

## Complications in Thalassaemia Patients Receiving Blood Transfusion

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### Abstract

Thalassemia is a genetic disorder that involves the decreased and defective production of hemoglobin, a molecule found inside all red blood cells (RBCs) that transports oxygen throughout the body. Normally, red cells survive for 120 days, but in thalassaemia, red cell survival is reduced. A study was conducted on a cohort of 40 thalassaemic patients registered at different hospital for their disease management by blood transfusion and chelation therapy. The aim of study was to observe number of children receiving blood and complications arising in them due to the blood treatment itself. It was of utter amusement that even after careful blood administration practices, the patient experience many complications both immediate and long-term. Major complications arising in thalassaemics were fever, allergic reactions and septic reactions. Some bitter truths about thalassaemia are that although, it increases the life span of patient; it prolongs the pain of both the patient and the family. It is concluded that careful screening procedures, standard blood administration practices, monitoring, management of complications, checking of effectiveness of therapy and comprehensive care can make a difference. Public awareness and preventive measures such as pre-marital and pre-natal testing should be done to eliminate this fatal disease.

**Keywords:** Thalassaemia, complications in thalassaemia, blood transfusion, chelation therapy.

### INTRODUCTION

Thalassaemia is a genetic disorder. Many different types of thalassaemia are present, of which  $\beta$ -thalassaemia is most common in the world.  $\beta$ -thalassaemia are a group of genetically inherited hemoglobin disorders characterized by chronic hemolytic anemia of variable severity. The genetic heterogeneity of this disorder results in a wide spectrum of clinical phenotypes that may vary from mild chronic hemolysis to a severe transfusion-dependent hemolytic anemia [1].

In Pakistan over 5-6% of our population is a carrier. This translates to approximately 3000 new cases of thalassaemia major each year. Without proper diagnosis and treatment most patients with severe thalassaemia die before the age of 5 years, but with the recommended treatment the prognosis can be greatly improved. Patients can live a normal life span with a relatively good quality of life.

As with all chronic illness prevention is the ultimate goal. Currently prenatal diagnosis is available and should be employed wherever possible. Early detection of carriers with prenatal diagnosis will help eradicate thalassaemia major. Thalassaemia is an Autosomal recessive disease with phenotypic

heterogeneity. As in all autosomal recessive disorders one will have a one in four chance of having a homozygously affected offspring in every pregnancy. Thalassaemia is characterized by severe anemia, growth retardation, skeletal disturbances, and iron overload, cardiac and endocrine abnormalities which cut short the life of the affected patients [2].

Thalassaemia can be diagnosed by tests such as CBC, Hb-electrophoresis, DNA testing. The various procedures used for prenatal diagnosis are: Chronic Villus Sampling (CVS), Amniocentesis, Fetal Blood Sampling, Fetal Cell analysis in maternal blood, Pre implantation diagnosis.

Blood transfusion is started once a definitive diagnosis of severe thalassaemia is made & hemoglobin is below 7gm/dl on two occasions more than two weeks apart. Blood and blood products which are available are packed red cell ideally leuco-depleted. Leuco-depletion may be done either by the blood bank, or by bedside filters, Washed red blood cells are especially useful in patients who experience blood transfusion reactions, Fresh blood (in many places the only available blood is fresh blood which is hanged and settled HBC used).

Blood transfusion is considered to be safe if donor blood is carefully matched for ABO blood group, Rh sub type, and minor blood groups including Lewis etc. if available. Since minor grouping is not available at a majority of centers, blood grouping should be done by the Coomb's method rather the slide method. It should be properly screened for hepatitis B, C, HTV and malaria. And the appropriate amount of blood volume to be transfused. The intervals between transfusions can vary between 2-5 weeks and should not exceed 20 ml/kg at any one time. They have to be adjusted according to the age, weight of the child and utility of quantity in one bag.

Common blood reactions associated with transfusions are Non-hemolytic reactions, Allergic reactions, acute hemolytic reactions, autoimmune hemolytic anemia, Delayed transfusion reactions, Transfusion related acute lung injury (TRALI) and graft vs. host disease (GVHD), Transfusion-transmitted infections are Hepatitis B, C, HIV, Malaria and syphilis.

