Hemorrhage after the preoperative use of complementary and alternative medicines

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The preoperative use of certain complementary and alternative medicines may predispose surgical patients to an acquired coagulation disorder resulting in excessive bleeding. Many herbs and dietary supplements inhibit platelet adhesion and aggregation or contain coumarins. We report the case of a patient undergoing breast surgery at the University of Colorado Health Sciences Center Denver, Colo, who had extensive postoperative bleeding requiring surgical re-exploration. Preoperatively the patient consumed vitamin E and several herbs with potential to alter the hemostatic process combined with the drugs quinine sulfate and sertraline hydrochloride. These combinations of alternative and conventional drugs may have contributed to inhibition of coagulation.

Key words: Anesthesia, complementary and alternative medicine, drug interaction, herbs, surgical patient.

Introduction
Widely self-prescribed complementary and alternative medicines are often considered to be safe food supplements because of minimal federal product labeling requirements. Between 17% and 51% of surgical patients may be self-prescribing alternative medicines prior to surgery. At least 15 million Americans are taking herbs, high-dose vitamins, or both, combined with prescription drugs. Some herbal products may cause adverse effects or interact with prescription medications. In a recent survey of preoperative surgical outpatients at our medical center, 27% of patients consumed multiple combinations of alternative medicines that could inhibit coagulation. The American Society of Anesthesiologists exhorts elective surgical patients to discontinue herbal medicines at least 2 weeks preoperatively.

We describe here a case report of a surgical patient at the University of Colorado Health Sciences Center, Denver, Colo, who had postoperative bleeding following a modified radical mastectomy and sentinel node biopsy. For several weeks prior to surgery, the patient consumed the herbs ginkgo, ginseng, and the Chinese herb huang qi, combined with vitamin E and the prescription drugs quinine sulfate and sertraline hydrochloride. A posteriori analysis revealed that this combination of alternative and conventional drugs could have caused a synergistic alteration in the hemostatic process that inhibited coagulation.
Case report

In September 1999, a 60-year-old woman with stage I breast adenocarcinoma underwent left modified radical mastectomy with sentinel node biopsy and right breast reduction. Because she was not interested in breast conservation, contralateral reduction for postoperative prosthesis matching was requested. She had no history of postoperative bleeding with previous surgeries of tonsillectomy, tubal ligation, hysterectomy, sinus surgery, or breast biopsy 2 weeks prior.

In May 1999, the patient complained of chest pain. After a normal cardiac evaluation, she was successfully treated for mycoplasma pneumonia with outpatient antibiotics. Although her exercise-induced asthma was well controlled, the preoperative chest roentgenogram reported mild emphysema. She was prescribed the following medications to treat her asthma: montelukast sodium tablets, albuterol sulfate, as well as inhalers salmeterol xinafoate, fluticasone propionate, and albuterol. She also was prescribed quinine sulfate for leg cramps and sertraline hydrochloride for depression. The patient’s preoperative physical examination was unremarkable with laboratory analysis revealing hemoglobin 14.4 g/dL, hematocrit 43%, and platelets 317,000. However, her prothrombin time was slightly prolonged at 15.6 (range, 10.2-12.3 seconds), partial prothrombin time was 25.2 s (range, 23.7 to 32.7 s) and international normalization ratio 1.27 (norm 1). No other preoperative laboratory tests were performed.

On September 8, the patient was examined in the preanesthesi testing clinic, where her alternative medication use was recorded. In the preoperative holding unit on the day of surgery, further querying revealed that in addition to her prescribed medications, she consumed the following herbs prior to surgery: bilberry, gingko (375 mg 4 times daily for 8 months), huang qi (300 mg twice daily for 5 months) and ginseng (300 mg 4 times daily for 6 weeks). Furthermore, she consumed the following vitamins preoperatively: vitamin C, vitamin B₁₂, and vitamin E (800 IU every day for 10 years). She had not discussed the use of herbs and vitamins previously and was unaware of any potential deleterious effects of alternative medicines. Due to the nurse anesthetist’s knowledge that these alternative medications may inhibit thrombus formation, the patient and surgeon were informed of the possibility of increased surgical bleeding and agreed to proceed with the surgery.

