Physiology of Hemostasis

The cellular and biochemical events leading to hemostasis begin with exposure of the site of endothelial injury, which occurs with the introduction and removal of the hemodialysis needle. The needle insertion site causes platelet adhesion, which bind together in the presence of von Willebrandt Factor (VWF), a circulating plasma protein also released by the vessel wall. Platelet adhesion results in the stimulation of additional platelets and subsequent platelet aggregation. Additional circulating platelets are recruited to the site of vascular injury, producing an occlusive platelet thrombus known as a platelet plug. The platelet plug is anchored and stabilized by the formation of a fibrin mesh.

Fibrin mesh formation begins with the release of tissue factor (TF) at the site of vascular injury, which binds to factor VIIa to form an complex leading to the activation of additional factors (IX, X, XI) in the clotting cascade. This cascade occurs mainly on the surface of platelet cell membranes and results in the conversion of prothombin to thrombin, the key enzyme in the clotting process. Thrombin converts fibrinogen into fibrin monomers, which then assemble into fibrin polymers. Thrombin also activates factor XIII to factor XIIIa, an enzyme which “cements” the fibrin strands together through the formation of covalent cross-bridges. Together with the platelet plug, the fibrin mesh seals the site of vascular injury and arrests bleeding. This entire process also requires the presence of calcium and additional cofactors to occur.¹

HEMODIALYSIS UNITS are well aware of the demands of puncture site hemostasis on patient workflow, staff overtime, and the potential risk of cross-contamination among patients. Bleeding tendencies inherent to the effects of renal failure and widespread use of antiplatelet agents and anticoagulants in this patient population also contribute to the scope of the problem. This article explores the physiology of puncture site hemostasis in renal patients, anatomic considerations in hemodialysis patients, current techniques for obtaining hemostasis, and future directions in this area.
Hemostasis in Hemodialysis Patients

Patients with end-stage renal disease may have prolonged bleeding times through a variety of mechanisms. Anemia of chronic renal failure is an independent contributor to this bleeding tendency. Although this effect can be reversed with the transfusion of washed red blood cells or treatment with erythropoietin, the exact reason for this phenomenon remains unclear. Chronic renal failure also causes platelet dysfunction through pathways that persist even when anemic patients have hematocrit corrected to normal levels. The first step of platelet adhesion at the site of vascular injury is defective in renal failure patients, possibly through impaired interaction of membrane glycoproteins with VWF. In addition to adhesion abnormalities, platelets of uremic patients exhibit abnormalities of calcium release, platelet activation (impaired arachidonic acid release and arachidonic conversion to thromboxane A2) and cellular microskeleton assembly. These effects on platelet adhesion are only partly corrected with dialysis.

Hemodialysis itself causes chronic low-level platelet activation, including actin formation, granule release and exposure on platelet membranes, and membrane protein release. This chronic activation renders platelets in hemodialysis patients relatively resistant to subsequent activation. Interestingly, these effects seem limited to hemodialysis as they resolve in patients who later initiate peritoneal dialysis.

Concurrent Medical Therapy

Hemodialysis patients have a high prevalence of cardiac, cerebrovascular and peripheral vascular disease. For this reason many hemodialysis patients receive long-term therapy with antiplatelet agents such as aspirin and clopidogrel, or chronic anticoagulation with warfarin. Aspirin inhibits platelet function through irreversible acetylation of the enzyme cyclooxygenase-1, which in turn blocks the cascade leading to the formation of the powerful platelet agonist thromboxane A2. This in turn impairs platelet aggregation and can result in longer bleeding times. Clopidogrel (Plavix) inhibits ADP-mediated platelet activation and aggregation in a pathway that is different than aspirin, so these drugs have a synergistic effect on inhibiting platelet function. Warfarin (Coumadin) affects the coagulation cascade and the formation of a fibrin mesh at the site of a platelet plug.

