
Oral surgery in patients on anticoagulant therapy

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Objective. Surgery is the main oral healthcare hazard to the patient with a bleeding tendency, which is mostly caused by the use of anticoagulants. The traditional management entails the interruption of anticoagulant therapy for dental surgery to prevent hemorrhage. However, this practice may increase the risk of a potentially life-threatening thromboembolism. Because this issue is still controversial, it is the aim of this paper to review the evidence, to highlight the areas of major concern, and to suggest management regimens for patients on the 3 main types of anticoagulants: coumarins, heparins, and aspirin.

Materials reviewed. The pertinent literature and clinical protocols of hospital dentistry departments have been extensively reviewed and discussed.

Results. Several evolving clinical practices in the last years have been detected: anticoagulant use is generally not discontinued; oral surgery is performed despite laboratory values showing significant bleeding tendency; new effective local methods are used to prevent bleeding; and patients at risk are referred to hospital-based clinics.

Conclusion. The management of oral surgery procedures on patients treated with anticoagulants should be influenced by several factors: extent and urgency of surgery, laboratory values, treating physician's recommendation, available facilities, dentist expertise, and patient's oral, medical, and general condition.

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Hemostasis in the healthy individual involves interaction between 4 biologic systems: the blood vessel wall, the blood platelets, the blood coagulation system, and the fibrinolytic system. Blood vessel constriction is an essential first stage; platelet adhesion and aggregation follow. The hemostatic mechanism is initiated at the site of injury by local activation of surfaces and release of tissue thromboplastin, resulting ultimately in formation and deposition of fibrin. The coagulation process is regulated by physiologic anticoagulants.¹ Activation of fibrinolysis is triggered by the presence of fibrin and tissue-type plasminogen activators at the site of fibrin formation, a process regulated by physiologic inhibitors such as α_2 -antiplasmin, histidine-rich glycoprotein, and plasminogen activator inhibitor.¹

Oral surgery induces changes of fibrinolysis in the oral environment; initially, the fibrinolytic activity of saliva is reduced because of the presence of inhibitors of fibrinolysis originating from the blood and the

wound exudates, but when the bleeding and exudation reduce, the fibrinolytic activity of saliva increases. Plasminogen and plasminogen activator are present in the oral environment in physiologic conditions because plasminogen is secreted into the saliva and tissue-type plasminogen activators arise from oral epithelial cells and gingival crevicular fluid. Thus, after surgery, fibrinolysis is triggered.²

Some patients have a tendency to bleed excessively after trauma. Surgery is the main oral healthcare hazard to the patient with a bleeding tendency, but regional block local anesthetic injections also may be a hazard because bleeding into the fascial spaces of the neck can threaten airway patency. Most bleeding tendencies are from the use of anticoagulants,³ usually prescribed to treat a number of cardiac or vascular disorders, including atrial fibrillation, ischemic cardiac disease, cardiac valvular disease, prosthetic cardiac valves, postmyocardial infarction, deep venous thrombosis, pulmonary embolism, cerebrovascular accident, and many others.⁴⁻⁶

Concern exists about intraoperative and postoperative bleeding in patients undergoing anticoagulation therapy and the best management for the situation. Many clinicians have recommended interruption of continuous anticoagulant therapy for dental surgery to prevent hemorrhage. However, with review of the available literature, no well-documented cases of serious bleeding problems from dental surgery in patients receiving therapeutic levels of continuous warfarin sodium therapy were identified, but several documented

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cases were found of serious embolic complications in patients whose warfarin therapy was withdrawn for dental treatment.⁷ Fundamentally, the surgeon and treating clinicians must balance the need for reducing anticoagulant therapy and preventing undue hemorrhage against the associated increased risk from the diminution of the therapeutic benefit of anticoagulation therapy resulting in potentially life-threatening thromboembolism.⁸ A recent survey showed that of more than 950 patients receiving continuous anticoagulant therapy (including many whose anticoagulation levels were well above currently recommended therapeutic levels) who underwent more than 2400 surgical procedures, only 12 (<1.3%) needed more than local measures to control hemorrhage.⁹

The recommendations concerning treatment emphasis, timing, and modifications of anticoagulant intake in relation to oral surgery have thus been controversial, and therefore, this paper reviews the current evidence, highlights the areas of major concern, and suggests management regimens. This paper discusses oral surgery management considerations for patients on the 3 main types of anticoagulants: the coumarins, heparins, and aspirin.

