

Anticoagulation for Haemodialysis

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Objectives

- Review normal clotting mechanisms
- Review altered clotting in uraemia
- Review place of anticoagulants within the clotting mechanism
- Review anticoagulants and extracorporeal circuit maintenance

Learning Outcomes

1. Discuss normal & altered coagulant cascade
2. Apply knowledge of circuits & anticoagulation in practice including
 - Circuit management
 - Anticoagulant regimes
 - Anticoagulant adjustments

Introduction

"Blood alone moves the wheels of history"
(Martin Luther King)

Anticoagulation of dialysis circuits is a routine part of every workday for haemodialysis practitioners. In order to provide safe care and effective treatment the practitioner must have a sound understanding of the many facets underpinning this part of our work. The normal physiological process of coagulation and the effects of uraemia on this need to be clearly understood. Practitioners also need an understanding of why and how extracorporeal circuits are anticoagulated together with the different types of anticoagulant available.

Physiology of Coagulation

Our bodies make clots as a means of preventing blood loss and haemorrhage in the event of a damaged blood vessel and to begin tissue repair. This is achieved through a complex series of chemical reactions termed the clotting cascade. The clotting cascade also stops the clot activation cycle and removes blood clots by fibrinolysis once no longer needed (Fischer 2007).

Two separate coagulation pathways have been explored in detail and described in the literature as the contact activation (formerly intrinsic) pathway and the tissue factor (formerly extrinsic) pathway. Originally the two pathways were thought to be of equal importance, now however; there is a strong belief that the tissue factor pathway is of prime importance. It is noted that people with deficiencies of factor XII, high molecular weight kininogen or prekallikrein (clotting factors active in the contact activation pathway) do not necessarily suffer bleeding disorders. More recently the coagulation pathways have been further described as a non-linear model involving feedback loops (Bombeli & Spahn 2004).

Historically, each newly discovered factor within the clotting cascade has been allocated a roman numeral. Many clotting factors have also been named (e.g. Prothrombin: Factor II, Thrombin: Factor

Key Words

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IIa, Stuart-Prower Factor: Factor X). Because these clotting factors were not all identified in the sequence in which they are activated within the cascade, the numbering system can confuse the unwary. Thus Factor VIII was identified and named prior to Factor X yet Factor X acts before Factor VIII in the sequence of normal clotting.

Disrupted vascular endothelium triggers a series of biochemical reactions designed to achieve haemostasis (Fischer 2007; Hedges et al 2007). The endothelial disruption may be a cut or tear or it can be a rough surface due to build up of lipid plaques (for example). Initially when platelets touch the damaged or rough endothelium several key ingredients including Tissue Factor (TF), collagen, fibronectin, thrombospondin, von Willebrand factor, laminins and microfibrils come into play (Fischer 2007; Hedges et al 2007 p 138). These ingredients or clotting factors allow platelet adhesion to occur. The factors activate or permit the platelets to become sticky.

The platelets have an additional effect through their secretion of ADP and other adhesive proteins. This first set of

Author:

Kirsten Black, RN, BN, NNCert is a Clinical Nurse Educator in the Nephrology Department at Royal Hobart Hospital

Correspondence to:

Kirsten Black, Dept. of Nephrology Royal Hobart Hospital, 3rd Floor, Carruthers Building, St John's Park, New Town, Tasmania 7008. kirsten.black@dhhs.tas.gov.au

clotting reactions results in a collagen and platelet plug forming at the site of endothelial disruption. A further set of reactions commencing with prothrombin (Factor II) results in the formation of thrombin (Factor IIa), which in turn converts fibrinogen (Factor I) to fibrin. Prothrombin and fibrinogen are both clotting proteins produced in the liver. Fibrin and thrombin are essential if a platelet / collagen plug is to be converted into a stable clot or thrombus. Blood cells become entangled in the insoluble Fibrin threads thus forming clots (Anthony & Thibodeau 1979, p. 362).