Anatomic Considerations

The optimal vascular access for hemodialysis is a native arteriovenous fistula. Fistulae have a superior performance over synthetic dialysis grafts and central venous catheters due to higher long-term patency, lower rates of infection and higher quality of life. In 2000, the majority of U.S. hemodialysis patients underwent placement of a permanent vascular access in the form of an arteriovenous synthetic graft. Most grafts were forearm loop or upper arm straight grafts constructed from polytetrafluoroethylene, so that relatively little anatomic variability existed among puncture sites of hemodialysis patients. The Fistula First initiative of CMS has resulted in a steady rise in the prevalence of native fistulae among hemodialysis patients. As of 2011, approximately 56 percent of patients now have a native fistula compared to less than 18 percent in 2000. This trend is expected to continue toward the goal of Fistula First and the K/DOQI consensus guidelines.

The most common configurations of native fistulae among U.S. dialysis patients are radiocephalic, transposed brachiobasilic and brachiocephalic fistulae. These fistulae, particularly radiocephalic fistulae, can develop areas of extreme tortuosity (Figure 1) and aneurysmal change making the use of currently available hemostasis devices challenging. The obesity epidemic in the United States also affects a disproportionately high percentage of hemodialysis patients due to high rates of comorbidities including diabetes mellitus and hypertension. From 1995 to 2002, the increase in body mass index (BMI) among U.S. patients starting dialysis grew at twice the rate as that of the general U.S. population. This higher rate of obesity among dialysis patients can make it difficult or impossible to apply circumferentially-applied hemostasis devices to some patients due to their body habitus.

Current Techniques for Obtaining Hemostasis

Manual compression applied by the nurse, technician, or patient is the standard of care following withdrawal of hemodialysis needles. Manual compression provides a mechanical arrest of bleeding while platelet plug and fibrin mesh form through conventional pathways. Manual compression is simple, inexpensive and ideally suited to patients who are compliant and physically capable of applying pressure to their own puncture sites. Patients who cannot or are unwilling to hold pressure for sufficient time for hemostasis are a challenge in busy settings.
hemodialysis units as these patients demand more time and effort from nephrology nurses. Recent changes in reimbursement for dialysis clinics have resulted in the need for greater documentation of dialysis adequacy, producing further demands on nursing time and resources.

Hemostasis Devices

The majority of dialysis units in the United States utilize, to a variable extent, a hemostasis device due to the demands on personnel time and the impact of manual compression on workflow. Medical devices used to promote hemostasis include spring-actuated pressure clamps, compression band devices, and hemostatic pads.

Pressure Clamps

Pressure clamps, commonly referred to as dialysis clamps or dialysis arm clamps are reusable devices similar to tongs that utilize a spring mechanism to provide pressure to the puncture site. An example of a pressure clamp is shown in Figure 2. The clamp also applies varying pressure to the puncture site; the more the device is opened, the greater force applied by the spring. This variable force is not dependent upon the needs of the patient, but rather the size of their limbs. These devices must be disinfected by the care provider and dried prior to their reuse on another patient. In a survey of members of the American Nephrology Nurses Association (ANNA) this disinfection process was performed by nurses in over 90 percent of clinics. The potential for cross-contamination among patients in whom clamps have been inadequately disinfected has been recognized by the Centers for Medicare and Medicaid Services (CMS). All clinics using reusable clamps must maintain compliance with Conditions for Coverage for End-Stage Renal Disease Facilities (42 CFR 494.30) mandating clamps are adequately disinfected, dried, stored and labeled. There is some anecdotal evidence among dialysis providers that the inability of clamps to adjust the amount of pressure applied to the puncture site may contribute to higher rates of thrombosis although no published data exist to support this claim. However, clamps have been discouraged from some hemodialysis units and chains.

Compressive Bands

Several compressive band devices have adjustable collars similar to a cable tie that has a molded pressure pad which contacts the puncture site. The device is placed around the patient’s arm and tightened similar to a tourniquet. An example of a device approved by the Food and Drug Administration (FDA) as an accessory to extracorporeal blood systems for broad indicated uses is the HemoBand (HemoBand Corporation Inc., Portland, Oreg.) Other band devices cleared by the FDA as vascular compression devices include the TR Band (Terumo Interventional Systems) and the RaDAR Vascular Compression Device (Advanced Vascular Dynamics). Indicated uses range from solely hemostasis of the radial artery (TR Band) to broader use for hemostasis of radial, arterial, venous, and dialysis punctures (RaDAR Vascular Compression Device). Additionally, the Comfort Band (TZ Medical) was cleared as a wound dressing for hemostasis for wounds, the skin surface at arterial/vascular sites and on patients on anticoagulation therapy. These devices pose challenges for use in the hemodialysis setting, since devices which encircle the patient’s arm cannot be tightened without the device moving off from the original point of alignment (Figure 3).

