Original Article

Efficacy of Chicory in Decreasing Serum Ferritin and Liver Enzymes in Major Beta Thalassemia Patients

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Abstract

Objective

Thalassemia major is a severe transfusion-dependent anemia that needs iron chalation therapy to remove iron overload. The objectives of the present study were to assess the iron overload liver response to inulin of chicory supplementation by evaluating the serum ferritin and liver enzymes.

Methods

Among 70 beta thalassemia patients, 50 were selected for chelating therapy using inulin of chicory. The initial dose was 1gr given twice a day. Twenty patients were excluded because of Hepatitis B and C and cardiac heart failure.

Results

From 50 patients, 47 patients tolerated chicory, which the majority showed dramatic responses. Mean serum ferritin level decreased from 3563.09 ng/ml to 1728.54 ng/ml. Mean serum AST level decreased from 25.44 u/lit to 22.25 u/lit. Mean serum ALT level decreased from 30 .861u/lit to 25.085u/iit. Serum ferritin level decreased significantly after treatment (PV≈ 0.00), but there was no significant difference in AST (PV=0.379) and Alt (0.367) after chicory treatment.

Conclusion

The present results suggest that chicory can reduce iron over load and liver enzymes. Significant differences in serum ferritin were found during intervention, but not in LFT enzymes.

Key words

Major beta thalassemia, Chicory, Ferritin, Liver enzymes

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Introduction

Beta thalassemia is caused by reduced synthesis or absence of the beta globin chain of the hemoglobin. Major thalassemia is a severe transfusion–dependent anemia, and thalassemia intermediate could change from the asymptomatic carrier state to the severe form (1). Management of thalassemia major consists of red blood cell transfusion and iron chelation therapy to remove iron overload (1, 2).

Iron overload complications include endocrine disorders like growth retardation, failure of sexual maturation, diabetes mellitus, insufficiency of the thyroid, parathyroid, pituitary and adrenal hormones ,dilated myocardiopaty, liver fibrosis and cirrhosis (3). So iron overload is a potentially fatal condition, which results from multiple blood transfusions. Deferoxamine which has been used as an iron chelator has limited efficacy due to its demanding therapeutic regimen (leading to poor compliance). Deferasirox, once daily oral iron chelator is more effective than deferoxamine (4). The plant cichorium intybus linn is commonly known as chicory or kasni is used for the treatment of liver diseases (5, 6, 7). Chicory was easy to use and well tolerated in all patients. Toxicity was not considerable even at maximal dose of 1 gr per day. Side-effects of chicory are contact dermatitis, skin allergic like hives, itching and skin irritation (8). However, in the rare instances nausea, headache, abdominal pain was seen and temporary discontinuation of it resulted in rapid disappearing of these symptoms and allowed carrying on therapy. Several studies suggest that inulin supplementation leads to up-regulation of the expression of genes encoding for Fe transporters, enzymes and ferritin in intestinal enterocytes (9).

The objectives of the present study were to assess the iron overload and liver response to inulin of chicory supplementation by evaluating of the serum ferritin and liver enzymes.

Materials and Methods

Among 70 major beta thalassemia patients, 50 patients were selected in between 2009 and 2010 and they participated in phase II clinical trial. Twenty patients were excluded because of hepatitis B and C, and cardiac heart failure. The patients included boys and girls aged 4 to 28 years old (mean age 16 year old). Oral chicory was started 1 gram twice daily, when patients was older than 2 years old with ferritin more than 1000ng/ml. Informed consent was obtained from all patients and their parents.

Medical history was asked and physical examinations were performed. Oral chicory was given 1 gram twice a day. All patients were followed over 3 months. Liver enzymes (AST, ALT) and ferritin were measured before and after treatment.

Statistical methods, paired T-test, Student T-test and ANOVA were done.

Results

From 50 major beta thalassemia patients, 47 patients tolerated chicory well. A dramatic response to the drug was observed in majority of them.

The mean serum ferritin and LFT Before and after treatment with chicory are shown in table 1. Mean serum ferritin level decreased from 3563.09 ng/ml to 1728.054 ng/ml ($p < 0.001$). Significant differences in serum ferritin were found during intervention, but the reductions of serum AST and ALT were not significant as shown in table 1.

Table 1: Ferritin and LFT status before and after treatment with chicory 1

Blood enzymes	Mean	Std.deviation	p-value
AST before AST after	41.42 u/lit 40.00 u/lit	22.257 u/lit 25.444 u/lit	0.739
ALT before ALT after	42.81 u/lit 38.64 u/lit	30.861 u/lit 25.085 u/lit	0.367
Ferritin before Ferritin after	3563.09 ng/ml 2692.13 ng/ml	1728.054 u/lit 1408.992 u/lit	0.000

1Numbere of patients =47. AST, ALT: liver enzymes
Only serum ferritin decreased significantly.