GENERAL POINTS

Anticoagulants present management problems in oral surgery mainly because of prolonged intraoperative and postoperative bleeding. However, about 90% of postextraction hemorrhage is from other causes, including the following³:

- excessive operative trauma, particularly to oral soft tissues;
- poor compliance with postoperative instructions;
- interference with the extraction socket or operation site (eg, by sucking and tongue pushing; plasminogen activators are present in saliva and oral mucosa and can thus cause fibrinolysis);
- inflammation at the extraction or operation site, with resultant fibrinolysis;
- inappropriate use of analgesia with aspirin or other nonsteroidal antiinflammatory drugs, which, by interfering with platelet function, induce a bleeding tendency (Table I);
- uncontrolled hypertension.

The following general points should be considered in patients for oral surgery on anticoagulant therapy:

1. Dental preventive care is especially important to minimize the need for surgical intervention.¹⁰
2. Systemic conditions that may aggravate the bleeding tendency can be present. These conditions include a wide range of disorders, including coagulopathies, thrombocytopenias, vascular disorders, such as

Table I. Drugs that may be used in patients for dental surgery that can impair platelets or their function

| |
|--|
| ANTIBIOTICS (β LACTAMS) |
| Amoxicillin |
| Ampicillin and derivatives |
| Azithromycin |
| Methicillin sodium |
| Penicillin G (benzyl penicillin) |
| Cephalosporins |
| Rifampicin |
| Sulphonamides |
| Trimethoprim |
| ANALGESICS (NONSTEROIDAL ANTIINFLAMMATORY DRUGS) |
| Aspirin |
| Diclofenac sodium |
| Diflunisal |
| Ibuprofen |
| Mefenamic acid |
| GENERAL ANESTHETIC AGENTS |
| Halothane |
| PSYCHOACTIVE AGENTS |
| Antihistamines (some) |
| Diazepam |
| Tricyclic antidepressants |
| Chlorpromazine |
| Haloperidol |
| Valproate sodium |

Adapted from George JN, Shattil SJ. The clinical importance of acquired abnormalities of platelet function. *N Engl J Med* 1991;324:27-39.

Ehlers-Danlos syndrome, liver disease, renal disease, malignant disease, and HIV infection.³

3. Drugs that cause increased bleeding tendency (eg, aspirin and other nonsteroidal antiinflammatory drugs) should be avoided^{6,11} (see next point).
4. Any surgical intervention can cause problems; thus, the possibility of alternatives to surgery (eg, endodontics) should always be considered. The patients should be warned in advance of the procedure of the increased risk of intraoperative and postoperative bleeding and intraoral/extraoral bruising. If the bleeding tendency is great, dental extractions, other surgical procedures, and some local analgesic injections (regional blocks) can cause serious problems.
5. Other interventions to avoid, if possible, include regional local analgesic injections (may bleed into fascial spaces of neck and obstruct airway; intraligamentary or intrapapillary injections are far safer) and intramuscular injections.³

WARFARIN (COUMARIN)

Coumarins are used in the treatment and prophylaxis of thromboembolic disorders (Table II). Warfarin (also used as rat poison) is the common one used. Warfarin is highly water soluble and rapidly absorbed from the stomach and the upper gastrointestinal tract; its plasma

Table II. Coumarin anticoagulants

| |
|-----------------------------|
| Warfarin |
| Acenocoumarol (nicoumalone) |
| Phenindione |

concentrations peak 60 to 90 minutes after oral administration. It binds to the enzyme vitamin K 2,3-epoxide reductase in liver microsomes, antagonizing the vitamin K-dependent synthesis of several coagulation factors, especially factors II, VII, IX, and X and proteins C, S, and Z, so that the prothrombin time (PT) and activated partial thromboplastin times (APTT) are prolonged.¹

