CHAPTER **46**

CONTINUOUS COUMADIN ANTICOAGULATION: Myth Versus Reality

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INTRODUCTION

Patients with a multitude of elective and emergency foot and ankle conditions from ingrown toenails to trimalleolar ankle fractures can present to the podiatric physician coincidentally receiving anticoagulation therapy with warfarin sodium (Coumadin, Dupont Pharma) to prevent complications from atrial fibrillation, thromboembolism or stroke. Continuous anticoagulation therapy is a lifesaving measure preventing fatal complications for these conditions. Paradoxically, coumadin therapy can place the patients at greater risk of hemorrhage following invasive podiatric procedures and trauma. Critical decisions then present themselves to the patient and podiatrist. These questions include interrupting the course of coumadin therapy and risking death or stroke; proceeding with an invasive treatment approach and risking hemorrhage by not stopping the anticoagulation, or risk not treating the presenting complaint appropriately. To stop, or not to stop the Coumadin is a major decision that should not be taken lightly and without consultation and discussion of the implications with the patient in terms of an informed consent process. The podiatric physician should be well aware of the potential risks involved in all phases of these types of decisions. The authors will review the literature concerning the risk of discontinuing continuous anti-coagulation therapy versus hemorrhage and discuss when it may be indicated to choose either option in foot and ankle surgical situations and the protocols available.

HISTORY AND DEFINITIONS

The first effects of oral anticoagulants, though harmful, were seen in dairy cattle in the 1920s and 1930s. In the early part of the century, farmers tried to find other sources of food for their cattle besides hay and corn, and sweet clover was thought to be a cheap source of food for the dairy cattle. Unfortunately, the sweet clover was easily spoiled by molds due to its own excessive moisture and it rotted. Due to the cows eating this rotted sweet clover, adverse effects of internal hemorrhaging and even abortions were noted. A compound known as bishydroxy-coumarin (synthesized as dicumarol), a counterpart of warfarin, was finally isolated in 1941 by Karl Link, and it was this compound that caused the death in cattle.

The interest in this anti-coagulant was over shadowed by the discovery of heparin, an intravenous anti-coagulant. Heparin, extremely valuable today as it was when it was first introduced for human therapeutic use in the 1930s, is still an integral part of medicine. However, the counterparts of warfarin did have an immediate role. It was commercially used as a rat-poison though an unsuccessful rodenticide. Further research into the anti-coagulant group continued and warfarin sodium was eventually synthesized.

The mechanism of action of warfarin sodium is the inhibition of the (vitamin K dependent) gamma-carboxylation of glutamate residues in prothrombin and coagulation factors II, VII, IX, and X. There are also blocking actions on the gamma carboxylation groups of Protein C and S. These blocking actions and antagonist effects on vitamin K, inhibit coagulation. The peak effect of warfarin occurs 36 to 72 hours after ingestion of the drug.

Warfarin has a biological half-life of 36 to 42 hours. It is usually given as the sodium salt, which has a bioavailability of 100%. It strongly binds to proteins, primarily plasma albumin (99% of racemic warfarin binds), and only the non-protein bound form has therapeutic effects. Hence, other drugs that bind to albumin can have an adverse effect on the binding properties of warfarin to plasma albumin, causing either an increase or a decrease in the prothrombin time. Increasing the prothrombin time can be dangerous. Drugs that cause an increase in the prothrombin time, and intensify the effects of warfarin include metronidazole, fluconazole, trimethoprim-sulfamethoxazole, disulfiram, amiodarone, cimetidine, third generation cephalosporins, allopurinol, ciprofloxacin, omeprazole, and tamoxifen. Drugs that cause a noticeable decrease in the prothrombin time, or decrease the effects of warfarin, include: rifampin, barbiturates, dicloxacillin, griseofulvin, nafcillin, and oral

contraceptives. Vitamin K and fresh frozen plasma are used to reverse the effects of warfarin.

Indications for warfarin sodium are acute or recurrent myocardial infarctions, atrial fibrillation, cerebrovascular disease, peripheral vascular disease, prosthetic heart valves, pulmonary embolus, valvular heart disease and venous thrombosis. Hemorrhagic disorders and abortions to the fetus can occur, as warfarin promptly crosses the placenta and is therefore contraindicated in pregnancy. Cutaneous necrosis can also occur. This is usually seen soon after prescribing warfarin.

DISCUSSION AND LITERATURE REVIEW

More often patients seem to present with podiatric care needs while taking continuous anticoagulation therapy with Coumadin. Continuous anticoagulation therapy is a lifesaving treatment that requires constant monitoring and periodic adjustments to maintain adequate therapeutic dosing. Any inadvertent dosage alteration can potentially result in life threatening complications. It is always best, whenever possible, not to interrupt the anticoagulation therapy for these patients. A key decision point for a patient is when to consent to and risk discontinuing anticoagulation therapy for an invasive procedure. Current literature helps in this decision process, but is not specific to the podiatric profession and foot and ankle surgery specifically. The dental literature and research has been very informative in suggesting guidelines that may be applicable to certain foot and ankle conditions.