Table 2: Ferritin and LFT status between drug groups before and after treatment with chicory

Blood tests	Deferoxamine	Osferal	L1+deferoxamine
AST before chicory AST after chicory	47.72 ±26.409 u/lit 40.28±19.650 u/lit	41.75±5.73 u/lit 46.50±19.68 u/lit	32.79±13.990 u/lit 31.53±15.218 u/lit
ALT before chicory ALT after chicory	47.44±35.807 u/lit 42.92±27.882 u/lit	49.50±27538 u/lit 60.50±14.708 u/lit	35.21±24.767 u/lit 27.16±17.199 u/lit
Ferritin before chicory Ferritin after chicory	3370.40±1346.3421 ng/ml 2422.80±1000.826 ng/ml	4135.00±1935.037 ng/ml 3355.00±1188.430 ng/ml	3591.84±2164.2012 ng/ml 2814.74±1859.786 ng/ml

1,2 p-value<0.001 AST,ALT= liver enzymes .L1=Deferiprone.
Significant differences were found between Deferoxamine and L1+deferoxamine, but in osferal group no significant differences were noticed.

Table3
Diff-Ferritin and Diff-LFT status between drug groups among treatment with chicory

Blood tests	Deferoxamine	Osferal	L1+deferoxamine	P-value
AST changes	-7.440±19.615 u/lit	4.750±18.920 u/lit	-1.263±17.106 u/lit	0.738
ALT changes	-4.520±24.752 u/lit	11.000±23.762 u/lit	-8.052±27.207 u/lit	0.410
Ferritin changes	-947.600±877.548ng/ml	-780.000±792.464 ng/ml	-777.105±755.949ng/ml	0.777

AST and ALT= Liver enzymes, L1= Deferiprone
Significant differences between drug groups were not noticed during treatment with chicory.

Discussion

The present results showed that root of chicory could reduce serum ferritin. These results emphasized on possible mechanisms of inulin enhance Fe^{++} absorption. In addition, inulin had a beneficial effect on the colon microbial colony (increasing the Bifidobacteria and Lactobacilli colonies) and up regulated the expression of mucin. One hypothesis for explaining the enhancing effect is that fermentation products of inulin in chicory enhance iron solubility in the intestinal lumen, thereby making more iron available for uptake by entrocytes. If this is the case, one would expect an increase in intracellular iron, which would be expected to down-regulate, not up-regulate, the expression of Fe-transporter genes. We observed the opposite; it appears that inulin effects the expression of these genes by other mechanism independent of intracellular iron concentration (9). E. Tako et al suggest that inulin and other fructans enhances Fe-bindin proteins that play an important role in Iron absorption in the intestine (6). Some data suggest that Iron absorption corrected from serum ferritin also did not differ among treatment (p = 0.490) (10).

Present findings are similar to those reported by others who showed decrease in iron over load was observed dramatic response in more than 90% of major beta thalassemia patients in our study (6,9). However, limited studies on major beta thalassemia patients were reported.

Liver is affected by secondary iron overload. Alternation in AST and ALT has been reported by Zafar R et al. results of their studies showed that Chicory could afford a protection against hepatocellular damage (11). Ahmed B et al described chicory normalized the tissues as neither fatty accumulation nor necrosis was observed (5). But our findings did not show significant differences in AST and ALT after chicory treatment (PV <0.05).

We suggest that inulin may contribute to the regulation of iron absorption through changes in bacterial population or by affecting mucus gene expression. One of the pathways by which inulin affects intestinal gene expression is increasing soluble Fe in the intestinal lumen (6). However, the mechanism by which inulin affects the gene expression regulation of enterocyte iron-related transporters and binding proteins remains to be elucidated.

In conclusion, this study results suggest that chicory can reduce iron over load but not liver enzymes. Significant differences in serum ferritin were found during intervention, but not in LFT enzymes.

References:

1.Gao A, Galanello R. Bata- thalassemia. Genet med. 2010; 12(2):61-67

2.Orkin S, Nathan D, Ginsburg D, Look A, Fisher D, Lux S. Hematology of Infancy and childhood. 7th Edition, Elsevier; 2009; pp1068

3.Galanello R, Origa R. Beta- thalassemia. Orphaned J Rare Dis. 2010; 21; 5(1):11.

4.Agarwal MB. Deferasirox: oral, once daily iron chelator- an expert opinion. Indian J Pediatr. 2010; 77(2): 185-91.

5.Bahar Ahmed, Tawfeq A, Al-Howiriny, and Abu B. Siddiqui. Anti hepatotoxic activity of seeds of cichorium intybus. J Ethnopharmacol. 2003; 87(2-3): 237-40

6.Tako E, Glahn RP, Welch RM, Lei X, Yasuda K, Miller DD. Dietary inulin affects the expression of intestinal enterocyte iron transports receptors and storage protein and alters the microbiota in the pig intestine. Br J Nutr. 2007; 10:1 -9

7.Kaur N, Gupta AK. Applications of inulin and oligotfructose in health and nutrition. J Biosci 2002:7-14

8.Ziaee S A, Mesgarpour B. Taking precautions and drug interactions (plants).1st Edition, Tabib; 2005;pp275

9.Tako E, Glahn RP, Welch RM, Lei X, Yasuda K, Miller DD. Dietary inulia affects the expression of intestinal enterocyte iron transporters receptors and storage protein and alters the microbiota in the pig intestine. British Journal of Nutrition 2008; 99:472-480

10.Van den Heuvel EG, Schaafsma G, Muys T, van Dokkum W. Non digestible oligosaccharides do not interfere with calcium and non heme-iron absorption in young, helthy men. Am J Clin Nutr 1998; 67 (3): 445-51.

11. Zafar R, Mujahid Ali S. Anti-hepatotoxic effects of root and root callus extracts of Cichorium intybus L. J Ethnopharmacol. 1998;63(3):227-31.