Case Report

Green Tea Consumption Prevented Iron Overload: A Case Report of Thalassemia Intermedia

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Abstract: *This is the first report of commercially available green tea preparation preventing iron overload in a thalassemia intermedia patient. After 11 months drinking 2 cups of infusion green tea made from one tea bag daily, the serum ferritin decreased from 1,090 mcg/L to 600 mcg/L. A 5-year follow-up with serial measurement of ferritin revealed that green tea consumption might prevent iron overload in thalassemia intermedia patient. No other side effect, except low serum zinc, was found.*

Keywords : ● *Green tea* ● *Thalassemia* ● *Iron overload* ● *Iron chelation*

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Introduction

Thalassemia, a worldwide health problem, is a form of anemia resulting from mutations in the α/β-globin genes, leading to decreased or no production of the globin chain.[1] The severity of thalassemia can be categorized as thalassemia major, thalassemia intermedia and thalassemia minor.[1]

Iron overload in thalassemic patients, practically being diagnosed with elevated serum ferritin, is caused by repeated blood transfusions and elevated dietary iron absorption. Labile iron promotes the formation of a reactive oxygen species (ROS)[2], which lead to oxidative stress, organ dysfunction and tissue damage. Green tea, a commonly consumed beverages in Asia, is thought to reduce the risk of iron accumulation. There are two reported mechanisms by which green tea decreases body iron: (a) it inhibits non-heme iron absorption from the gastrointestinal tract[3] and (b) it decreases in vitro non-transferrin-bound iron (NTBI) and erythrocyte oxidative stress in Hb E/β-thalassemic plasma via epigallocatechin-3-gallate and epicatechin-3-gallate.[4] Green tea effectively inhibits or delays the deposition of hepatic iron in regularly iron-loaded thalassemic mice.[5]

There was no *in vivo* evidence that green tea consumption prevents iron overload among thalassemic patients. This report is, therefore, the first evidence that commercially available green tea preparation prevents iron overload in a thalassemia intermedia patient.

Case report

A 17-year-old-girl, diagnosed with a mild Hb E/β-thalassemia when 6-year-old, had a baseline Hb level around 8-10 g/dL. She was transfusion-independent, received blood transfusions only once or twice a year when ill and/or anemic. Her serum ferritin was checked every 6 months, when she was in good health, by the accredited laboratory in our university hospital (ELIZA kit by Cobas® machine, Roche Diagnostics, USA). When the level reached > 1,000 mcg/L, desferrioxamine (DFO) 20 mg/kg/day was given via infusion pump

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subcutaneously for 10-12 h, 2-3 days/week from the beginning to 6 days/week in 2008.

The patient had an offer to study abroad for 11 months (2008). Two years before going abroad, her serum ferritin levels were 967, 1,125, 802 and 1,012 mcg/L. Before leaving Thailand, her serum ferritin was 1,090 mcg/L. We discontinued iron chelator treatments during her oversea study due to the lack of medical oversight and because the serum ferritin was borderline. We did, however, suggest her to drink tea as it might inhibit iron absorption.

While abroad, her host family prepared commercially available green tea preparation (standard 2 g sachets) for our patient to consume daily. In the morning, one teabag was put into a mug with approximate 240 mL near boiling water, steeped for 3 minutes and allowed to cool before drinking. The same teabag was reused in the same volume of hot water in the evening. Eleven months later, when she returned to Thailand, her serum ferritin was 600 mcg/L. Four months after her return, she was given a blood transfusion (10 mL/kg of leukocyte poor-packed red cells) because of dyspnea after exercise. Her serum ferritin remained low (612 mcg/L) and no side-effects were detected. No iron chelator was given.

She continued to drink commercially available green tea preparation regularly. Several brands of green tea were used as available. On average, she received a blood transfusion once annually and her serum ferritin levels were tested every 3-6 months for the first 3 years after returning. The results of her first 8 serum ferritin tests were 653, 761, 1,062, 964, 906, 653, 653 and 652 mcg/L (the normal range is 15-300). The levels of serum ferritin is demonstrated in figure 1. We found that her serum ferritin levels rose after each blood transfusion.