One of the most serious complications of blood transfusion is iron overload. This mainly occurs because of multiple transfusions, ineffective erythropoiesis and increased iron absorption from the GI tract. The most widely used and known iron chelator is desferrioxamine (Desferal® 500mg/vial). Splenectomy is required after massive splenomegaly. All children should be immunized 2 – 4 weeks prior to surgery with three vaccines: Pneumococcal, Meningococcal vaccine, Haemophilus influenza type B. Long-term chelation therapy also poses many problems. Abnormal findings in the visual, auditory, and somatosensory evoked potential recordings are mainly attributed to desferrioxamine neurotoxicity [3].

#### Objective

1. To study the effectiveness and rationale of blood transfusion and chelation therapy.
2. To emphasize the need for monitoring throughout the treatment.

3. To ascertain number of complications occurring in thalassemic patients.
4. To observe the risk: benefit ratio of therapy.
5. To study patient compliance with the treatment regimen.

#### MATERIALS AND METHODS:

Patients of age up to 20 yrs were observed. In this study, patients of definitive diagnosis of beta thalassemia major and thalassemia intermedia having in a critical need of blood were included. Type of blood to be administered includes fresh blood, washed red blood cells or packed red cell (ideally leuco-depleted). These are administered through BT (blood transfusion) set.

Whole assessment protocol, most importantly blood typing (ABO) and screening, was being observed before giving transfusion to patient. Patients' reports of complete blood count (CBC), Hb-electrophoresis and renal, hepatic and cardiac functioning tests were considered along with enzyme levels of liver and kidney.

The blood during transfusion is monitored carefully. One major problem is the need to overcome reactions that can occur during or after transfusion. Medications to surmount these reactions are anti-histamines, antipyretics etc. Iron overload is the devastating complication arising in thalassemic patient, most commonly due to multiple transfusion and ineffective erythropoiesis. Serum ferritin levels were checked and iron chelation therapy is given. Chelation therapy is given to patients of above 2yrs of age. It is administered through slow SC infusion over 8-12 hours of a 10% desferrioxamine solution using an infusion pump 5 nights/ week.

Other complications related and un-related to transfusion develops as the disease progresses. These include most commonly hepatomegaly, splenomegaly and growth retardation.

#### RESULTS:

The data of 40 thalassemic patients being conservatively managed by blood transfusion and chelation therapy in health care units (Sir Ganga Ram Hospital, Children Hospital and

Fatimid Foundation) were analyzed by a well-designed Performa and is illustrated as:

Fig.1 shows that gender distribution was found to be 50% female and 50% male. There is an equal chance of male and females to be effected by this disease.

Fig.2 describes that cause of thalassemia in the studied data was mostly consanguineous marriage which was 80%, environmental factors 5% and unknown 15%.

Fig.3 shows patients of thalassemia receiving blood when diagnosed were 97.5% and patient who receives blood after 1 year of diagnosis was found to be 2.5%.

Fig.4 shows blood transfusion rate given to patients was of 2hrs was in 37.5% of patient, 3hrs in 57.7% and 4hrs in 5% of patients. The rate of blood should be slower in case of patients of cardiac problem.

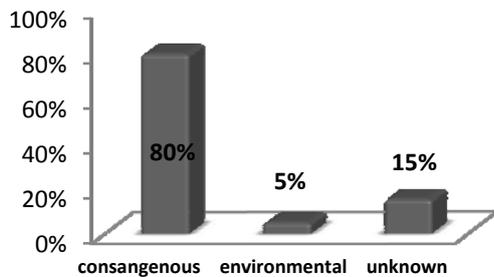
Fig.5 shows type of blood transfused was PCV in 27.5%, washed red cells 57.5%, filtered blood in 5% and fresh blood in 10% of patients.

Fig.6 shows type of blood transfusion reactions occurring was immediate in 87.5% and delayed in 12.5% of patients.