In a literature review published in the Journal of the American Dental Association in January of 2000 titled "Myths of Dental Surgery in Patients Receiving Anticoagulation Therapy" some very interesting points were noted that may be applicable to the podiatric physician. Serious embolic complications, including death, were 3 times more likely to occur in patients whose anticoagulation therapy was interrupted than were bleeding complications in patients whose anticoagulation therapy was continued (and whose anticoagulation levels were within or below therapeutic levels). Of 526 patients who experienced 575 interruptions of continuous anticoagulation therapy, 5 (0.95%) suffered serious embolic complications; 4 of the patients died. The author concluded based on a review of 2,400 surgical dental procedures that interrupting therapeutic levels of continuous anticoagulation for dental surgery is not based on scientific fact, but seems to be based on its own mythology.

In the New York State Dental Journal of November 2002 a paper was published titled "Stop the Nonsense Not the Anticoagulants: A matter of life and death." The authors state that the risk of a patient on Coumadin having a life-threatening thromboembolic event if the anticoagulation therapy is stopped is 3-5 times greater than the risk of the patient having postoperative bleeding that cannot be controlled with local measures. Their literature review showed no scientific evidence to support removing patients from anticoagulation therapy to perform routine dental procedures including uncomplicated extractions. Another literature review from 1998 published in Archives of Internal Medicine titled, "Dental Surgery in Anticoagulated Patients" reviewed complications of both stopping and not stopping continuous anticoagulation therapy. All cases found in the literature of excess hemorrhage could be managed locally and were noted in either multiple tooth extractions, concurrent antibiotic dosing, or poorly managed anticoagulation levels. The authors noted that it was time to stop interrupting Coumadin therapy for dental surgery. The authors further stated that those dentists that interrupt anticoagulation therapy are treating the doctor and not the patient. They felt those patients on anticoagulation within the therapeutic range are at no greater risk for hemorrhage than patients with normal coagulation.

The common theme through this literature is to try not to stop continuous anticoagulation therapy whenever possible. The podiatric literature, other than providing several thorough reviews, does not specify when or which procedures warrant alterations in continuous anticoagulation therapy. More research needs to be done in this area to help the podiatrist know how best to balance these choices. Dental extractions can certainly be likened to nail avulsions in terms of potential for hemorrhage complications. It would seem reasonable to extract from these reviews that both nail avulsions and nail avulsions with matrixectomies could be performed without fear of excess hemorrhage.

At the VAMC Augusta we have documented multiple patients and will continue to follow patients after nail surgery on continuous anticoagulation and have not noted any hemorrhage complications in patients who are in the therapeutic range with their anticoagulation therapy maintained perioperatively. Skin procedures such as excision of lesions or curettage of verucca may be considered as well to be exempt from alterations in anticoagulation therapy. Soft tissue digital surgeries or bunion procedures may require further research on risk of

hemorrhage complications. Such research would certainly be warranted given the risk of stroke or death when the anticoagulation is interrupted. Osseous forefoot and rearfoot surgeries would typically warrant alterations in anticoagulation therapy to avoid hemorrhage complications with the full knowledge of the risks explained and understood by the patient and documented.

PROTOCOL OPTIONS

Maintaining Dosing Unaltered

The best policy in terms of altering continuous anticoagulation therapy is to maintain dosing without changes. Nail and skin procedures would seem to fall into the range of dental extractions and be safely performed without worry or concern. Studies have shown, and experience dictates that if the internist is consulted preoperatively, the Coumadin dosing even for these minor procedures will be altered. If consultation with the internist is performed, it is suggested to focus on the stability of the patient on the medication, their compliance, and previous history of problems on the medication not on the decision to alter the Coumadin dosing, which is not necessary.

Scheduling elective nail or skin procedures just after any routine anticoagulation testing or repeating a test earlier on the day of the procedure is suggested especially in patients with a difficult anticoagulation control history. A study reported in "Periodentology" in 2000 suggested, based on their review of the literature, that as long as the prolongation of the prothrombin time (PT) is therapeutic at 1.5-2.0 times the normal clotting time or the international normalized ratio (INR) is maintained between 2.0 and 3.5 on the day of the procedure, no thromboembolic events or hemorrhage complications were noted. In the elderly or those with a high INR, a 3-day cessation protocol was suggested.

