

# Antithrombotic and antiinflammatory drugs for protection of microvascular anastomosis

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The results of microsurgical procedures in 43 patients who underwent replantation, as well as free tissue transfer were studied. The following scheme of antithrombotic medication was applied postoperatively: a) 330 mg acetylsalicylic acid and 75 mg dipyridamole; b) 440 mL low molecular weight dextran, divided in 2 doses; c) 60000 IU streptokinase and 15000 IU streptodanase; and d) 100 mg diclofenac. 29 of the patients were completely free

of complications. Transient vascular spasm was noted in 10 patients and 2 patients developed necrotic lesions distal to the microvascular anastomosis which resulted in two secondary amputations. These results suggest that although antithrombotic treatment can not be seen as a substitute for fine surgical procedures, it still remains powerful tool in the hands of microsurgeons.

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Since the development of clinical microvascular surgery, small vessel thrombosis has persisted as a major source of patient morbidity. Refinement of microsurgical techniques and methods have increased the successful outcome of microvascular procedures including both trauma and reconstructive cases. Despite instrumentation improvements and advancements in microsurgical technique, anastomotic thrombosis continues to complicate an estimated 5 to 20 percent of all clinical replantations and free-tissue transfer cases.

Pharmacologic agents such antithrombotic and antiinflammatory drugs have been widely used and tested for their efficacy and have been found a useful aid in maintaining patency at the anastomosis site, thus, facilitating perfusion of the replanted part or the transferred free tissue segment. Several antithrombotic schemes have been proposed in order to decrease the risk of thrombosis such as local anesthetic agents as smooth muscle relaxants, systemic antithrombotic therapy, antiplatelet agents (aspirin), low-molecular weight dextran, Dipyridamole and non-steroidal antiinflammatory drugs. The purpose of this report is to study the usefulness of certain antithrombotic and antiinflammatory drugs at the anastomosis site and evaluate their influence on the postoperative course in these patients.

## Patients and methods

43 patients with complete or incomplete amputations or large soft tissue defects were treated between 1986 and 1991. Microsurgical procedures included replantation and revascularization of amputated parts, as well as free tissue transfer. 41 of the patients were men and 2 were women, mean age 39 (8-70) years. 24 patients had an upper limb injury, 6 had a lower limb injury and 13 patients underwent free tissue transfer. Standard microsurgical techniques were used under regional anesthesia for the upper limb and epidural for the lower limb.

Antithrombotic medication was administered to all patients according to the following scheme: a) 330 mg acetylsalicylic acid and 75 mg dipyridamole; b) 400 mL low molecular weight dextran, divided in 2 dose; c) 60,000 IU streptokinase and 15,000 IU streptodanase; d) 100 mg diclofenac.

In cases which indicated that arterial inflow was diminished postoperatively, the limb was lowered, while in cases which presented with slow venous outflow, the limb was elevated. In addition, antibiotic and analgesic medication was administered. Special care was also taken to keep room temperature stable, while smoking and caffeine were prohibited as they are known to induce vasoconstriction. Follow-up examination of the microcirculation of the limb was done daily, as well as doppler examination on the 8th postoperative day.

## Results

10 days postoperatively, 29 patients were completely free of complications. Transient vascular spasm was noted in 10 patients. 3 patients developed necrotic lesions distal to the microvascular anastomosis. In 2 of these patients, successful skin grafting procedures were performed while in the third patient the middle finger was amputated. In one patient who had sustained a high energy injury presented with necrosis due to thrombosis proximal to the site of anastomosis. As a result the leg had to be amputated.

## Discussion

According to Poiseuille's law, which states that fluid flow through a vessel (F) is proportional to the pressure gradient (DP/L, change in pressure over length), the radius (r) and the fluid viscosity, blood flow in a vessel can be increased by either increasing the vessel radius (diameter), decreasing the viscosity and/or increasing the factor DP/L. The latter can be increased by increasing the perfusion pressure and/or decreasing the vessel resistance.

Smooth muscle fibers in the vessel wall of arteries, arterioles are under sympathetic control. The sympathetic system also regulates the response of the arteriovenous anastomoses to temperature. Sympathetic stimulation reduces skin and digital blood flow, while sympathectomy markedly increases the flow. In this regard, other than agents which affect the clotting mechanism, most adjunctive drug therapy is aimed at producing a chemical sympathectomy (Bergqvist 1983, Czervionke et al. 1979, Sweirstra et al. 1984). In addition, other local factors are important in regulating blood flow and perfusion of the anastomosis site. External pressure on the vessel wall from tight dressings, hematoma or edema may exceed the "critical closing pressure," especially in the venous system.

Tissue anoxia and decreased perfusion lead to increased capillary permeability and tissue edema, and a vicious cycle as that seen in compartment syndromes may occur. Both dextran and heparin appear to lower viscosity. Adequate hydration of the patient is also important not only in preventing vasoconstriction, but also in lowering viscosity (Bergentz and Bergqvist 1984, Clyne et al. 1987, Roth and Majerus 1975,

Aspirin which has an antiplatelet effect, prevents platelet aggregation by acetylating the enzyme cyclooxygenase and thus prostaglandin PGG<sub>2</sub> and PGH<sub>2</sub> as well as thromboxane A<sub>2</sub> synthesis (Pumphrey et

al. 1983, Roth and Majerus 1975, Weiss and Aledort 1967). The daily dose of aspirin varies between 50 and 600 mg, but most authors accept that 330 mg daily represents the optimal dose (Bochner and Lloyd 1986). The above mentioned effect of aspirin is amplified when it is combined with dipyramole, although the effect of the later is not completely understood.

On the other hand, low molecular-weight dextran appears to have both antiplatelet and heparin like effects (Bergentz and Bergqvist 1984, Sweirstra et al. 1984). Pharmacologically, it is indicated for the prophylaxis of deep vein thrombosis. There is a general agreement that dextran causes fewer hemorrhagic complications than heparin. Our rejection of the systematic use of heparin is based on the high incidence of side effects both at the site of anastomosis and systemically.

Our findings suggest that although antithrombotic treatment cannot be seen as a substitute for fine surgical technique, it still remains a useful tool to maintain vascular patency.

## References

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