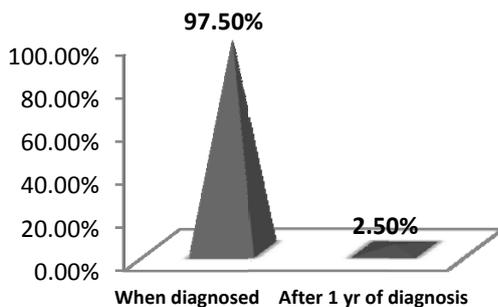
**Figure 1 :**Gender distribution of data population



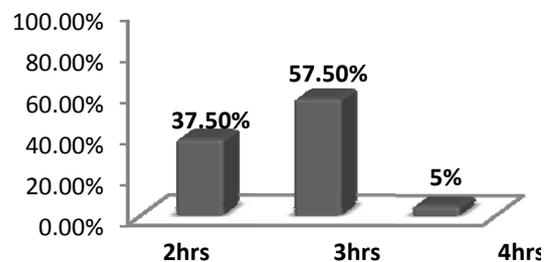
**Figure 2 :**Cause of thalassemia



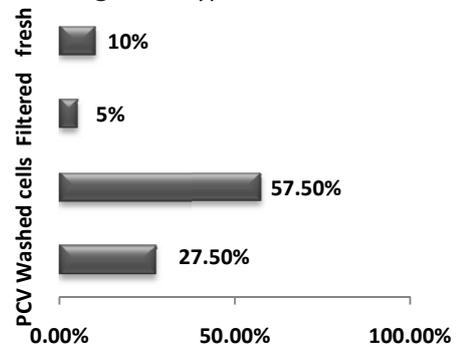
**Figure 3:** 1st blood transfused given



**Figure 4:** Blood Transfusion Rate



**Figure 5:** Type of blood transfused



**Figure 6:**Type of transfusion reactions

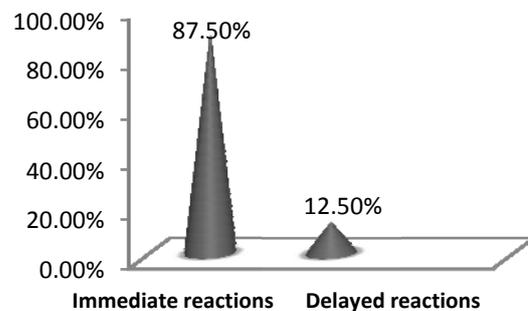
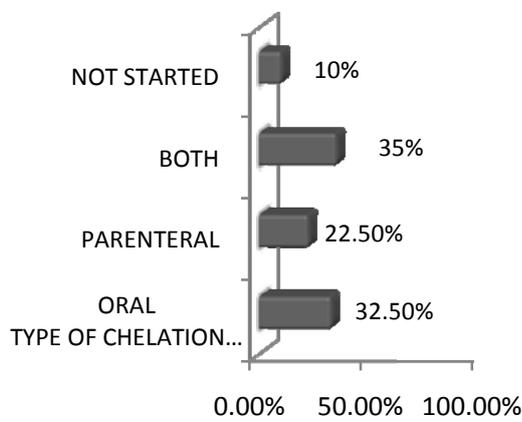


Fig.7 shows type of chelation therapy given was parenteral in 32.5%, oral 22.5%, both parenteral and oral in 35% and in patients not started at that time was 10%. Chelation therapy is usually started usually after 10-12 transfusions and atleast 2yrs of age.

Fig.8 shows that chelation therapy complications were visual problems in 15% of patients, hearing loss 7.5% and local reaction was 82.5%.

**Figure 7 :**Type Of Chelation Therapy



**Figure 8:**Chelation therapy complications

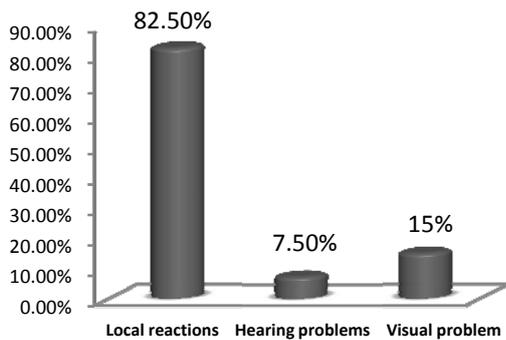
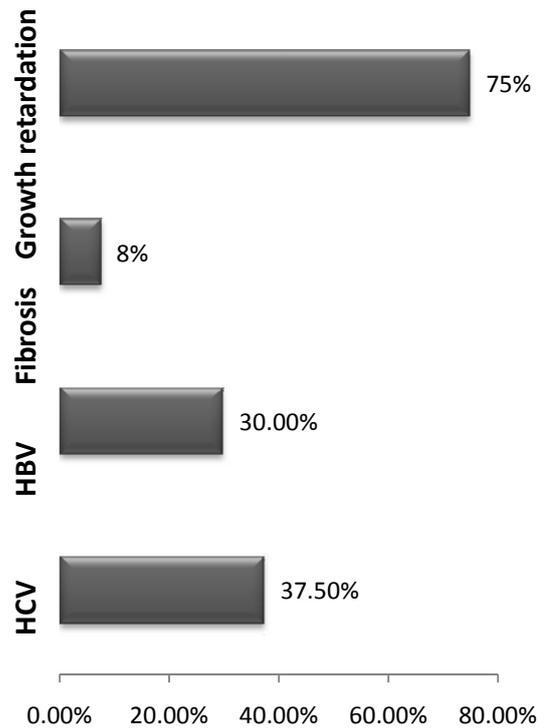


