Efficacy of Chicory in Decreasing Serum Ferritin in Transfusion Dependent ß-Thalassemia Patients: A Randomized Clinical Trial

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Introduction

- β-thalassemia is a group of inherited hemoglobinopathies caused by reduced or absent synthesis of β globin chains
- All patients with thalassemia major are dependent on lifelong blood transfusion from first few months of life.
- Regular blood transfusion leads to various complications, including iron overload.

- A unit of red blood cells contains approximately 250 mg of iron, while the body can excrete up to 1 mg of iron per day.
- In the absence of chelation, a thalassemia patient who receives 25 units per year, accumulates 5 gr of iron per year.
- Moreover, intestinal iron absorption increases in these patients.
- Excess iron is severely toxic to all cells of the body and can lead to serious and irreversible organic damage, such as heart disease, cirrhosis, growth retardation, and multiple endocrine problems.

- Therefore, iron-chelation therapy is essential to maintain iron levels considerably safe and prevent its deposition in various organs. There are several approved iron chelators: deferoxamine (Desferal®) , deferiprone(Ferriprox®), and deferasirox(Exjade®).
- To remove excess iron from the body, several years of great compliance is needed.
- As a result, looking for a drug with higher compliance and fewer side effects is beneficial.

- Cichorium intybus linn (also known as chicory or kasni) is a perennial plant, that has been used in herbal medicine for fever, diuresis, promoting digestion, curing jaundice, and benefiting liver and kidney function.
- It belongs to the family Asteraceae, and is widely distributed around the world, according to various benefits.
- Chicory has become an important vegetable and technical crop in many temperate regions over the last decade, especially in Europe, Asia and North America

- Also, Chicory is a rich source of bioactive compounds, such as flavonoids, saponins and tannins
- Chicory metabolites have been reported to have antioxidant, anticancer, anti-inflammatory, and anti-hepatotoxic effects.
- This agent is regarded as relatively safe and it can be tolerated up to 1000mg/kg/day.
- Potential complications of chicory includes contact dermatitis, hives, itching and skin irritation. Nausea, headache, and abdominal pain has been reported as temporary side effects in rare instances

- It has been reported that chicory has significant effects in reducing fasting serum glucose, HbA1C, AST ,and ALP concentrations.
- Furthermore, recent study by Shahvazian et al. suggest that chicory can reduce iron overload, serum Ferritin, and liver enzymes. However, this research didn't have a control group.
- For that reason, current study is aimed to investigate the efficacy of chicory syrup in decreasing serum ferritin in transfusion dependent ß-Thalassemia patients.

Methods

- This current double-blinded placebo-controlled study was conducted in Ali-Asghar hospital between December 2019 and July 2020.
- Inclusion criteria: Transfusion dependent thalassemia

  Ferritin level more than 1000 ng/ml
- Exclusion criteria: Patients with poor compliance.

- 50 children with transfusion dependent thalassemia major and intermedia
- Randomly selected and divided into:

  intervention(n=25) and control(n=25) group
- Patients in intervention group received 5cc of chicory syrup twice a day for 8 weeks, and patients in control group received a placebo with same color and appearance

- Chicory seeds and roots are obtained from the herbal medicine market. Thereafter, they are recognized in the herbarium section of the pharmacology faculty of Tehran University and receive a herbarium code. Seed and root aquatic extract are made using the maceration method.
- A 60% sugar syrup is made by adding the concentrated extract of chicory seed and root extract. The acquired syrup is standardized according to the total phenol and flavonoid.
- The syrup contains 417 mg seed extract and 417 mg root extract per 5 ccs.

- Both groups were given their regular chelation therapy through the experiment.

- Serum ferritin was measured at the beginning and end of the trial.
- Age, gender, genotype of thalassemia, drug administration and numbers of transfusions were extracted from patients' files.

Results

- A total of 50 thalassemia patients were studied, 25 patients for each groups. The mean age: 26.72 years (SD= 4.34)
- The youngest and the oldest patients were 17 and 35 years old respectively. The average weight: 54.46 kg (SD= 6.15).
- Twenty-six patients were male (52%) and 24 patients were female (48%).
- 45 patients were major thalassemia patients (90%) and 5 patients were intermedia type (10%).

- The initial ferritin amount between the placebo and the treatment group did not have a meaningful difference (P= 0.162).
- Two months after consuming the drug and the placebo, ferritin was checked again and it had decreased by 897.28 (SD=180.85) ng/ml and 799.2 (SD=145.07) ng/ml in both the treatment and the placebo groups respectively. According to the statistical analysis, the ferritin reduction in the treatment group was meaningfully superior to that of the placebo group (P=0.04).

- The mean AST and standard deviation were (53.92±23.38) U/L and (42.68±19.92) U/L in the treatment group and placebo group respectively. The AST amount did not have a meaningful statistical difference between both groups (P>0.05).
- At the end of the study, the treatment group witnessed a decrease (10.88±12.83) U/L and the placebo group's AST decreased (11.28±19.75); however, the statistical difference between two groups was not meaningful. (P= 0.93).

- ALT were (49.4 ± 26.88) U/L and (45.04±40.10) U/L in the treatment and the placebo groups respectively. The ALT amount did not have a meaningful statistical difference between both groups (P>0.933).
- At the end of the study, the ALT decreased in the treatment group (8.6±13.42) U/L and in the placebo group (2.8±6.65) but the difference between the groups was not statistically meaningful (P=0.061).

	Chicory	Control	pvalue
Ferritin	597.26 ±3111.6	2772.0 ± 1036.63	**0.162**
ALT	49.4 ±26.88	45.04 ± 40.1	**0.654**
AST	53.92 ±23.38	42.68 ± 19.92	**0.074**

	Chicory	Control	Pvalue
Ferritin	897.28 ± 180.85	799.2 ± 145.07	**0.04**
ALT	8.6 ± 13.42	2.8 ± 6.65	**0.061**
AST	10.88 ± 12.83	11.28 ± 19.75	**0.933**

Discussion

- In this study, chicory was effective in reducing serum ferritin in patients with beta- thalassemia.
- According to a similar study that done by Shahvazian and his colleagues in Yazd, the use of chicory root could reduce serum ferritin but did not show significant differences in AST and ALT.
- Alternation in AST and ALT has been reported in another survey by Zafar R et al. They showed that chicory could protect against hepatocellular damage. Also in similar study, Ahmed B et al described chicory normalized the tissues as neither fatty accumulation nor necrosis was observed.

- According to these studies, chicory has antihepatotoxic effects. These effects may be due to it contains, isoflavones, polyphenols, and other antioxidants, that can lower the activity of serum ALT and AST in situation of hepatotoxicity.
- Some studies showed that liver function can improved due to protective effect of antioxidants components in chicory extract.
- Moreover, chicory increases intracellular antioxidant enzyme activities and lower oxidative stress in tissues due to chicory extract improve endogenous antioxidant defense status. This hepatoprotection of chicory can prevent liver damage without any histopathological changes.

- Because high iron in patients with thalassemia is an oxidative stress and can have hepatotoxic effects, the use of drugs that can reduce these hepatotoxic effects will greatly help prevent liver damage.

Conclusion

- According to the fact that chicory extract had a good effect on reducing ferritin in thalassemia patients in this study, we propose that future studies should be conducted using larger sample sizes.
- So that we will be able to prove this effect with more certainty.
- Moreover, since the chicory herb has not had a particular side effect neither in this nor the previous studies, it is proposed that this medical herb can accompany the chelators available in the market as a complementary medicine.


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