Comparison between Conventional Iron Chelating Medicine and Natural Iron Chelating Substance on Transfusion Dependent Thalassemia Patients - A Study from West Bengal, India

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ABSTRACT

Aims: The aim of this study was to find a harmless, cost effective and easy available iron chelating agent for blood transfusion dependent thalassemia patients who developed iron overload due to repeated blood transfusions and subsequent failure of vital organs and need a concomitant use of iron chelating agent for survival.

Study Design: Sixty transfusion dependent thalassemia patients were selected to evaluate the role and efficacy of a natural substance bottle gourd (Lagenaria siceraria), as iron chelating agent.

Place and Duration of Study: Out Patient Department of Thalassemia Control Unit, Imambara

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Sadar Hospital, Chinsurah, Hooghly, West Bengal, India, between January 2016 and July 2016.

Methodology: The study was undertaken with serum ferritin level, liver function test, routine urine test, ophthalmic and auditory check up to assess the result of using natural chelating agent (bottle gourd) in comparison with commonly used medicine (deferasirox) as iron chelator.

Results: Deferasirox has shown different adverse effects in transfusion dependent thalassemia patients like increased hepatic enzyme level, proteinuria, auditory side effects, which were absent in its natural counterpart.

Conclusion: Natural substance bottle gourd has shown reduction of serum ferritin level without significant side effects and this is cost effective also.

Keywords: Thalassemia; iron chelation; deferasirox; bottle gourd.

1. INTRODUCTION

Thalassemia is one of the most common forms of inherited genetic disorder prevalent worldwide [1-4]. About 100,000 children with thalassemia major are born each year [5,6]. Thalassemia and other hemoglobinopathies are certainly the most common genetic non-communicable disorders and is one of the major public health problems in India [5,6].

In beta thalassemia, there is relative decrease or absence of β chain, which results an excess of α chains. Beta thalassemia major patients show severe hemolytic anemia that can be treated with multiple blood transfusions [7]. Compound heterozygous state HbE-beta thalassemia is also very common in India, where the affected child inherits HbE allele from one parent and β allele from another parent. HbE-beta thalassemia shows great variety in clinical expressions of the disease, as it ranges from nearly asymptomatic to severe transfusion dependent thalassemia. Due to repeated blood transfusions these thalassemia patients develop iron overload. Iron overload is the major cause of morbidity for thalassemia patients. It occurs very rapidly in patients who are on chronic transfusion program. The human body has no active mechanism for the excretion of iron [8,9]. So that the excess iron accumulates in our body and ultimately gives rise to different organ failure.

Under normal conditions the intestinal iron absorption is 1-2 mg/day approximately, and under stimulation the iron absorption may reach up to a maximum level of 3-5 mg/day, amounting to an annual iron accumulation of 1-2 g, approximately [10]. Transfused blood contain approximately 200 mg of iron per unit. Therefore, the patients who receive 2-4 units of blood per month, they will have an annual accumulation of 5-10 g of iron [10].

Ferritin is the principal form of iron store, found in the liver, spleen, bone marrow, endocrinal glands and to a smaller extent in the blood [11]. In the majority of clinical centers, the standard method of evaluating the total amount of body iron is measurement of the ferritin concentration in the blood [12].

To reduce the accumulation of iron in thalassemia patients, subsequent organic injuries and a reduction in survival, they must be treated with iron chelators. There are few iron chelators, has been in clinical use for several years. One of them is Desferrioxamine, which is a very potent iron chelator, but this can be used only by parenteral routes (either subcutaneous or intravenously) and has a lot of side effects like growth retardation, visual problems, agranulocytosis [13]. Next is Deferiprone, an orally active iron chelator. Some toxic side effects of Deferiprone therapy have been recognized including gastrointestinal symptoms, hepatic dysfunction, agranulocytosis and arthritis [14,15]. Another oral iron chelator is Deferasirox which is now widely used, but also has several adverse effects like hepatic dysfunction, renal problem, ophthalmic and auditory side effects [16].

That is why the study was tried with a natural substance, bottle gourd (Lagenaria siceraria) which can be beneficial for these transfusion dependent thalassemia patients by decreasing their iron overload as well as not having other systemic side effects. In vitro study reveals bottle gourd exhibits significant antioxidant activity ---- metal chelating and ferric reducing when compared with standard compounds [17].

2. STUDY SETTINGS

In Imambara Sadar Hospital, there is a (under State Thalassemia Control Program) thalassemia OPD for treating thalassemia patients along with a day care unit for blood transfusion as the curative side of the program and population
screening and subsequent counseling as the preventive part. The study was undertaken with randomly selected sixty patients, who are on regular blood transfusions schedule and with high ferritin count. It has been advised some of them to take uncooked Bottle gourd daily 100-200 g at least for six months. The total participated patients in this study were divided in three groups, each consisting of twenty patients. I. Those who were taking oral Deferasirox (30 mg/Kg body weight/day), II. Those who were taking both oral Deferasirox (30 mg/Kg body weight/day) and Bottle gourd (100-200 g per day) and III. Those who were taking only Bottle gourd (100-200 g per day).

Serum ferritin has been widely used as an easily accessible serum marker for transfusion induced iron overload. So the change in serum ferritin level indicates the efficacy of iron chelating agents in a transfusion dependent thalassemia patient. As deferasirox causes hepatic dysfunction, so the significant rise of SGOT and SGPT levels indicate early adverse effects of deferasirox, which also causes proteinuria, visual and auditory side effects.

