PERI-OPERATIVE CONSIDERATIONS IN THE ANTICOAGULATED PATIENT

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This paper will review the basics of hemostasis, discuss recognition of coagulopathies and give suggestions for dealing with the abnormal coagulation conditions.

At its most superficial level, adequate hemostasis allows for improved visualization of tissue, decreased surgical time, and decreased anesthesia exposure and risk. Also at a more fundamental level, adequate hemostasis keeps down excessive bleeding, complications, and ultimately decreases the risk of morbidity.

Perioperative coagulation is dependent on four mechanisms: the vasculature, platelet activity, protein cascade, and the fibrinolytic system. All four of these mechanisms interact to maintain the homeostasis of normal circulation.

REVIEW OF CLOTTING MECHANISMS

Normal Coagulation

Under normal circumstances blood circulates through the vasculature and the platelets and coagulation factors are shielded from exposure to endothelial collagen by a protective glycocalyx coating. This coating is made up of mucopolysaccharides and other components such as heparin sulfate, ADPase, and Prostacyclin (PGI_2), all of which help deter platelet aggregation and activation of the coagulation cascade. In addition to the physical barrier of the glycocalyx, circulating coagulation factors (such as thrombin) bind with receptor sites. In the case of thrombin, receptor site is thromboplastin. The binding of thrombin to thromboplastin causes the release of protein C.

This activates plasminogen and causes an increase in fibrinolysis thereby serving to maintain patent vessels.

The process discussed above maintains the status quo until an insult occurs which exposes the vascular endothelium directly to the platelets and coagulation factors. When this insult occurs, the coagulation cascade and platelets are activated.

Platelet interaction can be considered the body's first line of defense against hemorrhage. When a platelet is exposed to vascular collagen, adhesion immediately occurs to collagen and other platelets forming a platelet plug over the injured endothelium. This platelet plug achieves hemostasis and is then reinforced with fibrin, the final product of the clotting cascade.

Clotting Cascade

The clotting cascade is a complex series of biochemical equilibrium reactions which ultimately come together in the conversion of fibrinogen to fibrin. Control of the cascade is accomplished through a complex feedback/amplification system. The cascade can be somewhat artificially divided into an intrinsic and extrinsic system.

The extrinsic system is activated by release of tissue thromboplastin (Factor III) from damaged tissue. Factor III along with activated Factor VII (Proconvertin) and calcium ions catalyze the conversion of Factor X to its active form (X_A). This set of reactions rapidly (within a few seconds) forms active Factor X which leads directly to formation of thrombin and indirectly to formation of fibrin. This acts as the cement for a clot.

The intrinsic arm of the clotting cascade is dependent on the many coagulation factors present in circulating blood. Initially circulating Factor XII (Hageman Factor) is activated by exposure to collagen. Activated Factor XII then leads to conversion of Factor XI to its active form. Factor XI then in turn causes activation of Factor IX. Factor IX, along with circulating Factor VIII, and calcium lead to the activation of Factor X and continuation of the cascade beyond Factor X which is known as the final common pathway. This is the final common pathway since it is shared by the intrinsic and extrinsic arms of the cascade.

CLINICAL APPLICATION

Anticoagulation

Now that a basic understanding of coagulation has been reviewed, consider the anticoagulated patient. For the purposes of this paper the causes of anticoagulation can be divided into three groups: hereditary, disease states, and pharmacological.

Hereditary causes of anticoagulation include Van Willebrand's Disease, Hemophilia A, Hemophilia B, and other less common factor deficiencies. Most of the individuals with hereditary coagulation deficits will be aware of their deficiency and will relate it in a comprehensive new patient history and physical.

Certain disease states will also lead to coagulation deficiencies. Among these are liver disease and vitamin K deficiency. Liver disease may interfere with the formation of circulating clotting factors, all of which are synthesized by hepatic activity with the exception of Factors V and VIII. However, it should also be noted that levels as low as 30% to 40% of normal may be present and the patient still present with a normal prothrombin time (PT) and partial thromboplastin time (PTT).

A second possible cause of anticoagulation induced by a disease state is vitamin K deficiency. Vitamin K deficiency may be primary, as in lack of vitamin K intake. This type of vitamin K deficiency is rare, for the body is able to store several weeks' supply of vitamin K. Vitamin K deficiency due to gastrointestinal abnormality may also be noted. As vitamin K is a fat soluble vitamin, decreased ability to absorb fats from the intestinal surface will lead to vitamin K deficiency. This may be seen in patients with partial bowel resections or in patients on antibiotic therapy with decreased GI flora.

