



Possible interaction of warfarin with peppermint herbal tea: a case report

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ABSTRACT

Herbal medicine is usually safe and popular in Iranian communities. Peppermint herbal products may interact with warfarin, which is an essential lifelong drug used in patients with prosthetic heart valves. Herein, we report a case of possible interaction between warfarin and peppermint herbal tea.

We described a 68-year-old woman who was on warfarin treatment due to bileaflet mechanical aortic valve, and mitral valve replacement presented with severe dyspnea in the setting of large obstructive prosthetic mitral valve thrombosis diagnosed by echocardiography. Therefore, cardiac surgery was conducted in the emergent setting. Warfarin was started the day after the procedure. She developed melena with a volatile and elevated international normalized ratio (INR) of 4.8 and prothrombin time > 30 s on the 7th post-operation day. She reported no changes in drug or dietary habits except for drinking high amounts of peppermint tea the day before. After the discontinuation of warfarin and medical consultation for gastrointestinal bleeding, the INR level decreased to 1.8 within two days.

Consumption of peppermint herbal products are usually safe; however, caution should be taken with patients under warfarin treatment. Full disclosure for patients on anticoagulant treatment is necessary before discharge and during clinical follow-up.

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Introduction

All patients with valve replacement surgery undergo long-term warfarin therapy. Warfarin has been the most commonly used oral anticoagulants ever since its approval in 1954 (1). Oral anticoagulants, which are warfarin derivatives (e.g., warfarin), act as vitamin K antagonists by interfering with the effects of clotting factors II, VII, IX, and X. Warfarin, fumarin, kumaklor, bromadiolone, and brodifacum are other drugs in this class (2). The recommended dose of warfarin is based on reaching an appropriate international normalized ratio

(INR), considering age, diet, weight, and genetic differences. Warfarin reduces the risk of valve thrombosis and embolic events from 4% to 0.2% in year (3).

One important complication and morbidity of warfarin therapy is excessive hemorrhaging that is observed when INR is greater than 4 or 5 (4). The risk of major bleeding in patients with mechanical heart valve taking warfarin is between 0.34% and 1.32% each year (5). One out of every ten major bleeding cases leads to death; the

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mortality rate of major bleeding in patients taking anticoagulant drugs, such as warfarin, was reported 9-11% in each case (5). There are many risk factors for hemorrhaging following anticoagulant agents including warfarin, INR>4 or 5, age>75 year, hypertension, history of cerebrovascular accident, simultaneous use of antiplatelet drugs (e.g., Plavix-osivix and aspirin), and a history of bleeding. Approximately 50% of all warfarin-induced bleedings are life-threatening. The most prevalent sites of anticoagulant-dependent bleedings are gastrointestinal (GI) tract (40-60%), urinary tract (15%), intracranial cavity, and retroperitoneal space (15%) (6).

With progress in medicine, traditional medicine and medicinal plants have lost their popularity; however, in many parts of the world, such as Iran and China, they still have relative trust to these drugs. Almost one in six adults in the United States uses the prescribed drugs concomitantly with a herbal supplement. The centers for disease control and prevention recently reported that 38.3-40% of adults in the United States use alternative and complementary medicine. About 15 million people worldwide are at risk of drug interactions with herbal medicines, and consumers of these drugs have little information about the interaction of these medicines and their side effects (7).

Therefore, interactions with chemical drugs can be dangerous, and interactions that alter the anticoagulant effects of warfarin may be particularly acute and life threatening. There are many reports about herb-drug interactions. Some herb-drug interactions and their clinical importance have been verified by several case reports (8).

Peppermint tea (mint tea) is an herbal tea made from an infusion of peppermint (*Mentha piperita*). Peppermint tea, brewed from the plants leaves and the essential oil of peppermint are used in traditional medicine for different therapeutic purposes. Peppermint is a strong antioxidant that has significant antimicrobial, antiviral and antitumor activities, and some antiallergenic potential in vitro (9).

Peppermint has known properties in relieving symptoms of indigestion and irritable bowel syndrome (IBS). Several clinical trials examining the effects of peppermint oil on IBS symptoms have been conducted, and it seems to be effective in relieving indigestion, symptoms like diarrhea and colic, and the aforementioned IBS (9). However, human studies of peppermint tea are limited and clinical trials on peppermint tea are absent.

Adverse reactions of peppermint tea have not been reported, although caution has been urged for peppermint oil therapy in patients with gas-

trointestinal reflux, hiatal hernia, and renal calculus (9,10). According to the national institutes of health, peppermint tea falls into the "likely safe" category when used as a culinary herb, and "possibly safe" when taken in concentrated amounts as medicine (10). In the present study, we described an important suspected drug-herb interaction resulting in a highly elevated INR accompanied by clinically significant GI bleeding.

