Turning to the Use of GP IIb/IIIa Inhibitors, an Emerging Pharmacologic Approach for CLI: An Interview With Craig Walker, MD

Interview by Jennifer Ford

VDM: Can you comment on the increased prevalence of peripheral arterial disease (PAD) and critical limb ischemia (CLI) in the US population?

Walker: Peripheral arterial disease has reached epidemic proportions. And THE SAGE GROUP has reported that CLI currently afflicts up to 3.4 million US patients with PAD. By 2030, the US prevalence of CLI is forecasted to exceed 4 million.[1] As our population ages and the incidence of diabetes continues to increase, it is reasonable to postulate that the incidence of PAD and CLI will continue to rise.

VDM: What are some of the changes in medical practice regarding the diagnosis and treatment of PAD and CLI in recent years?

Walker: Peripheral arterial disease is now recognized as an important marker of major cardiovascular risk and death. Whereas not all patients with PAD require a surgical or percutaneous intervention, all require at a minimum a medical intervention stressing smoking cessation, control of hypertension, lipid control, and evaluation of global atherosclerosis. We have become more vigilant in diagnosing PAD, even in asymptomatic patients. We typically only intervene in patients with disabling claudication despite medical management and in patients with critical limb ischemia. Typically, an interventional first therapy is utilized. Improved crossing techniques allow successful intervention in the overwhelming majority of patients. Utilization of CO_2 angiography and/or ultrasound guidance allows treatment of patients with severe re-nal impairment and those with serious contrast allergy. New interventional techniques are resulting in limb salvage even in cases with severely impaired outflow where surgery is not feasible. Patients with multiple comorbid medical conditions are now being treated routinely with less risk.

Craig Walker, MD
Cardiovascular Institute of the South
Tulane University School of Medicine
Louisiana State University School of Medicine
Lafayette, Louisiana

VDM: Antiplatelet therapy in individuals with symptomatic atherosclerotic lower-extremity PAD received a class I recommendation, level of evidence A, in 2011 ACCF/AHA guidelines. What are your thoughts on the need for antiplatelet agent(s) during peripheral vascular interventions?

Walker: It is my opinion that antiplatelet drugs are crucial in peripheral intervention. Multiple studies have shown that PAD patients are more prone to have thrombotic complications than other atherosclerotic conditions. Peripheral interventions substantially increase that risk, because there is typically additional vessel injury.

VDM: How important is it to have a glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitor on board for peripheral vascular interventions?

Walker: GP IIb/IIIa inhibitors are quite useful in peripheral interventions. I utilize them whenever there is suspicion of recent thrombus, when there is poor run-off, "no reflow," and in patients who have experienced repeat thrombosis despite good initial result with outflow.

VDM: What are your concerns/thoughts on the risk of bleeding in the PAD setting, especially related to GP IIb/IIIa agent use and/or the choice of access route? What strategies can be utilized to mitigate the bleeding risk(s)?

Walker: Peripheral vascular interventions are associated with more thrombotic and bleeding complications than coronary interventions as we are entering diseased vessels with less elastic recoil. In particular, brachial and antegrade femoral entry have more associated bleeding risk. I try to use braided sheaths to avoid kinking. In the case of antegrade puncture I have been using external closure devices. I wait approximately 1 hour post infusion to utilize manual compression. I have not experienced significant increased bleeding using this protocol.

VDM: What is your experience with tirofiban hydrochloride (Aggrastat) injection in the PAD setting? What are the advantages of tirofiban, compared to other agents in the class, within this specific setting?

Walker: I use tirofiban in the settings that I've mentioned earlier. When I use this therapeutic in cases of "no reflow" I typically administer the agent directly into the vessel, occasionally using a proximal occlusion balloon to prevent the drug from washing out quickly. Several in vitro studies suggest that high concentrations of these agents can result in disaggregation of platelet rich thrombi.[2] Compared to eptifibatide, which is also effective, tirofiban causes less pain (tirofiban pH is near neutral compared to that of eptifibatide). Abciximab is also effective and is not associated with pain but allergic reactions can occur if there has been prior utilization as it is murine derived.

VDM: How is tirofiban administered in your practice in the PAD setting? Are there any differences in terms of dosing and infusion length compared to its use in acute coronary syndrome interventions?

Walker: I typically utilize a bolus directly into the affected artery utilizing the same dosing algorithm used in coronary intervention (25 mcg/kg within 5 minutes). This is often followed by an infusion for 3 hours to 6 hours in cases where "no reflow" had occurred (0.15 mcg/kg/min).

VDM: Can you specify, using the Rutherford scale, which PAD patient population would most see a benefit from GP IIb/IIIa inhibitor, such as tirofiban?

Walker: I have found this to be most useful in CLI patients and in patients who have had relatively recent stent thrombosis particularly when lytic therapy is contraindicated.

VDM: Is there a role for tirofiban in reducing the frequency of amputation in the most extreme cases of PAD (i.e. Rutherford 6 level patients)? If so, what would this role be?

Walker: I believe that this class of agents can help when there is poor outflow initially post intervention.

VDM: Recently, the FDA approved a new, more concentrated format of the high-dose bolus of tirofiban (premixed, ready to use, at 250 mcg/mL in a 15 mL vial). Do you foresee any clinical advantages that the new concentrated vial format of tirofiban may provide?

Walker: I think this will be helpful. The more concentrated dose should allow less fluid administration and should achieve a higher dose concentration within the affected artery.

VDM: Do you see benefit in administration that the new vial format of tirofiban may have over the IV bag format for the clinician?

Walker: Yes, the new vial format could provide a benefit for interventionalists by enabling easier administration for the operator.

VDM: What is your preferred strategy for postoperative antiplatelet management for PAD and/or CLI patients?

Walker: As mentioned earlier, I may utilize Aggrastat for 3 hours to 6 hours following the index procedure, after which time I use dual antiplatelet therapy indefinitely.

REFERENCES

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