After uneventful induction of general anesthesia by the nurse anesthetist and attending anesthesiologist, a left modified radical mastectomy with sentinel node biopsy and right breast reduction were surgically performed. Although no preoperative or intraoperative medications that affect coagulation such as ketorolac or anticoagulants had been administered, the surgeons complained of oozing from the surgical wound. Upon thorough examination prior to surgical closure, no bleeding vessels were found. Blood loss was estimated at 250 mL, and 1,900 mL intravenous fluid was administered for the 2-hour procedure.

In the postanesthesia care unit, the patient’s left breast, chest, axilla, and right breast were marked with significant ecchymotic discoloration, and she complained of throbbing and numbness of her left arm. Although her pulse rate was 80/min and blood pressure 100/58 mm Hg, after the surgical drains collected 269 mL of grossly bloody fluid her hematocrit fell to 26% and hemoglobin to 10.1 g/dL. Consequently, she required an emergency surgical re-exploration and evacuation of hematomata.

For induction of general anesthesia for the second procedure, the attending and resident anesthesiologists administered etomidate, 10 mg; fentanyl, 100 µg; and rocuronium, 40 mg, intravenously. After induction of anesthesia, she exhibited a 20-minute episode of hypotension to 80/60 mm Hg and pulse rate of 100/min requiring vasopressor treatment with ephedrine, 10 mg intravenously and intravenous fluid bolus. After surgical evacuation of a hematoma, three 1-mm diameter arterial bleeding vessels on her left pectoralis major surface were electro-coagulated. The estimated blood loss for the second procedure was 50 mL and she required 2,400 mL of intravenous fluid. Smooth emergence from anesthesia was noticed with little incidence of coughing and bucking during or after extubation. Upon arrival in the postanesthesia care unit, the patient’s pulse rate was 128/min and her blood pressure was 108/50 mm Hg.

The remainder of her postoperative recovery was unremarkable. She had no residual neurologic abnormality in her left arm. Her hemoglobin stabilized at 7.2 g/dL and hematocrit at 21.3%. Although she exhibited symptoms of postural hypotension upon standing, the patient opted against transfusion. She was discharged on the third postoperative day with prescriptions for ferrous sulfate and docusate sodium. At her postoperative visit 1 month later, her hemoglobin was 12.1 g/dL and her hematocrit was 36.8%.
Discussion

Cancer patients commonly consume complementary and alternative medicines alone or in combination with conventional treatments. Seeking salutary remedies, many surgical cancer patients may unwittingly self-prescribe alternative medicines that affect coagulation. Patients who are scheduled for elective surgery should avoid consuming herbs with thrombocytopenic or antiplatelet effects that might inhibit coagulation or promote hemorrhage (email communication with Francis Brinker, ND, in March 2000), as has been reported with heavy garlic intake prior to surgery.9

Vitamin E, taken by 20% of surgical patients at our medical center,4 reduces platelet adhesion and aggregation in doses of 400 IU per day.10 Gingko affects platelet aggregation by inhibiting platelet activating factor.11 Huang qi is used for its immunostimulatory properties, yet its effect on platelet aggregation and fibrinolysis markedly inhibits the synthesis of thromboxane A2 and increases prostaglandin I2.12

Ginseng is an herbal medicine that contains coumarins.13 Coumarins are widely distributed in botanical products.14(p75-76) The discovery that coumarins in the spoiled hay of sweet clover (Trifolium repens) inhibited the formation of prothrombin lead to investigation and synthesis of dicoumarol-type anticoagulants,15(p124) which are derived from a sweet clover plant, Melilotos officinalis.14(p75-76) Because coumarin-drug interactions occur with a number of therapeutic substances, in 1954 the US Food and Drug Administration banned the use of coumarin and coumarin-containing materials, such as tonka beans (Dipteryx odorato) for flavoring purposes.14(p75,490)