Her thyroid and parathyroid functions and electrolytes were normal. Serum zinc levels were not

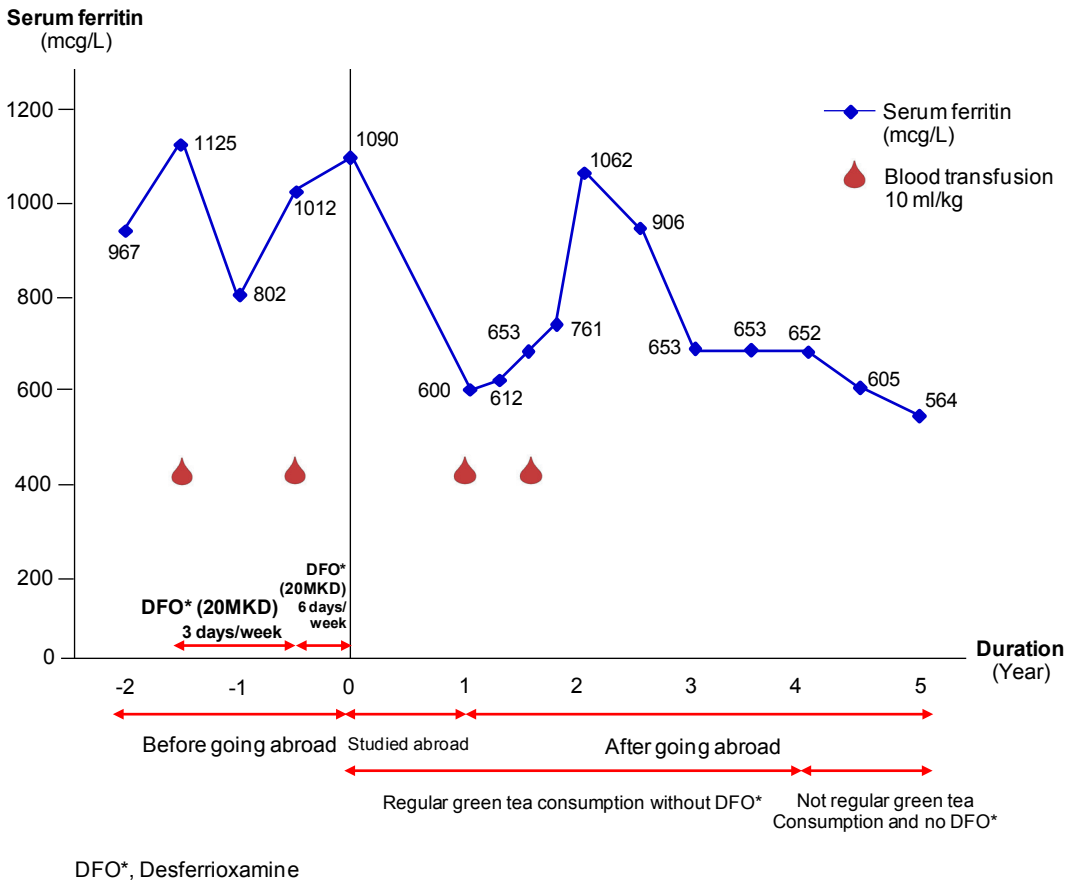

Figure 1. Changing of serum ferritin before and after green tea consumption.

available initially, but as the test became available using atomic absorption spectrometer (Spectr AA-200, Varian, Australia), we found she had low serum zinc (≤ 0.30 mcg/L; normal is 0.50-1.50). We, therefore, gave her one zinc sulfate tablet (15 mg) every day. Her serum ferritin levels were around 600 mcg/L at the same time, so we advised her to stop drinking green tea. She continuously had low serum zinc (≤ 0.30 mcg/L) despite 6 months of zinc supplementation without green tea consumption, which resolved after one year of zinc supplementation (serum zinc 3.54 mcg/L) and supplements were discontinued. Her food pattern was the same when she was in Thailand and abroad and she had normal menstruations.

In May and October 2013 without any iron chelator, her respective serum ferritin levels were 605 and 564 mcg/L. She had been drinking green tea in the form of a beverage once or twice weekly. By October 2013, her serum zinc had again declined to ≤ 0.30 mcg/L. We advised her to take one tablet of zinc sulfate daily. Her echocardiography was normal and revealed no pulmonary artery hypertension.

Discussion

In thalassemia, the organs affected by iron-overload include the liver, cardiovascular and endocrine systems.[6] Iron chelation therapy aims to decrease the levels of accumulated iron to achieve safe levels of body iron by removing plasma NTBI or reducing the intracellular labile iron pool (ICLIP), which can temporarily reverse iron-mediated disease.[7] Parenteral DFO reduces tissue iron stores, prevent iron-induced organ damage, and improved survival, with minimal serious toxicity except in high dosages.[7] Prolonged continuous infusion (8-12 h) is inconvenient and many patients could not comply to the treatment. Deferiprone, an oral iron chelator, is more toxic than DFO;[8] (its serious adverse effects include neutropenia and agranulocytosis). Deferasirox, a newer oral iron chelator, though effective[9], is costly for patients in developing countries.