Hemostatic Pads

Hemostatic pads are disposable materials made by a variety of manufacturers that are used in conjunction with manual compression provided by nursing personnel or the patient. These devices may consist simply of woven gauze, or may contain an agent to promote hemostasis such as cellulose, kaolin, thrombin, or chitosan. These pads may accelerate the hemostasis process through a variety of mechanisms, as long as the device material is in contact with blood in the hemostatic puncture site. An example of this device is the Syvek Patch (Marine Polymer Technologies, Inc), made from poly-N-acetyl glucosamine isolated from seaweed algae. A recent case-control study compared hemodialysis patients receiving manual compression for hemostasis compared to a poly-N-acetyl...
Fig. 4. The HemCon bandage and other hemostatic pads contain agents which promote or accelerate the coagulation cascade, and are applied directly to the puncture wound.

glucosamine patch. In patients where the patch was used up to 70 percent of the time a 16 percent lower risk of graft thrombosis was observed compared to control patients, and a 60 percent reduction in thrombosis risk was observed when the patch was used more than 70 percent of the time. The high cost of this device ($20 per puncture site, $40/patient encounter) precludes routine use for most dialysis centers. Other examples of hemostatic pads include the TipStop, a compression dressing with an alginate surface (Gambro Hospital AG) the QuikClot, a hemostatic pad containing kaolin within an absorbent gauze (Z-Medica), and the HemCon bandage which contains chitosan-acetate (HemCon Medical Technologies) (Figure 4).

Future Directions

Future hemostasis devices for hemodialysis units will need to address the demand for providing controlled, localized pressure to puncture sites which can be adjusted according to the needs of each individual patient. These devices also need to enable nurses, patient care technicians and additional care providers to perform other critical functions. Future devices will also be needed to function effectively in obese persons, who currently exceed 30 percent of the adult U.S. population. For these reasons, an optimal device would allow an application to the wide range of anatomiic sites currently present in U.S. hemodialysis patients—radial and brachial fistulae, synthetic grafts, forearm, upper arm, chest, and thigh accesses. Infection risk is an additional concern. Hepatitis B virus (HBV), for example, can remain viable on environmental services for up to a week at room temperature, and HBV surface antigen (HBsAg) has been found in dialysis centers including clamps, dialysis machine control knobs, scissors and doorknobs.

The transmission risk of HBV, hepatitis C and HIV within inadequately disinfected hemostasis devices has the potential to be reduced through sterile, single use hemostasis devices that are simply removed and discarded once hemostasis is achieved. Access site infection through bacterial transmission also has the potential to be reduced with future approaches, thereby avoiding risks of cross contamination and lost dialysis treatments from infected access sites. It has been estimated that the cost of an acquired bloodstream infection is between $10,000 and $20,000. While this cost is not directly borne by dialysis clinics today, CMS has increased data collection and reporting of dialysis adequacy requirements so that reimbursement levels will increasingly be influenced by quality of care benchmarks. In 2014 the ESRD Quality Incentive Program (QIP) will implement a revised Total Performance Score for dialysis facilities which includes three new reporting measures, including “dialysis safety events” to the National Healthcare Safety Network (NHSN) of the Centers for Disease Control and Prevention. Moreover, additional costs of treating vascular access infections such as antibiotics will no longer be paid separately under the ESRD Prospective Payment System. 11 (PPS)(11).

Conclusion

Puncture site hemostasis remains an ongoing challenge for dialysis patients and providers. Increasing demands on dialysis clinic personnel, the greater tendency for dialysis patients to experience prolonged bleeding following needle removal, and the need for minimizing infection risk will influence future devices and techniques to achieve hemostasis.

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References


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