Coumarin anticoagulant therapy should maintain a PT of 1.5 to 2.5 times the control.⁸ Warfarin effects are delayed for 8 to 12 hours and are maximal at 36 hours but persist for 72 hours.^{5,11} The plasma half-life of warfarin is about 37 hours.¹¹ Warfarin is metabolized mainly in the liver and by the cytochrome p450 complex, and its effect is reversible with vitamin K.¹

International normalized ratio

The World Health Organization recommends the use of the international normalized ratio (INR) for reporting PT values (Table III). The INR is the PT ratio (patient PT/control PT) that would have been obtained if an international reference thromboplastin reagent had been used.

For a PT within the normal range, the INR is approximately 1. An INR of 2 to 3 is the usual therapeutic range for deep vein thrombosis, and an INR of up to 3.5 is required for patients with prosthetic heart valves.¹²

MANAGEMENT OF PATIENTS ON WARFARIN AND OTHER ORAL COUMARIN ANTICOAGULATION THERAPY

Traditionally, patients on oral anticoagulant therapy were placed into 1 of the following 3 categories, which dictated the appropriate anticoagulation therapy: 1, low-risk procedures required no change in anticoagulation medication¹³; 2, moderate-risk procedures indicated withdrawal of coumarin 2 days before the procedure and verification of INR the day of the procedure¹³; and 3, for high-risk dental procedures, a heparin protocol was strongly recommended.¹³ The management of patients on anticoagulant therapy should certainly take into consideration the type of the surgical procedure, the INR value (Table III), the presence of other risk factors (Table IV), and a great deal of clinical judgement, but the INR should be used as a guideline to care, not a commandment (Tables V and VI), because stopping warfarin does not necessarily reduce bleeding

Table III. Oral anticoagulant therapy and oral surgery

| | Prothrombin time | Thrombotest | INR |
|--|---------------------|-------------|------|
| Normal level | <1.3 | >70% | 1 |
| Therapeutic range | 2-4.5 | 5%-20% | 2-5 |
| Levels at which minor oral surgery can be carried out* | <2.5 | >15% | <3.5 |

*Uncomplicated forceps extraction of 1 to 3 teeth.

Table IV. Factors that increase bleeding risk in coumarin recipients

| |
|--|
| Aspirin intake |
| Presence of another coagulopathy or liver disease |
| Alcohol intake |
| Use of coumadin anticoagulant effect-enhancing medications |
| Severe gingivitis |
| Traumatic surgery |

but may cause hypercoagulability. Stopping warfarin before surgery has led to rebound thrombosis, which damaged prosthetic cardiac valves and even caused thrombotic deaths in dental patients.⁷ So, unless serious bleeding is anticipated, the warfarin should be continued.

In any case, anticoagulant treatment should never be altered without the agreement of the clinician in charge,⁶ and trauma should be kept to a minimum. The INR should be checked on the day of operation or, if that is not possible, the day before. For patients with constant INR levels of up to 2.5 needing emergency surgery, the authors' departments rely on the last known INR level, provided it was determined within 1 week before surgery. A bedside device, the CoaguChek (Roche Diagnostics), may be used. An independent study showed that although statistically significant INR differences were seen between CoaguChek and the international reference preparations ($P < .001$), the mean relative deviation of the INR was not greater than 0.104 and these test strips achieved a clinically acceptable level of accuracy.¹⁴

With limited oral surgery, such as uncomplicated forceps extraction of 1 to 3 teeth, with international normalized ratio of less than 3.5, and with no other risk factors

Limited oral surgical procedures can be performed without adjustment of coumadin dose in patients with an INR less than 3.5 with local or topical measures only.^{4,15} Local methods, such as resorbable gelatin sponge and multiple sutures, either alone or accompanied by fibrin glue or a mouthwash with tranexamic acid, give satisfactory hemostasis.⁴ If postoperative

