NON-SURGICAL VASCULAR THERAPY

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Although vascular grafting is the most widely applicable, definitive treatment for lower extremity vascular insufficiency, non-surgical vascular therapy also plays an important role in treatment options. Non-surgical forms of treatment are less invasive and less expensive than their surgical counterparts, and can in specific circumstances prove to be equally effective. Approximately 15% of patients now considered to be surgical candidates may be eligible for non-surgical revascularization. An additional group of patients not suitable for reconstructive surgery may also benefit.

Non-surgical therapy of vascular disease includes all conservative and interventional treatments not requiring traditional open surgery. These non-surgical methods fall into two general categories: pharmacological and percutaneous techniques.

PHARMACOLOGICAL TECHNIQUES

Pentoxifylline (Trental®)

Pentoxifylline (Trental®) is indicated for the treatment of chronic occlusive arterial disease with symptoms of intermittent calf claudication. This drug and its metabolites improve the flow properties of blood by decreasing the viscosity and in effect increasing the "flexibility" of the red blood cell. Although initial effects of the medication can be seen in two to four weeks, continuation of the drug for four to six months is recommended for optimal effect. Because this drug is a xanthine derivative, Trental should be avoided in anyone with an allergy to caffeine, theophylline, and theobromine. The usual dose is 400mg po t.i.d.

Anti-Coagulant Therapy

Anti-coagulant therapy is indicated for prevention of thrombus formation and thrombo-embolic phenomena. The primary agents used in this therapy are heparin and warfarin. Heparin has a half-life of only 6 hours and its immediate effects in the intrinsic coagulation cascade are seen through elevation of the PTT. Coumadin (Warfarin) has a half-life of two and one-half days and its effect on the extrinsic coagulation cascade is measured by the PT. For treatment of arterial thrombosis and the threat of embolic phenomena, maintenance of these parameters is usually kept at 1.5 - 2 times the normal value. Heparin is only available in parenteral form, and hospital administration is usually required. After an initial bolus of 5,000 - 10,000 U, a maintenance level of heparin is then infiltrated at roughly 1,000 U/hour.

Traditionally, heparin therapy is initiated in a case of acute arterial thrombus. Heparin achieves its therapeutic effect almost immediately while coumadin requires several days. Coumadin can be started concomitantly with heparin. The heparin is then discontinued when the PT values show the coumadin to be therapeutic. Coumadin is given at 2 - 10 mg qd.

Thrombolytic Therapy

Thrombolytic therapy is an effective treatment regimen designed to stimulate the endogenous thrombolytic system for the purpose of clot lysis. It converts plasminogen to the enzyme plasmin. Plasmin degrades fibrin clots along with fibrinogen and other plasma proteins. The aim of this

therapy is the production of sufficient amounts of plasmin for the lysis of intravascular deposits of fibrin. Before commencing therapy, the following labs should be taken: Thrombin time (TT), Prothrombin time (PT), Activated partial thromboplastin time (APTT), Hemoglobin/Hematocrit (H/H), and platelet count. Heparin should be discontinued during use of these drugs and the TT and APTT should be less than twice the upper limits of normal before initiating therapy.

The three currently available products include; Streptokinase (Streptase®), Urokinase (Abbokinase®), and Human tissue plasminogen activator. Traditionally, these drugs have played an important role in the treatment of pulmonary embolism and coronary artery thrombosis. Streptokinase, elaborated by beta-hemolytic streptococci, was the initial thrombolytic agent discovered. This agent acts systemically and has been associated with a high (40-50%) complication rate. Urokinase is currently the thrombolytic agent of choice due to decreased antigenicity, and a more predictable thrombolytic effect. However, Urokinase is less effective than Streptokinase in plasminogen activation and requires local administration through an arterial catheter to the proximal aspect of the thrombus.

Vasodilation Therapy

Another avenue of non-surgical treatment includes the area of peripheral vasodilation. Vasodilators can achieve their effect through different mechanisms of action. Relative constriction and dilatation of the peripheral vasculature is mediated by sympathetic innervation, largely the adrenergic receptors. Alpha adrenergic (a1 and a2) receptors primarily act to constrict the peripheral circulation, while beta adrenergic receptors function in the opposite effect or vasodilatation. Direct blockage of alpha receptors, either both in combination or individually will effectively increase peripheral circulation. Drugs such as Phenoxybenzamine, Prazosin, and Thymoxamine are several examples of direct acting alpha adrenergic antagonists. Methyldopa can also act in this capacity by centrally inhibiting alpha receptors. Sympatholytic therapy with Reserpine and Guanethidine are also effective in counteracting catecholamine-mediated vasoconstriction. Reserpine depletes Norepinephrine from arterial stores and Guanethidine interferes with the release of Norepinephrine from sympathetic junctions.