Fig.9 shows that after long- term therapy complications, HCV infection occurs in 37.5%, HBV in 30%, Fibrosis in 7.5%, growth retardation occurs in 75%.

Fig.10 shows that Hepatomegaly occurs in 72.5%, Splenomegaly in 92.5%, cirrhosis in 2.5% and liver failure occurs in 5% of patients.

**Figure 9:** long-term therapy complications



**Figure 10 :**Hepatic and Spleen complications

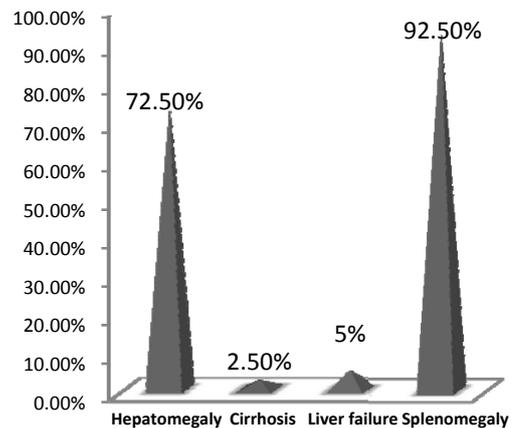
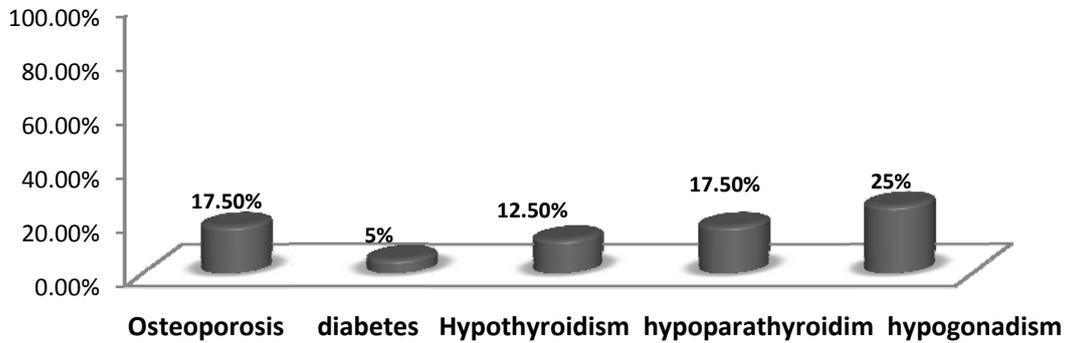


Fig.11 shows endocrinopathies observed in patients were osteoporosis in 17.5%, hypothyroidism in 12.5%, Diabetes in 5%, Hypoparathyroidism occurs in 17.5% and Hypogonadism occurs in 25%.