Table V. Management of patients on coumarins needing oral surgery in dental clinics

| |
|--|
| 1. Careful history taking including: |
| Underlying medical condition (need of antibiotic prophylaxis?) |
| Presence of increasing bleeding risk factors |
| Previous bleeding experience in oral surgery procedures |
| Habits (ie, alcohol intake) |
| Mental condition |
| 2. Careful oral examination to determine: |
| Degree of urgency of planned surgical procedure |
| Extent of planned surgical procedure |
| Gingival condition |
| 3. Order INR |
| 4. Decision of whether to treat or to refer with consideration of following factors: |
| Result of history taken |
| Result of oral examination |
| Result of INR |
| Logistical considerations: distance to hospital or emergency care facility, patient mobility |
| 5. Referral always to hospital in presence of either one of following conditions: |
| INR > 3.5 |
| Need of more than simple surgical procedure |
| Presence of additional bleeding risk factors or logistic difficulties |
| 6. Performance of surgery in office without INR provided: |
| Need of surgery cannot be postponed |
| History of stable INR up to 2.5 |
| Previous available INR value obtained within last week |
| 7. If surgery to be performed in office, following materials should be used: |
| Absorbable packing hemostatic agents |
| Sutures |
| Hemostatic mouthwashes |

bleeding occurs, in an emergency, an antifibrinolytic agent (tranexamic acid; see subsequent) can be used topically to control hemorrhage. Vitamin K 1 mg is sometimes used.⁴

With more than simple or minor surgery, with international normalized ratio of more than 3.5, and with other risk factors present

The patient should be treated in hospital, and consideration should be given to the bleeding tendency. With the agreement of the clinician in charge, the anticoagulation therapy will probably need to be modified, possibly with a change to heparin during the preoperative period. If anticoagulants are to be continued after the operation, vitamin K should be avoided because it makes subsequent anticoagulation difficult. Usually, discontinuation of the warfarin for 2 or 3 days before surgery is simply best; a recent study confirms a 2-day suspension to be a simple and safe policy for patients with prosthetic heart valves who are undergoing anticoagulation therapy. For prevention of postop-

erative bleeding, an antifibrinolytic agent (tranexamic acid; see subsequent) can be used topically to control hemorrhage.

Drug interactions with warfarin

Patients on oral anticoagulant therapy are especially at risk of postoperative hemorrhage if the drug is displaced from its protein-binding sites or if its metabolism is reduced.¹⁶ If a risk of serious hemorrhage from such a drug interaction with warfarin exists, then use of these drugs is best avoided. Warfarin effect may be enhanced by the following therapies.

Antimicrobials.

ANTIBACTERIALS. These include cotrimoxazole and other sulphonamides, quinolones, benzyl penicillin, chloramphenicol, doxycycline, isoniazid, neomycin, metronidazole, erythromycin, cephalosporins, ampicillin, and amoxicillin plus clavulanic acid.^{11,17-19} However, it is unlikely that any of the other antibacterial drugs need to be contraindicated with warfarin. If infection is present, no elective surgery should be done until the patient has been treated with antibiotics and is free from acute infection.⁵ In case of emergency, careful hemostatic control should suffice.¹¹

ANTIFUNGALS. Treatments with azoles (fluconazole, itraconazole, ketoconazole, miconazole) and griseofulvin¹¹ have resulted in bleeding in dental patients. Even topical miconazole gel has caused such problems.²⁰

ANTIVIRALS. Treatment with saquinavir mesylate¹¹ and ritonavir is included in this group.²¹

Analgesics. Aspirin and other nonsteroidal antiinflammatory agents also can interfere with platelet function and cause gastric bleeding. Cyclooxygenase inhibitors (rofecoxib and celecoxib) appear not to have a significant effect on platelets or INR.^{11,5}

Paracetamol (acetoaminophen) in excessive and prolonged administration can enhance warfarin presumably by inhibiting its metabolism.^{22,23} An intake of less than 6 tablets of 325 mg of paracetamol per week has little effect on INR; however, 4 tablets a day for a week significantly affects the INR.²² Paracetamol will effect the INR within 18 to 48 hours of administration.