Green tea is one of the most commonly consumed beverages in the world[10]. It is made from the unfermented dried leaves of *Camellia sinensis*.[10] Like other natural product, the leaves of *C. sinensis* contain an array of phytochemicals; that vary in concentration according to the harvest season, climate, plant age, environmental and processing conditions.[11] The predominant composition of green tea, up to 35% of the dry weight, are polyphenols (including flavonols, flavones and flavan-3-ols), 60-80% of which are flavan-3-ols commonly known as catechins.[10]

Green tea catechins have 3′, 4′-dihydroxy and galloyl groups accounting for their antioxidant property and potentially binds iron.[12-13] The current report suggests an *in vivo* therapeutic effect of commercially available green tea preparation in an iron-overloaded thalassemic patient without the use of any other iron chelator. We documented a zinc deficiency which required treatment and follow-up.

All polyphenol-containing beverages were potent inhibitors of iron absorption and the degree of absorption is dose-dependent. Beverages containing 20-50 mg of polyphenols reduced iron absorption from bread meal by 50-70% whereas beverage containing 100-400 mg of polyphenols reduced iron absorption by 60-90%.[14] Inhibitory effect of iron absorption by black tea was higher, 79-94%.[14] This might explain that when the patient stopped regularly drinking green tea but had been drinking green tea in the form of a beverage once or twice weekly, her serum ferritin was still low. Blood transfusion, however, was not given during this period.

Drinking black tea had an inhibitory effect of intestinal iron absorption in patients with congenital hemochromatosis.[15] The inhibitory effect was seen only with black tea and not with Japanese green tea. Tannins or polyphenols content of tea or other food is a major determinant of the inhibitory effect on non-heme iron absorption.[16] To produce black tea, leaves are harvested and withered and then crushed, torn, curled, or rolled and allowed to oxidize before being dried. As a result, the leaves are darken and develop a stronger flavor and aroma.[17] The level of

fermentation was inversely correlated with the levels of total catechins and epigallocatechin gallate (EGCG). The levels of EGCG and total catechins were higher in green tea than in oolong tea and black tea.[11]

Although green tea typically has less caffeine than black tea, this is not always true. Caffeine content may vary depending on the plant varietal, processing, and brewing methods. The caffeine content of green tea ranges from 24-40 mg per cup and black tea ranges from 14-61 mg per cup.[17]

Concerning side effects of green tea or black tea, a systematic review of anti-obesity medicinal plant demonstrates that *C. sinensis*, catechin enriched tea or black tea had no significant adverse effect.[18] Safety of these plants still remains to be elucidated by further long-term studies. Our patient had experienced low serum zinc, therefore green tea might have an inhibitory effect on zinc absorption from the gastrointestinal tract. Interestingly, the study in rats showed that consumption green tea decoction significantly increased serum zinc but decreased serum iron.[19]

There has had no evidence of green tea consumption preventing iron overload *in vivo* in thalassemic patients before. This case report provides a strong rationale for more clinical research in thalassemic patients on green tea alone or in combination with other iron chelators to discover possible biochemical changes that would account for the evidence. Thereafter, an evidence-based generalizable recommendation could be made.

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ผลของการดื่มชาเขียวกับการป้องกันภาวะธาตุเหล็กเกินในผู้ป่วยธาลัสซีเมียอินเทอร์มีเดีย 1 ราย

อรุณี เจตศรีสุภาพ พัชรี คำวิลัยศักดิ์ และ สุรพล เวียงนนท์

ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

บทคัดย่อ *รายงานนี้เป็นรายงานครั้งแรกถึงผลของการดื่มชาเขียวกับการป้องกันภาวะธาตุเหล็กเกินในผู้ป่วยธาลัสซีเมีย 1 ราย ผู้ป่วยดื่มชาเขียวที่หาซื้อได้วันละ 2 แก้ว โดยชงจากชาเขียวซองเดียวกันทุกวัน ในระยะเวลา 11 เดือน ค่าซีรัมเฟอร์ริตินลดลงจาก 1,090 เป็น 600 ไมโครกรัม/ลิตร ในการติดตามผู้ป่วยเป็นเวลา 5 ปี พบว่าชาเขียวอาจป้องกันภาวะธาตุเหล็กเกินในผู้ป่วยธาลัสซีเมีย อาการข้างเคียงที่พบในผู้ป่วยรายนี้คือมีค่าสังกะสีในซีรัมต่ำแต่ไม่พบอาการข้างเคียงอื่นๆ*

คำสำคัญ : ● *ชาเขียว* ● *ธาลัสซีเมีย* ● *ภาวะธาตุเหล็กเกิน* ● *การขับธาตุเหล็ก*

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