Calcium channel blockade within the artery can effectively relax smooth vessel contracture. These drugs are especially effective in inhibiting vascular responses evoked by alpha 2 receptor activity. Of the calcium channel blockers available, Nifedipine has proven to be the most consistent in alleviating vasospastic episodes and increasing peripheral circulation. Diltiazem and Verapamil have shown promise in several clinical trials, but the success seen with Nifedipine is much more impressive.

New interest in vasodilator therapy has also been seen in experimentation with prostaglandins. Prostacyclin and Prostaglandin E1 and E2 all exhibit good vasodilatory action coupled with an inhibition of platelet aggregation. IV infusions of these drugs have shown clinical improvement that has lasted up to several weeks.

PERCUTANEOUS TECHNIQUES

Percutaneous techniques are also considered to be viable alternative methods for the treatment of peripheral vascular disease. These therapies are classified as endovascular interventional modalities and include percutaneous transluminal angioplasty and a variety of laser systems and arthrectomy devices. All of these systems are attractive because of their potential for effective treatment and low morbidity. With short term follow-up, percutaneous techniques have indeed proved promising in treatment of vascular thrombus. Long term studies are necessary, however, for definitive answers. Critics have stated that all arterial trauma induces an inflammatory healing response, and this response may lead to fibrointimal hyperplasia. Even if these procedures are immediately successful, the healing process may cause acceleration of a future occlusive process and ultimately cause more harm.

Percutaneous transluminal angioplasty (PTA) was the first of the non-invasive angioplasty techniques introduced in 1964 by Dotter and Judkins. It is still considered to be the "gold" standard among the variety of percutaneous techniques available today. Percutaneous re-perfusion is accomplished by successful inflation of a balloon-tipped angiocath into the residual lumen of a stenotic artery. Angioplasty re-establishes physio-

logic lumen diameter by causing intimal fracture and media stretching; the plaque itself is unaffected. According to Vieth, et al., the morbidity rate is less than 8%, and the mortality rate is less than 1%, with 50% of patients deriving benefit for at least two years. Successful angioplasty is linearly dependent upon the length of the occlusion, with 85% success reported for stenosis of 1 - 7 cm. Higher long term success is also seen with more proximal lesions such as the iliac versus the femoral vessels.

Laser assisted PTA has been under development since the mid-1980s and has gained increased popularity. Recent developments include transmission of laser light energy into a hot tip which can actually vaporize plaque on contact. The laser tip operates at approximately 500 degrees Celsius and creates a 2mm tract thru the occluding plaque. The laser cannulation is an attempt to convert a complete occlusion to a concentric stenosis. A PTA balloon can then be passed through the tract, dilating the lesion as described above. Initially, this technique was believed to produce less arterial trauma than PTA and a lower rate of restenosis. Interestingly, experience has shown that the heat generated from the laser actually caused more intimal damage with eventual collapse and a higher rate of re-occlusion.

Another device utilized with initial promising results is the Excimer Laser introduced in 1988. The high energy light emitted is selectively absorbed by the arterial plaque and leaves the arterial intima untraumatized. The potential for treating multiple and tandem lesions with this device is exciting, although it is still in the experimental stages.

Percutaneous arthrectomy is a technique capable of removing short eccentric plaques by mechanical means. These plaques are usually treated poorly by other angioplastic techniques. A cylindrical cutting blade placed inside an outer protective catheter shaves off intruding plaque thru a rectangular window. A non-dilating balloon opposite this window is inflated during arthrectomy to insure good blade-plaque contact. In 1988, Schwarten reported a success rate of 88% in arthrectomy procedures alone, and up to 100% success when supplemented with balloon angioplasty techniques.

Restenosis has been seen in a percentage of post PTA procedures. Causes of restenosis are commonly due to elastic recoil and extensive dissection. Intravascular stenting has been proposed in conjunction with angioplasty procedures for better postoperative success rates. The function of the stents is to oppose elastic recoil of vascular stenosis, providing increased internal support.

Two major types of intravascular stents are presently available: balloon expandable and self-expanding. Balloon expandable stents function by balloon mediated expansion. The stent is mounted onto a balloon and delivered to the target site within a protective sheath. Once the target site is reached, the sheath is withdrawn allowing expansion of the stent as the balloon is inflated. The balloon is then deflated and removed. Self-expanding stents function by two basic mechanisms. One mechanism is a resumption of the stent configuration triggered by thermal memory at body temperature. This is possible by utilizing a nickel and aluminum alloy known as nitinol. Nitinol has the ability to assume two distinctive crystalline structures interchangeable with small variations in temperature. Once inserted within the target region, the surrounding vessel and soft tissue structures will allow this alloy to expand to a functional design. Secondly, self-expanding stents also function by removal of a constraining membrane. Once in position, the constraining membrane is rolled away triggering expansion of the stent. Intravascular stents have become popular since the early 1980s, and studies have shown that stenting in iliac arteries provide immediate post-procedural hemodynamic improvement superior to that of PTA alone. These findings have shown intravascular stenting to be a favorable addition to PTA.

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