Other factors that influence warfarin. Warfarin effect can also be influenced by irregular tablet taking; liquid paraffin use, which theoretically leads to loss of vitamin K₃; disease such as diarrhea, liver disease, and malignant disease, which can increase the INR²²; and diet (avocados, beets, broccoli, brussel sprouts, cabbage, chick peas, green peas, green tea, kale, lettuce, liver, spinach, and turnips, which are high in vitamin K and can reduce the INR).²² Alcohol ingestion can inhibit warfarin but can have the converse effect on liver disease.¹¹

Table VI. Guidelines for warfarin therapy after surgery³⁴

*Day 1: Obtain baseline INR.

Start warfarin with 10-mg dose on night of surgery. Use lower doses (2 to 5 mg) if patient is elderly, chronically malnourished, has liver disease, or is on medication that can potentiate warfarin. Alternatively, can use patient's known usual maintenance dose.

†Day 2: Check INR (reflects first dose only).

If INR < 1.5, give same dose.

If INR > 1.5, give lower dose.

‡Day 3: Check INR (reflects first 2 doses).

If INR < 1.5, it suggests that a higher than average maintenance dose (>5 mg) will be necessary.

If INR is 1.5 to 2.0, it suggests that average maintenance dose (approximately 5 mg) will be necessary.

If INR > 2.0, it suggests that lower than average maintenance dose (<5 mg) will be necessary.

*Warfarin therapy should be initiated simultaneously with heparin unless contraindication exists or if patient is suspected of having hypercoagulable state.

†Discontinue heparin once INR is at necessary therapeutic level. Generally, heparin and warfarin overlap for approximately 4 days.

‡Arrange for follow-up INR with patient's physician within 3 days of discharge.

OPERATIVE CARE

Whenever possible, potentially problematic surgical procedures are best carried out in the morning, allowing more time for hemostasis before nightfall, and early in the week, to avoid problems at the weekend when staffing may be less intense. Surgery should be performed with 2% lidocaine (lignocaine) with 1:80,000 or 1:100,000 epinephrine (adrenaline) unless the patient is also an active cocaine abuser or a cardiac patient, in which case epinephrine should be avoided.

Surgery should be carried out with minimal trauma to both bone and soft tissues. Local measures are important to protect the soft tissues and operation area and minimize the risk of postoperative bleeding.

In the case of difficult extractions, when mucoperiosteal flaps must be raised, the lingual tissues in the lower molar regions should preferably be left undisturbed because trauma may open up planes into which hemorrhage can track and endanger the airway. The buccal approach to lower third molar removal is therefore safer.³ Minimal bone should be removed and the teeth should be sectioned for removal where possible.³

Meticulous curettage of the extraction site is essential to avoid excessive bleeding⁴ because when postoperative bleeding occurs, the cause is not necessarily the prolonged INR but may be local infection. In the case of multiple extractions, postoperative bleeding does not occur in all extraction sites; rather, it usually occurs in only 1 site, often a location associated with severe periodontitis.

Bleeding should be assessed intraoperatively, and if there is concern, one should place in the extraction site an absorbable hemostatic agent such as: oxidized regenerated cellulose; resorbable gelatin sponge; collagen (synthetic or microcrystalline or porcine); cyanoacrylate; or fibrin glues, which consist mainly of fibrinogen and thrombin and provide rapid hemostasis and tissue sealing and adhesion. Commercial, viral-inactivated products are available in Europe, Canada,

and Japan, but recombinant fibrin products will find more favor. Suturing is desirable to stabilize gum flaps and to prevent postoperative disturbance of wounds by eating. Resorbable sutures are preferred because they retain less plaque. Nonresorbable sutures should be removed at 4 to 7 days.³ Gauze pressure (a tranexamic acid-soaked gauze helps; see subsequent) should be applied and, after 10 minutes of biting on gauze, hemostasis should be assessed. If bleeding is controlled, the patient should be dismissed and given a 7-day follow-up appointment and the phone number of the office with instructions to call if bleeding occurs. The occurrence of additional risk factors for bleeding should prompt the treating clinician to be more cautious (ie, to place more sutures and to prescribe in advance the use of an antifibrinolytic agent, such as topical 4.8% tranexamic acid, for up to 7 days).

