Inhibition of Warfarin Anticoagulation Associated with Chelation Therapy

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Chelation therapy originally was administered exclusively to patients with heavy metal poisoning. Now some physicians are administering this therapy for numerous conditions, most commonly coronary heart disease. A 64-year-old man experienced impaired warfarin anticoagulation after undergoing chelation therapy. His international normalized ratio (INR) fell from 2.6 the day before to 1.6 the day after therapy was administered. Whether chelation therapy decreases the effectiveness of warfarin anticoagulation is uncertain. However, because of this potential interaction, clinicians should consider increased INR monitoring in patients undergoing chelation therapy.
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Chelation therapy originally was intended for treating patients with heavy metal poisoning. The compounds, including ethylenediaminetetraacetic acid (EDTA) and dimercaptopropane sulfonate, indiscriminately bind and remove minerals and metals such as aluminum, arsenic, cadmium, copper, lead, nickel, and mercury from the body. Administration of chelation therapy expanded to other conditions, such as heart disease, in the 1950s. While treating workers in the battery industry for lead accumulation, Norman Clarke, Sr., M.D., noticed that some patients had improved angina after chelation therapy.[1, 2] In theory, progression of atherosclerosis depended on copper, iron, or other minerals, such as calcium, and chelation therapy could bind these minerals and inhibit the process. Chelation therapy for patients with heart disease fell out of favor in the 1960s. In 1972, the remaining proponents of chelation therapy founded the American College for the Advancement of Medicine to promote and perform research on chelation therapy.[2] Today, more than 1000 physicians practice chelation therapy in the United States.[1, 3] However, whether the potential benefits of this therapy outweigh the risks still remains highly controversial.

Our patient experienced impaired warfarin anticoagulation after treatment with chelation therapy. To our knowledge, this case report is the first to describe this occurrence.

Case Report

A 64-year-old Caucasian man came to the anticoagulation clinic for management of his warfarin therapy 3 days after being discharged from the hospital for bilateral pulmonary embolism. His warfarin dosage was 15 mg/week. His medical history was significant for coronary artery disease, myocardial infarction, coronary artery bypass grafting (on two occasions), hypertension, hyperlipidemia, peptic ulcer disease, and obsessive-compulsive disorder. He was taking atenolol 50 mg/day, lisinopril 10 mg/day, atorvastatin 10 mg at bedtime, nitroglycerin 6.5 mg 3 times/day, triamterene 37.5 mg–hydrochlorothiazide 25 mg/day, omeprazole 20 mg/day, nizatidine 150 mg every night, and enteric-coated aspirin 325 mg/day. He also took a liquid multivitamin preparation daily that contained spinach and broccoli extract. He denied taking any other substances, such as herbal products, dietary supplements, vitamins, or minerals.

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Table 1. Ingredients in Intravenous Chelation Therapy Administered over 3 Hours

Ingredient	Volume (dl)	Osmolality (mOsm)
Sterile water	500	—
Sodium EDTA 3 g	20	26.80
Magnesium chloride 2 g	10	29.50
Procaine HCl	10	1.40
Heparin 2500 U	0.5	0.46
Vitamin C 7 g	14	81.20
Potassium chloride 2 mEq	1	4.00
Pyridoxine (vitamin B_6)	1	1.11
Thiamine (vitamin B_1)	1	0.62
Sodium bicarbonate 840 mg	10	17.90
Trace elements	1	—

EDTA = ethylenediaminetetraacetic acid.

Table 2. Warfarin Dosing and INR Values in a Warfarin-Treated Patient Who Received Chelation Therapy

Date (2000)	INR[a]	Warfarin Dosage
2/7	1.0	10 mg/day (first dose in hospital)
2/8	1.0	7.5 mg/day
2/9	1.3	No change
2/10	1.8	No change
2/11	2.5	5 mg/day (discharged from hospital)
2/14[b]	3.4	15 mg/wk (skip 2/16, then 5 mg Th, Sa; 2.5 mg F, Su)
2/21	3.5	17.5 mg/wk (skip 2/21, then 5 mg F, 2.5 mg all other days)
2/28	2.1	25 mg/wk (5 mg MWF, 2.5 mg all other days)
3/6	2.6	No change
3/8[c]	1.6	10 mg x 1 dose, then 25 mg/wk (5 mg MWF, 2.5 mg all other days)
3/14	2.8	25 mg/wk (5 mg MWF, 2.5 mg all other days)
3/21	2.3	No change
4/17	2.7	No change
5/8	2.3	No change
6/5	2.6	No change
7/3	1.5[d]	No change
7/10	2.7	No change
8/11	2.7	No change

INR = international normalized ratio.
[a]All INRs were obtained at a Munson Healthcare facility laboratory that uses the same blood draw technique (venipuncture), equipment (CA 1000), and thromboplastin value (international sensitivity index = 2.0) for all INR calculations.
[b]Patient visited anticoagulation clinic.
[c]Day after patient received chelation therapy.
[d]Patient reported missing 2 doses.

Approximately 3 weeks after starting warfarin, the patient received chelation therapy at his primary care provider's office (Table 1); his international normalized ratio (INR) on the previous day was 2.6. The patient returned to the clinic the next day for a scheduled visit, and his INR had fallen to 1.6 (Table 2). The patient denied missing any warfarin doses; he was taking 25 mg/week. He reported no drug or dietary changes and had no new illness that could have affected his INR. He was instructed to take warfarin 10 mg that day and then restart the previous regimen of 5 mg on Monday, Wednesday, and Friday and 2.5 mg on Tuesday, Thursday, Saturday, and Sunday, for a total of 25 mg/week. With this dosing regimen the patient's INR remained stable within the therapeutic target range (2.1–2.7). He did not receive further chelation therapy.

In vitro, EDTA inhibits coagulation by binding to calcium ions that are required for the progression of blood coagulation. One would expect EDTA to have an anticoagulant effect and increase INR. Prolonged prothrombin times have been reported, although infrequently, in patients receiving chelation therapy.[4] The mechanism of this potential interaction is not clear. One possible explanation is that the high dose (7 g) of vitamin C in the chelation therapy might have contributed to the decreased anticoagulation effect of warfarin.[5] Whether vitamin C actually interacts with warfarin is a controversial issue and has not been verified. Furthermore, in theory, oral administration of vitamin C decreases warfarin absorption. Our patient was given vitamin C intravenously, so the interaction would not be expected to occur. Other possible explanations for the drop in his INR, such as missed doses, laboratory errors, or other factors, cannot be ruled out.

Conclusion

Based on our experience with this patient, we cannot determine with certainty whether chelation therapy decreases the effectiveness of warfarin anticoagulation. In fact, this case seems to contradict previous findings. However, since chelation therapy can consist of numerous ingredients, different formulations may have various effects on warfarin. Clinicians may see increases, decreases, or no change in the INR of warfarin-treated patients who receive chelation therapy. Until more is known about how chelation therapy might affect warfarin, clinicians should consider increased INR monitoring in patients undergoing chelation treatment.

References

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