**Figure 11 :Endocrinopathies**



**Figure 12 :Cardiac Complications**

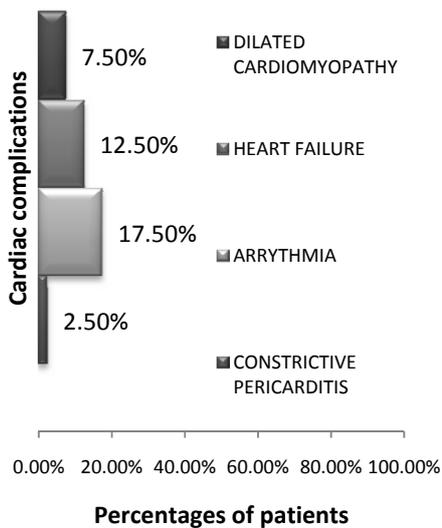
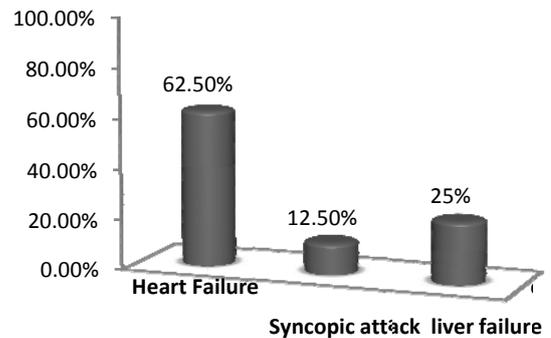


Fig.12 shows cardiac complications occurring in thalassemic patients were arrhythmia in 17.5%, constrictive pericarditis in 2.5%, Heart failure in 12.5% and dilated cardiomyopathy in 7.5%.

Fig.13 shows that complications arising in thalassemic patient causing death of patient were liver failure in 25%, syncopic attack in 12.5% and heart failure in 62.5%.

**Figure 13 :Complications causing death**



**Figure 14 : Record Maintained**

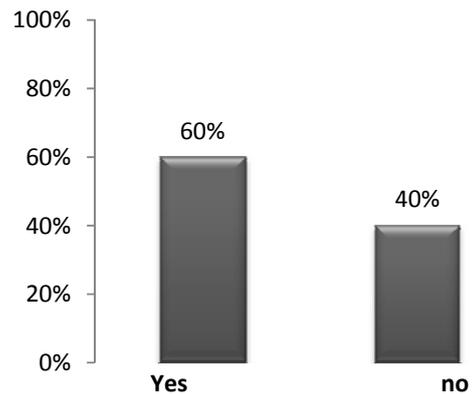


Fig.14 shows that patient records were maintained in 92.5% but in 7.5% records were not maintained.

**DISCUSSION:**

In thalassaemia care there are many challenging areas because many problems are produced due to the treatment itself. In the past 10 years, although, new therapies have greatly improved the quality of life and life expectancy in thalassaemic children but complication still occurs.

Thalassaemia are mostly managed by blood transfusion. The ultimate cure of the disease is stem cell transplantation, but it is a very risky procedure and the availability of the fully matched donor is not always possible.

In order to evaluate frequency of complications in thalassaemia patients, systematic study was carried out. CBC and Hb-electrophoresis were the major determinant for the diagnosis of thalassaemia. Some thalassaemia intermedia patients are asymptomatic until adult life, whereas others are symptomatic from as young as 2 years of age [4]. In our study, patients of thalassaemia receiving blood transfusion were selected only.

After diagnosis, the type of blood required, volume of blood to be transfused and intervals between transfusions are then decided on the basis of individual patient requirement. Type of blood required by patients may vary, like Packed cells (PCV), Washed Red cells, Leuko-reduced or filtered blood and fresh blood. Patients experiencing severe blood transfusion reaction are transfused washed red cells. The Blood before transfusion is passed through various tests and checks. Blood typing and compatibility testing is done and then the blood is sent for screening of major transfusion-transmittable infections like HCV, HBV, HIV, malaria, syphilis, HTLV etc. Some infectious viral agents like CBV and EBV may be transmitted with blood; creating problem in immunocompromised patients, in these patients administration of leuko-reduced RBCs may be helpful. Patients at high risk for contracting blood-borne viruses are with chronic liver disease, intravenous drug users and recipients of blood and blood products, as compared to voluntary blood donors and pregnant women [5]. Transfusion-induced malaria may be a

serious threats to the life especially those who have undergone splenectomy [6].

The volume of blood to be transfused and blood transfusion rates are set according to individual body weight, age and requirement. Patient specifications and allergy profile is strictly considered before transfusion. The transfusion is stopped quickly as soon as the reaction occurs and vital signs are checked. The occurrence of immediate transfusion reaction is more as compared to delayed reactions. An anti-allergic or anti-histamines are given to avoid allergic reactions (rash, urticaria, and pruritis) after transfusion [7]. If patient experience elevation of temperature after blood is transfused, anti-pyretics are given. In case of septic reactions (e.g vomiting, hypotension, fever, chills), antibiotics may be given after performing blood culture test. Severe allergic reactions are may be compensated by administration of Adrenaline or steroids (anaphylaxis, flushing). It has been found that hemoglobinopathies caused by blood transfusions are far more common than previously reported [8].