Postoperative care

Careful mouth toilet after surgery is essential. After surgery, the patency of the airway must always be ensured. Care should be taken to watch for hematoma formation, which may manifest itself with swelling, dysphagia, or hoarseness. Many patients can be managed after surgery with antifibrinolytic agents given topically as a mouthwash during the first 7 to 10 days. The best known agent is tranexamic acid, which is not Food and Drug Administration approved for use on the US market, where epsilon amino caproic acid is an alternative.

Antifibrinolytics. Tranexamic acid is a synthetic derivative of the amino acid lysine, which exerts an antifibrinolytic effect through the reversible blockade of lysine-binding sites on plasminogen molecules.²⁴ Systemic tranexamic acid does not result in therapeutic concentrations in saliva. Topical tranexamic acid is effective even when the anticoagulant therapy remains unchanged.²⁵ At least 3 double-blind randomized controlled studies have shown the efficacy and safety of

Table VII. Double-blind randomized controlled trials of topical tranexamic acid used as 4.8% to 5.0% mouthwash for 2 minutes, 4 times daily for 7 days after tooth extractions, showing percentage bleeding for more than 20 minutes after surgery

| First author | Year | Patients | | Control subjects | |
|-----------------|------|----------|----------|------------------|----------|
| | | Number | Bleeding | Number | Bleeding |
| Sindet-Pedersen | 1989 | 19 | 5.3% | 20 | 40% |
| Borea | 1993 | 15 | 6.7% | 15 | 13.3% |
| Ramstrom | 1993 | 44 | 0 | 45 | 22.2% |

tranexamic acid mouthwashes, which also do not have unwanted systemic effects. Overall, tranexamic acid reduced bleeding complications to 0 to 7% from 13% to 40% in control subjects (Table VII).²⁶⁻²⁸ Tranexamic acid is used topically as 10 mL of a 4.8% to 5% weight/volume solution used as a mouthwash for 2 minutes, 4 times daily for 7 days. Epsilon aminocaproic acid (250 mg/mL) 25% syrup 5 to 10 mL is an alternative for use as a hemostatic mouth rinse. Infection also appears to induce fibrinolysis, and therefore, antimicrobials such as oral penicillin V 250 to 500 mg 4 times daily should be given (or clindamycin) after surgery for a full course of 7 days to reduce the risk of secondary hemorrhage. Additional caution is necessary in these cases to prevent the risk of drug interaction with warfarin, which may enhance bleeding.²⁹

For postoperative pain management, paracetamol (acetaminophen) is recommended as the general analgesic and antipyretic of choice for short-term use in patients on oral anticoagulant therapy and is preferred over nonsteroidal antiinflammatory agents¹¹ because it does not affect platelets. Codeine or a cyclooxygenase inhibitor are suitable alternative analgesics. A diet of cool liquid and minced solids should be taken for several days.¹⁰

Postoperative prolonged bleeding

Patients should receive the surgeon's pager number or be instructed to visit an emergency room if they cannot reach the surgeon.²⁹ If there is bleeding, biting on a moist gauze, or a gauze pad soaked in tranexamic acid, or a moist tea bag with firm pressure for 30 minutes might eliminate the bleed. With a bleeding patient, it is important to establish whether the situation is urgent and when the patient will need admission for intravenous fluids or reversal of anticoagulation. This may well be the case if the patient is losing large quantities of blood or is hypotensive (hypovolemic).