Interrupting Dosing

Where more invasive procedures or surgeries are to be performed, alterations in Coumadin dosing are generally recommended. The medication is generally stopped 2 days prior to the procedure and begun again on the day of the surgery. A prospective cohort study on dental procedures published in "Clinics in Applied Thrombosis and Hemostasis" in 2000 showed no major bleeding or thromboembolic events following this protocol in 104 consecutive patients undergoing 123 dental procedures whose INR values were between 2.0 and 4.5. Monitoring of anticoagulation levels showed a mean decrease in INR levels of 1.0U at the 2-day mark. Seven days after the suspension of Coumadin the INR returned to therapeutic levels in 90% of patients. The average time spent at an INR of less than 2.0 (critical value) was 28 hours. This protocol was deemed safe and effective, but still left the patients potentially vulnerable for a 28 hour period and 10% of patients required greater than a week to return to safe therapeutic levels of Coumadin dosing. Literature reviews show thromboembolic complications more likely as a result of more prolonged alterations in Coumadin dosing whether planned or accidental and patients with older heart valve replacements from the 1960s.

Cessation of Dosing

Cessation of continuous anticoagulation therapy is considered if the medication is stopped for 4-5 days and then restarted after a procedure. The effects of the Coumadin over this period of time are eliminated. The chance of hemorrhage from the procedure is eliminated, but an increased risk of a thromboembolic event is very real. This approach is generally considered too risky and usually unnecessary for most dental procedures. We can extract from this research that any patient confusion over shorter duration interruption type protocols concerning when to stop or start the Coumadin of even several days, places them at far greater risk for a serious thromboembolic event.

Substitution Therapy

This protocol involves discontinuing the long-acting Coumadin and substituting the shorter acting Heparin in what is termed a Coumadin-Heparin-Coumadin switch. The Coumadin is stopped 2-3 days prior to the procedure and Heparin is begun as a substitute. The Heparin is held preoperatively for 8 hours minimizing the period of interruption of anticoagulation. Coumadin is then restarted postoperatively and the Heparin withdrawn. This protocol can be costly and may require hospitalization and is generally reserved for patients at greater risk of thromboembolism. Use of Vitamin K and fresh frozen plasma are reserved for emergency situations and are not generally employed for elective type procedures.

ADDITIONAL STRATEGIES FOR THE PODIATRIC PHYSICIAN

Skin and nail surgeries may not warrant alterations in anticoagulation therapy. The chance of uncontrolled hemorrhage is low, but measures can be taken to help avoid this potential complication. Digital tourniquets are typically employed in nail procedures especially when

matrixectomy is planned. Short-term use over 15-20 minutes of a very firm compression dressing that is removed and replaced with a lighter compression dressing prior to discharge can be very helpful. This approach permits inspection of the wound as well for assurance of hemostasis. Chemical hemostats such as thrombin can be applied and absorbable hemostats such as oxidized cellulose and microfibrillar collagen can be incorporated into the dressings.

Recent or day of procedure PT and INR testing should be routinely reviewed prior to any invasive procedure. This is especially important in patients with a difficult management history where more than periodic adjustments in dosing are noted. Questioning or physical examination of the patient for bruising or evidence of a bleeding problem should be reviewed with the patient. Generally patients on continuous anticoagulation therapy are reasonably well versed in their condition and management history.

Concurrent use of a multitude of medications can interact with Coumadin and either potentiate or reduce its activity increasing the chance of hemorrhage or thromboembolic event. A number of medications that potentiate Coumadin activity are commonly used by the podiatric physician especially in the perioperative period. These medications include antibiotics commonly used in prophylaxis such as the penicillins and cephalosporins as well as erythromycin. These antibiotics are commonly noted in the literature when hemorrhage issues and cases are presented. Pain medications must be considered as well such as acetaminophen, salicylates and the NSAIDs, as well as propoxyphene. Other medications common to the podiatry profession that can potentiate the effects of Coumadin include ketoconazole and the corticosteroids. Medications common to the podiatric profession that oppose the effects of Coumadin include ascorbic acid, dicloxacillin, and nafcillin.

CONCLUSION

Further research is needed concerning the surgical podiatric patient under continuous anticoagulation therapy. Questions need to be answered concerning when the podiatrist should consider altering Coumadin dosing and when best not to alter the dosing in elective podiatric surgery. Nail and skin procedures would seem to be exempt from alterations in Coumadin therapy based on dental research and research currently under way. Possibly soft tissue procedures about the forefoot could be included as procedures where no alteration of anticoagulation treatment may be needed, if the therapeutic levels of the medication can be assured preoperatively. Further research is likewise needed to establish which protocol is best suited for the podiatric profession when alterations in anticoagulation are deemed necessary.

The high risk patient would seem to warrant consideration of Heparin substitution protocols to ensure the best safety against a thromboembolic event. Protocols that discontinue Coumadin for 2-3 days may be considered when there is a greater risk for intraoperative hemorrhage to maintain as low a risk for a thromboembolic event and yet maintain good hemostasis. This protocol has been successfully reported in the dental literature and seems reasonable for most podiatric procedural situations. The myths of Coumadin need to be replaced with the facts of research to help ensure safety from either a thromboembolic event or hemorrhage in the podiatric patient.

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