The lower incidence of fractures was observed in patients in which pre-transfusion haemoglobin levels greater than 9gm/dl were maintained in the early part of the disease, due to emphasis on hyper-transfusion regimen from a young age [9]. Hyper-transfusion therapy has significantly increased the life expectancy. However, this type of treatment has also increased the frequency of complications due to iron overload [10]. The excess of iron in the body is to be excreted otherwise it will soon get accumulates in different organs of the body i.e. heart, liver, kidney etc. Chelation therapy is given to these patients by orally and parenterally or both. Regular lifelong transfusion and chelation therapy in Thalassaemia Major prevented premature heart disease and pulmonary hypertension [11]. The most widely used iron chelator is desferrioxamine (Desferal® 500mg/vial). Inj. Desferal® is injected SC by infusion pump for up to 8-10 hours. The injection can also be given IV by means of drip for up to 8 hours.

Some hospitals use both oral and parenteral treatment regimen. Medications usually prescribed are folic acid®, ferriprox®, hepamarz® and Ca-supplements.

Serum ferritin is a good and practical method to monitor iron overload. Serum ferritin level should be maintained below 1000ng/ml or soon it will get accumulate in different body organs leading to various cardiac, hepatic and endocrine complications. The most common complications are related to iron overload. The heart is the main site where iron deposition causes life-threatening problems [12]. Physician prescribes monthly tests of serum calcium, serum potassium, LFT, RFT and serum ferritin to check levels of electrolytes and functioning of organs in the body. Some patients have undergone surgery of splenectomy and cholecystectomy due to complications of blood transfusion and due to compensatory reaction of the disease itself. Growth retardation and hepatosplenomegaly were the most commonly seen complications. Cardiovascular complication, most notably congestive heart failure was the most common cause of death in patients with  $\beta$ -thalassemia [13]. Some studies have shown that Hepatitis C, iron-related organ dysfunction, and complications of iron chelation therapy are age-dependent, though other factors may be involved [14]. The transfusion-chelation therapy is used for preventing rather than treating anemia related problem [15].

The life of thalassemic patients is miserable. Most of them can't reach the age of adolescence. The matrimonial rate of thalassemic patient is very low because patients often reach the age of marriages. While on our exploration period, social history was also considered. Most of them can't bear the expenses of treatment. Adverse impact of thalassemia was perceived in the domains of education and sports, most thalassemics were not satisfied with their body image. Thalassemic patients are extremely stressful and they face a variety of physical, psychological and social problem. Also culture

and education plays a major role in illness experiences and its treatment.

The patients receiving blood are recommended to avoid iron containing food, Pickles & Vinegars, and Vitamin C. Vitamin E, Tea & Coffee, Folic Acid should be included in diet. Physical Activity may be helpful to these patients.

Counseling should be done by the physician dealing with the patient. It is important for the patients and their families to know about the disease, its prognosis, available treatment regimens and the availability of preventive facilities.

## CONCLUSION

Looking after a thalassemics patient according to standard management is tedious and very expensive. All efforts should be concentrated on prevention of disease. It can be done by Public awareness, Population screening for carriers, Genetic counseling and Prenatal Diagnosis. Blood transfusion, in past, was looked on as relatively risk free. If blood transfusion was risk free, the current intense evaluation of transfusion practice would not come under systematic scrutiny. Major complications arising in thalassemics are fever, allergic reactions and septic reactions. Patients who receive allogenic blood transfusions experience increased morbidity, hospital stays, and cost. In the critically ill patient, the risk of a blood transfusion-transmitted infection is not the major, what is of more consequence is the evidence suggesting that blood transfusion has profound negative effects on the immune system. As a result, the patients after multiple transfusions become HCV, HBV positive even after screening. The transfusion-chelation therapy itself is not adequate treatment, rather it creates more complications. It is concluded that careful screening, standard blood administration practices, monitoring, management of complications, checking of effectiveness of therapy and lastly, meticulous comprehensive care can make a difference.

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