To stop oral bleeding, clots should be washed out with warm saline solution, the bleeding area should be identified, a local anesthetic injection containing epi-

nephrine (adrenaline) should be administered, a sterile gauze pad soaked with tranexamic acid should be pressed firmly over the extraction socket for 10 to 15 minutes, and suturing of the socket should be considered, with silk sutures to enable a tighter suturing. If the patient continues to bleed, desmopressin acetate (deamino-8-D arginine vasopressin) may help. This synthetic analogue of vasopressin induces the release of factor VIIIc, von Willebrand's factor, and tissue plasminogen activator from storage sites in endothelium. Desmopressin offers an alternative to blood products to control bleeding risk in patients with moderate and mild hemophilia.³⁰ It is given as an intranasal spray (1.5-mg desmopressin per mL with each 0.1-mL pump spray delivering a 100- to 150-microgram dose.)

HEPARIN

Heparin is a parenteral anticoagulant, which is often used for acute thromboembolic episodes or for hospitalization protocols that include significant surgical procedures. Heparin is administered subcutaneously or intravenously to prevent deep venous thrombosis and pulmonary emboli.^{6,11}

Heparin is a sulphated glycosaminoglycan originally obtained from liver (hence, heparin) but now from beef or porcine lung or gut. It acts on the following aspects of hemostasis¹: blood coagulation; activated factors IX to XII, particularly via its binding to and catalyzing antithrombin III to inactivate thrombin (it acts immediately, mainly by inhibiting the thrombin-fibrinogen reaction); and platelets, increasing aggregation but inhibiting thrombin-induced platelet activation. In addition, autoimmune thrombocytopenia can occur within 3 to 15 days or sooner if there has been previous heparin exposure. The PT, APTT, and thrombin times are therefore prolonged. Most patients are monitored with the APTT and are maintained at 1.5 to 2.5 times the control value (the therapeutic range). Large doses of heparin can increase the INR. Platelet counts also should be monitored if heparin is used for more than 5 days because heparin can cause a thrombocytopenia.¹¹

Heparin is available as standard or unfractionated heparin or low-molecular weight (LMW) heparins. The anticoagulant effect of standard or unfractionated heparin has an immediate effect on blood clotting, which is usually lost within less than 6 hours of stopping heparin. Low-dose heparin therapy (used to reduce deep vein thrombosis), may have little effect either on the APTT or on postoperative bleeding.³

LMW heparins, which include ardeparin, certoparin, dalteparin sodium, enoxaparin, and tinzaparin (Table VIII), are more completely absorbed from subcutaneous sites, have a longer duration of action⁶ but less effect on platelets, and may have little effect either on

Table VIII. Low-molecular weight heparins

| |
|-------------------|
| Certoparin |
| Dalteparin sodium |
| Enoxaparin |
| Reviparin |
| Tinzaparin |

the APTT or on postoperative bleeding.³ They are used primarily for prophylaxis of postoperative deep vein thrombosis, and there is no need to monitor APTT.

Management of patients on heparin anticoagulation therapy (Tables IX and X)

Heparin has an immediate effect on blood clotting but acts for only 4 to 6 hours, so that no specific treatment is needed to reverse its effect. The effect of heparin is best assessed by the APTT.

In general, heparin use is a challenge that surgeons can easily overcome. For uncomplicated forceps extraction of 1 to 3 teeth, there is usually no need to interfere with anticoagulant treatment involving heparin or LMW heparins or antiplatelet drugs.

Medical consultation should be sought before more advanced surgery in a patient with heparin treatment.⁶ Withdrawal of heparin is adequate to reverse anticoagulation where this is deemed necessary, or in an emergency, this can be reversed with intravenous protamine sulphate given in a dose of 1 mg per 100 international units of heparin,¹¹ but a medical opinion should be sought first. Protamine is less effective at reversing LMW heparins (Tables IX and X). When heparin therapy is stopped, any surgery can safely be carried out after 6 to 8 hours, when the effects of heparinization have ceased.