In actuality, it may be difficult to separate vitamin K deficiency from liver disease since with hepatocellular liver disease, the liver is incapable of properly storing vitamin K. Also even if vitamin K is adequately available, the liver may not be producing one or all of the vitamin K dependent co-factors (II, VII, IX, and X) thus possibly giving the appearance of vitamin K deficiency. To further complicate matters, protein C and protein S production are also dependent on vitamin K availability. (These proteins aid in physiological anticoagulation.)

In addition to pathological causes of anticoagulation, it must also be noted that there are quite a few indications for pharmacological anticoagulation. Included among these are previous myocardial infarction, and various hypercoagulation disorders.

Historically, the mystical amount of anticoagulation desired has been approximately 1.5 to 2.0 times the baseline PTT/PT. However more recent literature has shown this to be unnecessary and that in actuality all that is needed is 1.3 to 1.6 times the baseline. This change in thought is partially due to changes in laboratory technique.

History of pharmacological anticoagulation should be examined carefully and evaluated via the appropriate laboratory test. The common pharmacological anticoagulants are heparin and coumarin. They differ in route of administration, mechanism of action, and method of monitory therapy.

Heparin

Heparin may be administered intravenously or subcutaneously. Heparin inhibits coagulation by increasing the conversion of antithrombin III from the inactive to the active form. Heparin acts as a catalyst and is released unchanged in the reaction. The presence of heparin increases the rate of reaction by 1000 fold, acts quickly, and is cleared fairly rapidly following discontinuation of heparin therapy. Should an excessive dose of

heparin need to be reversed it may be done with protamine sulfate, 1 mg per 100 unit excess of heparin. It should be noted however that protamine in excess amounts also has anticoagulant activity.

Coumarin

Coumarin is dosed via oral administration. Coumarin achieves its desired effect by blocking the X-carboxylation of glutanic acid residues in prothrombin as well as Factors VII, IX, and X. This causes the involved factors to be biologically inactive for coagulation. The alpha-carboxylation is linked to deactivation of vitamin K. The mechanism of action is thereby seen to be the sum of inhibited synthesis and intact degradation of vitamin K dependent cofactors VII, IX, X, and II (listed by order of half lives: 6, 24, 40, and 60 hours respectively). The time for onset of action is generally felt to be 8 to 12 hours and recovery of normal pre-therapy levels of factors are dependent on their individual half lives. Should a rapid reversal of coumarin be required, it may be achieved with the administration of large doses of vitamin K and fresh frozen plasmas or Factor IX concentrate.

Monitoring of heparin and coumarin therapy is accomplished via the PTT and PT respectively. If one is planning on starting the patient on heparin or coumarin therapy a baseline PTT/PT should be obtained first. This includes cases where the patient is being placed on mini dose heparin for deep vein thrombophlebitis (DVT)/ pulmonary embolus (PE) prophylaxis, in spite of the theory that this should not have a significant effect on these laboratory values.

An alternative to anticoagulant therapy (pharmacological) for DVT and PE prophylaxis is the pneumatic external compression (PEC) boot. The function of the PEC device is to increase the velocity of blood returning from the extremity. The PEC significantly increases the velocity of venous flow in the deep femoral veins thereby decreasing stasis. More importantly it has been discovered that there is normally a drop in the circulating levels of antithrombin III following surgery. This decrease is not observed in patients who have had PEC used.

CONCLUSION

From the information reviewed, one can appreciate the complexity of normal coagulation function, as well as see the need of being able to recognize and understand the anticoagulated patient.

In addition to understanding the implications of the anticoagulated patient, one should also understand the indications for and mechanism of action of anticoagulant therapy. Virchow's triad of stasis, hyper coagulable state, and endothelial damage may be used as a guide for when to heparinize a patient. Along with the triad one must consider the surgical time of the procedure since the risk of DVT increases by 40% as the surgical time is increased from one to three hours.

Recognition of the anticoagulated patient should be via close scrutiny of a thorough history and physical, then ordering and analyzing the results of laboratory studies if indicated.

Finally it should be stated that anticoagulation is not necessarily a contraindication to surgery since there is no direct correlation between an increased bleeding time of less than 1.5 times normal and the incidence of hemorrhage. However, if the bleeding time is greater than 1.5 times normal then there is an increased risk of excessive bleeding in surgery. If bleeding time is greater than 2.0 times normal then the risk of excess bleeding is definitely increased.