oral iron-chelating agent that can be used, under supervision, in transfusion-dependent iron overloaded children. It decreases iron overload without causing considerable side-effect, since the evidence shows that the possible risk of toxicity are reversible, controllable and manageable. The recommended oral dose is more that 75mg/kg/day.

With respect to transplantation, there is sufficient evidence that sibling donor bone marrow transplantation is safe and effective, and more cost effective compared to blood transfusion therapy. While sibling bone marrow transplantation is most effective, there is also evidence of effectiveness of bone marrow transplantation from unrelated and alternative donors, cord blood transplantation and peripheral blood stem cell transplantation.

The role of modulators of fetal hemoglobin synthesis like Hydroxyurea, Butyrates, 5 Azacytidine and Erythropoietin is still largely experimental and cannot replace the need for regular blood transfusions and regular chelation therapy. The institution of gene therapy to replace bone marrow transplant appears to be still unattainable in the near future. There is no reported medical literature on psychological support for these patients and their families.

There is insufficient evidence on the effectiveness of other treatment modalities like nutrition support and vitamins.

5. RECOMMENDATION

Prevention and screening programm

It is recommended that a screening and prevention programme for the control of β-thalassaemia trait be instituted. Screening of school students and screening of relatives of known carriers should be carried out. Pre-marital and prenatal screening services should be offered for those who request for it.

Treatment

Blood transfusion

1. Thalassaemic children should receive leukocyte-reduced red cells for transfusion .
2. Use of neocytes is not recommended because of the high costs involved. All blood should be screened for ABO and Rh(D) compatibility, while Rh (C and E) and Kell may be undertaken in centers capable of carrying them out.

Chelation therapy

Chelation therapy, it is recommended that Desferoxamine and Deferiprone be used to prevent or improve serious complications of the Thalassaemia. Combination therapy should be considered in patients with inadequate doses of DF due to its high cost or side-effects.

Bone Marrow transplantation

Bone Marrow Transplantation should be offered to patients as soon as possible especially if there is a HLA compatible sibling/ family member. Bone marrow transplantation from unrelated and alternative donors, cord blood transplantation and peripheral blood stem cell transplantation services can also be offered where indicated

Other treatment modalities

There is insufficient evidence to recommend other treatment modalities.