In patients for renal dialysis, or patients with cardiopulmonary bypass or other extracorporeal circulation with heparinization, nonelective surgery is best carried out on the day after dialysis because the effects of heparinization have then ceased and there is maximum benefit from dialysis. LMW heparins appear to have little effect on postoperative bleeding,³ despite their longer activity (up to 24 hours). However, the advice of the hematologist should be sought before surgery in patients on these or antiplatelet drugs.

ASPIRIN

Salicylic acid (SA) irreversibly decreases platelet aggregation^{11,31} and is used chronically in the prevention of cardiovascular events and stroke in patients at risk.¹¹ In large doses, SA may cause hypoprothrombinemia. Even small doses of SA increase the bleeding time and decrease platelet adhesiveness.

Table IX. Initiation and modification of heparin therapy³⁴

1. One to 2 days before hospitalization, discontinue coumadin.
2. Check baseline APTT, INR, complete blood cell/platelet count.
3. Give bolus of heparin at dose of 80 U/kg intravenously.
4. Start drip infusion of heparin at 18 U/kg/h intravenously.
5. Check APTT 6 hours after initial bolus of heparin.
6. Adjust dose of heparin as per sliding scale:
 - APTT <35 seconds 80 U/kg bolus
Increase drip by 4 U/kg/h
 - APTT 35 to 45 seconds 40 U/kg bolus
Increase drip by 2 U/kg/h
 - APTT 46 to 70 seconds No change because level is therapeutic
 - APTT 71 to 90 seconds Reduce drip by 2 U/kg/h
 - APTT >90 seconds Hold heparin for 1 hour
Reduce drip by 3 U/kg/h
7. Monitor/continue heparin therapy with guidelines in Table X.

Table X. Guidelines for monitoring heparin therapy³⁴

1. Check APTT 6 hours after initial bolus and 6 hours after any dose change. Adjust heparin infusion as per sliding scale guidelines in Table IX until APTT is therapeutic (46 to 70 seconds).
2. When 2 consecutive APTTs are therapeutic, order APTT every 24 hours only (and adjust drip as needed).
3. Dosages of heparin when calculated by weight are rounded off to nearest 100 U/h.
4. Order complete blood cell and platelet count every 3 days during heparin therapy.
5. Stop heparin 4 hours before surgery. After surgery, restart heparin immediately with same rate used before surgery when APTT was therapeutic.

Management of patients on salicylic acid therapy

In general, SA intake is a challenge that surgeons can readily overcome. For uncomplicated forceps extraction of 1 to 3 teeth, there is usually no need to interfere with aspirin treatment. In patients receiving up to 100 mg SA daily, bleeding during oral surgical procedures is controllable with suturing and direct packaging with gauze,³¹ resorbable gelatin sponge, oxidized cellulose, or microfibrillar collagen. If oozing still is seen, tranexamic acid topically will help.

In patients receiving higher doses of SA, if there is concern, the current value of bleeding time should be established. If it is higher than 20 minutes, surgery should be postponed. However, if emergency surgical treatment is needed, in consultation with the treating physician, desmopressin acetate may be given.^{5,32} More problematic is a patient on SA and on other anticoagulation medications or with some bleeding tendency, such as hemophilia, or uremia. In those cases, medical advice should be sought to discontinue the use of aspirin intake 7 days before oral surgery procedures.³³

Table XI. Other parenteral anticoagulants

| Heparinoids | Hirudins | Prostacyclin | Antiplatelet agents |
|-------------|------------------------|--------------|---|
| Danaparoid | Lepirudin Desirudin | Epoprostenol | Aspirin Clopidogrel bisulfate Dipyridamole Ticlopidine hydrochloride Abciximab Eptifibatide Tirofiban |

OTHER PARENTERAL AGENTS THAT INFLUENCE THROMBUS FORMATION

These agents include heparinoids, such as danaparoid; hirudins, such as lepirudin and desirudin; antiplatelet drugs, such as clopidogrel bisulfate, dipyridamole, ticlopidine, and epoprostenol; and glycoprotein IIb/IIIa inhibitors (abciximab, eptifibatide, and tirofiban; Table XI). They have little effect either on the APTT or on postoperative bleeding.³

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