Medications containing coumarins may inhibit vitamin K-dependent coagulation factor II (prothrombin), and factors VII, IX, and X.16(p124) Coumarins compete with vitamin K and inhibit the hepatic production of prothrombin, an essential coagulation factor. Any influence that decreases vitamin K or decreases coagulation in other ways would enhance the effects of these prothrombin-lowering (prothrombopenic) anticoagulants.16(p166-167) Hemorrhage is the most common symptom in vitamin K deficiency possibly attributed to disruption of the clotting factors or interference with vitamin K activity such as hypoprothrombinemia, which also may occur with oral anticoagulants, salicylates, and some antibiotics.16(p205)

The patient also consumed the herb bilberry (Vaccinium myrtillus). Bilberry leaves have a documented ability to lower blood sugar; however, no detrimental drug interactions or absolute contraindications are known, nor is bilberry known to inhibit coagulation.16(p264) Additionally, vitamins B12 and C18 have no known effects upon coagulation and may be therapeutic in the prevention or treatment of cancer.

The inhalers montelukast sodium19(p664), fluticasone propionate,19(p671) and albuterol19(p671) have no known effects upon coagulation. Although sertraline hydrochloride was prescribed for depression, this medication rarely alters platelet function, and it is unclear whether sertraline has a causative role in abnormal bleeding.20

However, quinine may depress the hepatic enzyme system that synthesizes the vitamin K-dependent clotting factors and enhances the action of warfarin and other oral anticoagulants.19(pp1374-1375)

Hence, the complementary and alternative medicines with antiplatelet or hypoprothrombinemic effects that this patient self-prescribed preopera-

<table>
<thead>
<tr>
<th>Common name</th>
<th>Scientific name</th>
<th>Coagulation effect</th>
<th>Medicinal use</th>
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</thead>
<tbody>
<tr>
<td>Gingko</td>
<td>Ginkgo biloba</td>
<td>Inhibits platelet function, lowers fibrinogen levels, and decreases plasma viscosity</td>
<td>Improves memory, used for dementia syndromes and peripheral vascular disease</td>
</tr>
<tr>
<td>Huang qi</td>
<td>Astralagus membranaceous</td>
<td>Inhibits platelet aggregation and fibrinolysis</td>
<td>Immunostimulant</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Eleutherooccus ginseng</td>
<td>Inhibits platelet aggregation, contains coumarins</td>
<td>Stress reduction and to improve vitality</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>D-alpha tocopherol</td>
<td>Reduces platelet adhesion and aggregation</td>
<td>Potent antioxidant used for cardiovascular disease</td>
</tr>
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</table>
tively (Table)\textsuperscript{10,11} either alone or in drug-herb interactions with the prescription drugs quinine sulfate or sertraline hydrochloride, may have resulted in an acquired coagulation disorder or vitamin K deficiency and contributed to her significant postoperative blood loss. In disorders of vitamin K deficiency, the prothrombin time is prolonged, and assays demonstrate low levels of factors II, VII, IX, and X. The administration of vitamin K usually reverses these deficiencies unless synthetic function of the liver is markedly compromised.\textsuperscript{21}

Thirty-five percent of the alternative medicines taken by our surgical patients had potential to inhibit coagulation.\textsuperscript{5} Specific knowledge of the pharmacognostic mechanisms of action of herbal or other unconventional medicines is imperative to distinguish which complementary and alternative medications have potential beneficial vs adverse effects. These reported drug-herb combinations or interactions could be contraindications for surgical patients. Further study of the potential adverse effects or interactions of preoperative alternative medicines with concurrently administered anesthetic drugs is necessary to distinguish drug-herb interactions or synergisms that could potentially affect coagulation in the surgical patient.

REFERENCES


AUTHORS

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