During this second phase of clotting several more clotting factors come into play. One of these, glycoprotein 1b/IX has been implicated in platelet dysfunction of uraemia (Hedges, Dehoney et al 2007, p. 139). Calcium, phospholipid and vitamin K are also all required for coagulation to take place (Anthony & Thibodeau 1979; Fischer 2007; Hedges et al 2007). The tissue factor and contact activation pathways merge after activation of clotting factors VIII, IX and X, forming the common pathway. Thrombin becomes paramount at this point and the prothrombotic state is maintained until anticoagulant pathways commence.

Uraemic Effects on Coagulation

It has been accepted for over a century that uraemia induced by renal insufficiency can have an effect on the body's clotting mechanisms (Fischer 2007; Hedges et al 2007). Specifically, platelet dysfunction leading to decreased ability to clot or conversely protein C and protein S deficiencies and an increased likelihood of thrombus formation (Fischer 2007; Hedges et al 2007; Viganò, Schieppati & Remuzzi 1996). These altered coagulation effects can have marked impact on some ESDR patients including an increased incidence of pulmonary embolism, development of atherosclerosis and thrombosis formation

in arterio-venous dialysis access (Fischer 2007; Viganò, Schieppati & Remuzzi 1996).

Coagulation and Extracorporeal Circuits

Both the tissue factor and contact activation pathways may trigger clotting in an extracorporeal circuit. Turbulence and shear stress cause platelet activation of the contact pathway and ultimately release of TF, or TF may be triggered directly through the tissue factor pathway (Fischer 2007). Known predisposing factors implicated in circuit clotting include slowing, stagnation and turbulence of blood or any interface between air and blood (Fischer 2007). The likelihood of circuit clotting will also be increased by thickened blood, through high haematocrit, excess fluid removal or addition of thickening agents (e.g. packed red blood cell transfusion) (Fischer 2007). (Table 1)

Signs of a Clotting Circuit

A circuit may clot gradually or quite suddenly. There are a number of indications that clotting may be occurring in a circuit; gradually increasing venous pressure and increasing or decreasing arterial pressure (with no attendant vascular access problem); increasing trans membrane pressure; darkening blood; and/or visible clots forming in either the venous chamber or arterial-side dialyser header (Davenport, Lai, Hertel & Caruana 2007). Pressure changes may also help indicate exactly where in the circuit the clotting is occurring. Online clearance monitoring can be used as a guide to impending clotting within the dialyser. When fibres clot within the dialyser, the membrane surface area available for solute transfer diminishes. When the rate of clearance falls or the estimated end clearance falls during a dialysis session this is most probably due to clotting within the dialyser. Thus the various machine

tools can aid in determining whether anticoagulation is effective, efficient and adequate, so adjustment can be made immediately.

Prevention of Clotting in Extracorporeal Circuits

Anticoagulant Drugs

The clotting cascade can be interrupted at several stages depending on the anticoagulant chosen (Fischer 2007). Heparin has for many years, and remains today, the drug of choice for preventing coagulation in extracorporeal circuits (Davenport, Lai, Hertel & Caruana 2007). Heparin binds with the naturally occurring antithrombin, thus triggering early cessation of clotting. This process means heparin interferes with the cascade at the stage of factor Xa activation. With high dose heparin Factor IIa may also be inactivated. Side effects can include osteoporotic changes, elevated lipid profile, allergic reaction including pruritus, thrombocytopenia with heparin-induced thrombocytopenia (HIT) is a rare but life-threatening complication.

Generally a loading dose is given immediately prior to commencing treatment with a maintenance dose given by continuous infusion throughout the treatment. These doses are individualised for all patients with recommendations (European Best Practice Guidelines for Haemodialysis) of 50IU/kg for load and 500 to 1500IU for infusion (Fischer 2007). The Caring for Australians with Renal Impairment Guidelines do not specify dose recommendations, focusing chiefly on the connection between anticoagulant type and dialysis adequacy (CARI 2005). Antidote for heparin is Protamine Sulphate.

Alternate anticoagulants are low molecular weight heparin (LMWH) (e.g. Enoxaparin, Dalteparin), danaparoid, lepirudin, argatroban, fondaparinux, melagatran and citrate). Alternately,

anticoagulation of the circuit only can be achieved with regional citrate infusion.

