Other Support Measures

1. Vitamin C

Vitamin C should only be given if the patient is on regular desferal therapy. It is usually given after the first month of desferal therapy. The dose for children less than 10 years is 50 mg/day and for those who are older than 10 years it is 100 mg/day.

2. Folic Acid

Folic acid at 5 mg/day should be given to all patients who are under transfused.

3. Splenectomy

Splenic enlargement is an almost invariable feature of children with thalassaemia who are not on regular blood transfusion program. The spleen size in thalassaemia generally corresponds to the marrow dyserythropoiesis. An enlarged spleen causes pooling of blood in its substance which results in increasing transfusion requirements. The development of splenomegaly can be controlled by putting the patients on a regular hyper transfusion program. However, those who have large spleens and require frequent blood transfusions may be considered for splenectomy. The patients of thalassaemia who have enlarged spleens due to poor transfusion regimen may show splenic regression when they are put on regular blood transfusions. The splenectomy should be delayed until the patient is five years of age.

The indications for splenectomy in thalassaemia major are:

1. Annual blood requirement exceeding 200-220 ml/kg.
2. Massively enlarged spleen that is a source of abdominal discomfort.
3. Significant leukopenia or thrombocytopenia.

The patients undergoing splenectomy should be immunized against Pneumococcal infections at least two weeks before the operation. Prophylactic antibiotics (oral penicillin 250 mg bd) should be continued for at least 2 years. Prophylaxis against malaria should be done with weekly chloroquine (5 mg/kg/week). If the platelet count remains persistently high, prophylaxis against thrombosis by low dose aspirin should be given.

4. Hydroxyurea treatment

Hydroxyurea has been effectively used in thalassaemia intermedia. Studies from Iran, Pakistan and India have shown hydroxyurea to be effective in reducing the frequency of blood transfusions, at least in the short term, in 30-40% of the patients with β-thalassaemia major. Less is known about the long-term benefit and the complications of hydroxyurea treatment in thalassaemia major.

Hydroxyurea is also effective in reducing the serum ferritin in these patients. The latter could be because of the reduced transfusion frequency or reduced absorption of iron from the intestine.

No clear explanation is available on how hydroxyurea reduces the transfusion requirements in thalassaemia major. If it was only the augmentation of Hb-F production, hydroxyurea should have been effective in all patients of thalassaemia major. The beneficial effect of hydroxyurea in thalassaemia could also be due to its cytotoxic effect. Rapidly dividing ineffective erythroid cells are the main cause of cortical erosion and expansion of the marrow cavities in thalassaemia. The cytotoxic effect of hydroxyurea on erythroid precursors could significantly reduce the marrow expansion and consequently improve the anaemia due to red cell pooling. The net result would be a reduction in the frequency of blood transfusions. This effect should last as long as the expansion of the marrow cavities remains controlled.

Hydroxyurea is usually started at a dose of 5-10 mg/kg body weight/day and it may be gradually increased to a maximum dose of 20 mg/kg/day. The blood counts should be monitored regularly during the hydroxyurea treatment.

Genetic testing before hydroxyurea treatment

A patient with homozygous β^{o}-thalassaemia mutation is completely unable to form Hb-A. Similarly most of the β^{+}-thalassaemia mutations in Pakistan are also severe enough to exclude the possibility of any significant β-globin synthesis under the influence of hydroxyurea or any other compound like that. There is "no sense" in testing for β-thalassaemia mutations to predict the responsiveness to hydroxyurea. Almost 97% of the patients of β-thalassaemia major in Pakistan are not capable of forming >5% Hb-A. They only have the capability to form Hb-F. Consequently whatever success hydroxyurea can achieve would be either through enhancing Hb-F production or by reducing the expanded marrow cavities due to its cyto-toxic effects. The C–T SNP at position -158 to the Gγ-globin gene (Xmn-I polymorphism) and the *BCL11A* gene correlate well with an enhanced capacity to produce Hb-F. The two SNPs can be used to ascertain the phenotype in β-thalassaemia. But the same can also be inferred from the overall clinical behaviour of the patient.

In a country like Pakistan with resource constraints it would be a luxury to use expensive molecular genetic tests for predicting the response to hydroxyurea. The best approach should be:

1. Selection of patients on clinical performance.
2. Give hydroxyurea at the recommended dose for at least three months.
3. Continue the drug if the patient fulfils the response criteria otherwise the drug should be discontinued.

5. Psychosocial aspects of Thalassaemia

A comprehensive management plan for thalassaemia should also include the management of psycho-social aspects of the disease. The lack of awareness about thalassaemia and its diagnosis usually result in referral of the children from one place to another. Once diagnosed the recurrent problem of getting blood transfusions starts. The high cost of treatment and physical stress of the disease become an increasing burden for the whole family. Consequently most of the affected couples become isolated. The affected children are also miserable. Under these circumstances the affected families often need the help of a psychologist. The following may help:

1. Finding ways to minimize the stress of diseases and its complications.
2. Helping the patients in finding activities during blood transfusions.
3. Engaging the patients at improving self-esteem.
4. Encouraging the patients to meet other individuals with similar illness.