So, the study was undertaken with serum ferritin level, liver function test (particularly SGOT and SGPT), routine urine analysis (to check for proteinuria), and checked ophthalmic (for lentical opacity) and auditory (for conductive deafness) problems before starting the therapy and after six months of continued therapy. We've used the chi-square test to test the significance among the variables and p value <0.05 as the level of significance.

Written informed consent was taken from adult participants in our survey and in case of children, from their parents (as per guidelines of the institutional ethics committee).

3. RESULTS

Among twenty patients, who were on both oral Deferasirox and uncooked Bottle gourd, 14 (70%) of them have shown significant reduction in serum ferritin level. In this group of patients (n=20) serum ferritin level decreased from an initial mean (+/-SD) of 3020.4 +/- 1439.4 ng/ml to final of 2529.8 +/-1083.5 ng/ml despite of taking repeated blood transfusion, and seven (35%) of them have shown reduction in hepatic enzyme levels, while nine of them developed side effects like significant rise in serum SGOT and SGPT level (45%) or developed auditory problems (5%).

Among the last group of twenty thalassemic individuals, who have taken only uncooked Bottle gourd as iron chelating agent, twelve (60%) of them have shown significant decrease in serum ferritin level. In this group of patients (n=20) serum ferritin level has decreased from an initial mean (+/-SD) of 2261.45 +/- 684.58 ng/ml to final of 2111.9 +/-669.97 ng/ml, despite of taking repeated blood transfusion. Neither of them has shown those side effects. Also thirteen patients (65%) of them have shown significant reduction in hepatic enzyme level. When the results were compared to other groups, difference was statistically significant (P<0.0001).

The result has been summarized in Table 1.

4. DISCUSSION

It is clearly evident from the above findings that bottle gourd definitely has some ingredients in it which is responsible for iron chelation. The significant metal chelating activity reveals that bottle gourd contains antioxidants which act as chelating agent [17]. Also it has some additional property to reduce hepatic enzyme level, thereby reducing hepatic dysfunction. Both are having immense importance regarding health of thalassemia patients. Patients with transfusion-dependent thalassemia who are able to control iron overload successfully at a safe level with bottle gourd should be encouraged to continue with this approach to chelation therapy. Being an easy available natural fruit (widely used as vegetable) it contains no harm for the thalassemia patients and also would not be a costly one to afford for poorer population. One major problem can be solved in near future if natural iron chelating substance like bottle gourd becomes widely accepted among the thalassemia patients as well as among the clinicians. Although we have focused on the use of bottle gourd for thalassemia patients, bottle
Table 1. Statistical data after taking oral iron chelating agents continuously for 6 months, in comparison with that of before initiation of therapy

<table>
<thead>
<tr>
<th>Total number of patients (N)</th>
<th>On Deferasirox</th>
<th>On Def &amp; Bottle g.</th>
<th>On Bottle g.</th>
<th>Chi-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced ferritin (N, %)</td>
<td>Yes</td>
<td>13 (65%)</td>
<td>14 (70%)</td>
<td>12 (60%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7 (35%)</td>
<td>6 (30%)</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Side effects (N, %)</td>
<td>Yes</td>
<td>18 (90%)</td>
<td>10 (50%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>2 (10%)</td>
<td>10 (50%)</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>Increased level of liver enzymes (N, %)</td>
<td>Yes</td>
<td>14 (70%)</td>
<td>9 (45%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6 (30%)</td>
<td>11 (55%)</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>Proteinuria (N, %)</td>
<td>Yes</td>
<td>2 (10%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>18 (90%)</td>
<td>20 (100%)</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>Auditory side effects (N, %)</td>
<td>Yes</td>
<td>2 (10%)</td>
<td>1 (5%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>18 (90%)</td>
<td>19 (95%)</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>Reduced liver enzymes level (N, %)</td>
<td>Yes</td>
<td>0</td>
<td>7 (35%)</td>
<td>13 (65%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>20 (100%)</td>
<td>13 (65%)</td>
<td>7 (35%)</td>
</tr>
</tbody>
</table>

Gourd may also have an important role in the treatment of patients with other anemias who accumulate iron at lower rates than do those with thalassemia. Further studies of the benefits associated with bottle gourd should take place, and all patients receiving this natural agent should be closely monitored.

5. CONCLUSION

“Life is short and science is long, opportunity is elusive, experiment is dangerous, judgement is difficult.” ‘Hippocrates’ [18].

Thalassemia is mainly spread in developing countries like India and in majority of cases the sufferers are people of low socio-economic background, mainly due to their lack of awareness. Cost of the iron chelating medicines is too high for them. Though recently there is an initiative from West Bengal government to provide iron chelator free of cost to all thalassemia patients, still this facility is not available in other parts of the country. On the other hand, there is wide range of systemic side effects caused by the conventional iron chelating drugs. Therefore if some natural substance like bottle gourd is introduced as iron chelating agent, which is cost effective as well as devoid of any toxic adverse effects on these patients who are on regular blood transfusion, this will be a great relief for the patients, their family and over all to the economy of the country. With this hope in mind we are inviting other clinicians and researchers to give a look in our primary work and research in this sector of natural chelating agents which could be further exploited and could lead to discovery of new iron chelating drugs.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