Case report

We presented a 56-year-old woman with history of rheumatic heart disease who underwent median sternotomy and replacement of mitral and aortic valves (mechanical sj. No. 29 and mechanical sj. No. 21, respectively) in 2011. The patient was discharged without any complications. She was referred routinely for her follow-up, advised to take warfarin, as well as regular control of INR.

Despite a positive follow-up over the past four years, the patient referred to our cardiac surgery emergency department with dyspnea and one episode of hemoptysis. Chest X-ray showed pulmonary edema configuration, and INR of the patient was 1.2, despite regular warfarin administration. Transthoracic and trans-esophageal echocardiography (TEE) and fluoroscopy of the heart valves were performed for her. On examination, the mitral valve had severe malfunction status and was suspected to have thrombus formation; thus, emergent reoperation was planned for her. Before we started the resternotomy procedure, femoral artery access was provided.

Resternotomy was performed under general anesthesia without cardiac rupture or any other cardiac complications. After opening the left atrium, an inspection of mechanical prosthetic mitral valve was performed. A malfunction of the prosthetic valve, which was due to fixed and severe thrombosis of leaflet, especially the anterior leaflet, was noted. The clot removal and complete thrombectomy was carried out, and function of prosthetic mitral valve was perfect. The patient had an uneventful recovery and was transferred to the cardiac surgery department. Intravenous heparin (5000 u/q6) and warfarin (5 mg/day) were administered; furthermore, prothrombin time (PT) and INR (2/day) were controlled for three days after the operation.

On the fifth post-operative day, melena was detected, INR was 4.8, and PT> 30 s. Due to these results, we discontinued warfarin and heparin. Medical treatment such as gastric lavage, omeprazole dosage, and a blood transfusion uneventfully stopped the patient's GI bleeding. Two days later, a subsequent exam revealed elevated INR, which then rose to 1.83 and doses of warfarin at

2.5 mg began. The INR was within the acceptable range for another two weeks. The patient was discharged eight days later.

The patient stated that she had drunk three cups of peppermint tea five days after the operation to ameliorate indigestion, which caused warfarin intoxication. She reported no other changes in dietary habits or lifestyle. Laboratory examinations, such as complete blood count (CBC), showed that liver function was normal.

Discussion

Herbal medicine is popular in Iranian culture and many diseases had been treated with these types of medications in the past. An important key is the interaction between herbal medicine and the conventional drugs that are used in modern medicine. Unfortunately, due to the unconscious and arbitrary consumption of some herbal supplements and their interaction with many drugs, especially heart medications - vascular complications may be irreversible, so the beneficial effects of medicinal herbs should be compared with adverse effects and their possible interaction with other drugs. For example, some herbs interfere with anticoagulant drugs and may cause increased drug effect and bleeding. More than 1300 natural coumarin have been identified. Coumarin that is in similar structure with warfarin has also anticoagulant effects. Patel et al. reviewed the published clinical literature and case series published from 1971 to 2007 to investigate the interactions between various herbs and warfarin. Out of the 72 documented case reports of herb-warfarin interaction, 84.7% of cases had suggested possible interactions (61/72) and 15.3% cases (11/72) reported as probable interactions of medicinal herbs with warfarin. Cranberry juice was involved in 34.7% of (25/72) the case reports. The most common herb was ginkgo, and ginseng was another highly common herb that interacted with warfarin (8).

Some herbal supplements that interact with warfarin are ginger, alpha plant, garlic, green tea, urtica dioica, turmeric, onions, mango and grapefruit, and Chinese herbs including danshen (*Salvia miltiorrhiza*), gegen (*Pueraria lobata*), seven tannin (diuretic and astringent herb), chamomile tea, trigonella foenum, graecum fenugreek (Hlbh), fenugreek, lycium barbarum (Goji), hodiola rosea, fish oil, soy milk, cranberry juice, coenzyme, Q-Devil's claw, dong quai, ginseng, vitamin E, papaya, St. John's wort, bee pollen, safflower, licorice, and peach kernel.

This case report emphasizes on the limited knowledge of patients treated with warfarin regarding the potential interaction between herbal

products and warfarin.

Conclusion

Considering our findings and despite the fact that peppermint tea falls into the "likely safe" category of herbal medicine, we recommend avoiding mint tea for patients with artificial heart valves as well as patients under warfarin treatment. Further human and in vitro studies on the interaction between warfarin and mint tea are necessary.

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Conflict of Interest

The authors declare no conflict of interest.

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