Alternate Methods

When the circumstances call for heparin-free or anticoagulant-free dialysis alternate means to prevent or reduce clotting are required. Intermittent flushing of the circuit with normal saline is commonly used. Different dialyser membranes are promoted as having more biocompatibility, thus reducing the likelihood of clotting initiation.

Monitoring Anticoagulation in Circuits

Standard laboratory testing of blood for clotting times is unsuitable for monitoring anticoagulation during dialysis due to the cost, time and location constraints involved. Effectiveness of unfractionated heparin can be monitored onsite during dialysis by using a small, portable activated clotting time (ACT) machine. Most dialysis units will have their own protocols for expected ranges for ACTs during dialysis with a reduced clotting time range for any patient who has a concomitant coagulopathy or other indication for reduction in anticoagulant. In the event of severe coagulopathy or H.I.T. a heparin-free dialysis will be required.

Excessive Anticoagulation

It is not possible to over anticoagulate a dialysis circuit but, a patient can suffer adverse effects from too much anticoagulant. These effects can range from extended bleeding time post cannula removal to more severe haemorrhage such as gastrointestinal bleeds.

Adjusting Circuit Anticoagulation

At commencement on a haemodialysis program each new ESRD patient will require establishment of an individualised

anticoagulation regime. With a sound knowledge of the physiological effects uraemia has on normal clotting mechanisms a nephrology practitioner will be able to judge when and how to adjust such a regime. Many differing clinical pictures will arise during which a previously established anticoagulant regime will require alteration. Examples include the immediate pre and post-operative periods; when an unexpected bleed occurs (e.g. GI ulcer bleed) and during pregnancy, an uncommon event in dialysis patients which necessitates many adjustments. Pregnancy creates a hypercoagulative state, which results in the need for increased anticoagulation during dialysis (Wilkinson 2007, p. 39).

The common term for such adjustment is heparin modelling. When a patient is found to have an unpleasant side effect from heparin, e.g. hair loss or headaches, an alternative will be required. Thus it may be more accurate to describe this as anticoagulant modelling. The tools available, both on dialysis machines and separately, will be useful in establishing individual requirements in line with unit protocols.

In the case of patients with acute renal failure anticoagulation will also need close monitoring by the vigilant practitioner. In the event of a diagnosis

of H.I.T., heparin and L.M.W.H. will be ruled out completely (including for central access locking). Alternative anticoagulation for circuits can be found.

Questions and Activities

The following questions and activities are designed to make us think about our everyday practice. See if you can answer them on your own, or find an advanced practitioner who is willing to help you explore the possibilities.

- Q: Explain why some clotting factors have an 'a' after their roman numeral whilst others do not
- Q: What pressure changes will occur when clots form in different parts of the circuit? (You may find it helpful to draw a dialysis circuit showing where the clots would be forming when the following pressure changes occur \uparrow VP, \downarrow VP, \uparrow AP, \uparrow TMP)
- Q: How are patients at high risk of falls and anticoagulation related?
- A: Investigate (or start to develop) your unit's anticoagulation protocol
- Q: Under what circumstances should anticoagulation be reviewed?
- A: find out the drug of choice in your hospital for anticoagulation in the event of H.I.T.
- Q: How would you ensure biochemical safety for a patient undergoing regional anticoagulation with citrate?

Table 1 Causes of blood clotting in a dialysis circuit

<ul style="list-style-type: none"> • Blood-air interface • Slow flow • Turbulence • Shear stress • Haemoconcentration caused by; <ul style="list-style-type: none"> • High haematocrit • Access recirculation • Excessive fluid removal with inadequate vascular refilling • Blood transfusion during dialysis
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Suggestion

Next time you prime a circuit look at the different points where air becomes easily trapped. These are points where clots can easily form if our practice is marred by distraction, inattention or too much haste!

And remember:

“Every drop is sacred. Every drop is great. If a drop is clotted, solutes can’t equate.”

(With apologies to the Monty Python team)

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