

## INTRAARTERIAL STREPTOKINASE INFUSION IN ARTERIAL OCCLUSIONS Arteriyel tıkanmalarda intraarteriyel streptokinaz infüzyonu

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**Summary:** Acute limb ischaemia poses a threat to both the limb and life of a patient. Until recently, attempted revascularization by thromboembolectomy or vascular reconstruction held the best chance of limb salvage. Thrombolytic techniques afford an alternative method of management for this condition and are effective in selected patients. In this study, 4 patients with acute limb ischaemia were treated intra-arterial streptokinase and effective lysis was achieved in all cases.

**Key Words:** Thrombolytic therapy, Embolectomy

**Özet:** Akut ekstremitte iskemisi hem ekstremitenin hem de hastanın hayatının tedavisi için gereklidir. Son zamanlara kadar tromboembolektomi veya vasküler rekonstrüksiyon gibi revaskülarizasyon çabaları ekstremitteyi kurtarmak için en iyi yöntemlerdi. Seçilen olgularda etkili olan trombolitik teknikler bu durumun tedavisinde alternatif bir metod olmuştur. Bu çalışmada intraarteriyel streptokinaz ile tedavi edilen ve başarılı sonuç alınan akut ekstremitte iskemili 4 vaka sunuluyoruz.

**Anahtar Kelimeler:** Trombolitik tedavi, Embolektomi

Acute non-traumatic limb ischaemia is usually caused by arterial embolism or thrombosis of atherosclerotic vessels, and is associated with death in approximately 25% and major amputation in 20-40% of patients (1,15). The management of embolism is usually by balloon embolectomy which provides the best chance of preserving life and limb function (1,8,11). Unfortunately, this procedure fails to reperfuse the limb in a significant proportion of cases, a failure that results in amputation or death (1,3,13,20). One reason for this is incomplete clearance of thrombus; studies of intraoperative arteriography have shown this to occur in up to 30% of patients (1,3,8,17). It can be particularly difficult to clear all of the calf vessels because of the anatomical configuration (1,2,7,8,11).

Since Tilled and Garner observed the fibrinolytic activity of proteases produced by streptococci in 1933, the search has continued for safe, effective methods of achieving in situ thrombus dissolution

with pharmacological agents. In the 1960s intravenous streptokinase (SK) was given to patients with acute limb ischaemia with only limited success and a worrying number of haemorrhagic complications (2,4). Since Dotter et al. described regional fibrinolysis using one-twentieth the concentration of SK given through an indwelling arterial catheter (5), the technique has been shown to be effective with relatively fewer bleeding complications (6,7). This report presents the early results of intra-arterial SK treatment in 4 patients.

### METHODS

The study included 4 patients with acute limb ischaemia; there were one upper limb (digital artery thrombosis in the left hand) and 3 lower limb occlusions. There were 3 men and 1 woman, of median age 54 years (range 35 to 69 years). All patients had ischaemic pain at rest. There was cyanosis in the fingers of the patient with digital artery thrombosis. The duration of ischaemic symptoms ranged from 6 hours to 1 week. The patients were given a detailed examination on admission, including documentation of pulses and ankle pressure. Angiography was not performed, both to minimize the risk of local haemorrhage and

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inability to organization with radiology department. Vascular access was gained by use of the seldinger technique via the common femoral artery or radial artery. A 18G gauge teflon catheter was inserted into the artery and 250.000 IU a loading dose of SK was given. Subsequently 100.000 IU/hour SK was infused by mechanical pumps. Thrombolytic therapy was terminated when antegrade flow was established and perfusion restored to the distal vessels. Intravenous heparin, 5000 IU 4-6 time daily was administered for at least 7 days after termination of the SK infusion. During SK infusion patients were monitored in the intensive care unit, and the coagulation status was assessed every 12 hours by measurement of hemotocrit, platelet count, prothrombin time, fibrinogen level and fibrinogen degradation products (4,5,7,16,18,19). Most patients received thrombolytic therapy for 24 hours (range 24 to 48 hours). Contraindications to thrombolytic therapy included serebrovascular accident within two moths, operation within the preceding two weeks, recent liver biopsy, active coagulopathy, gastrointestinal tract bleeding, history of an allergy to SK, pregnancy or early postpartum period, aneurysm, arteriovenous malformation or a degree of ischaemia that would not permit observation for the duration of thrombolytic therapy (2,4,6,11,13,14)

## RESULTS

Intra-arterial SK therapy produced lysis of occluding thrombus with restoration of distal pulses in all patients. No complication was seen during and after SK treatment.

## DISCUSSION

Balloon-catheter extraction of a clot from an acutely occluded vessel or graft is the most reliable technique for prompt restoration of perfusion. Although embolectomy is a relatively simple method of rapidly removing arterial thrombus it is not without problems. Restoration of arterial flow may be incomplete due to the distal location of emboli, thrombus propagation beyond the range of the catheter and atherosclerotic obstruction that prevents passage of the catheter into occluded

distal arteries (3,8,11). Repeated futile attempts to retrieve thrombi under these circumstances may cause significant damage to the intima and on occasion may perforate the vessel wall (3,7). These limitations and complications may cause failure to restore pedal circulation, rethrombosis, or bleeding into the soft tissues (7). Embolectomy is commonly performed "blind" without radiological control despite several studies that have reported incomplete clearance of distal thrombus in up to 30% of cases (3,8).

For some patients in whom operative intervention is not possible, enzymatic thrombolysis with SK or urokinase (U) can restore arterial circulation. These commercially available agents activate plasminogen to plasmin and have usually been administered in high doses by intravenous infusion (18). Although this approach has been largely successful in achieving thrombolysis, systemic therapy has been associated with considerable rates of morbidity and mortality (5,12). The incidence of serious complications with systemic infusion has been reported to be as high as 30% to 50% (5,18). Complications include major and minor haemorrhage, stroke, cerebrovascular accident, distal embolization, allergic reaction (2,9,11,15, 18,19).

In an effort to reduce the morbidity associated with thrombolytic therapy, several investigators have employed selective arterial infusion of SK (4,9,10,11,18).

Thrombolysis is now established as a therapeutic alternative in the management of selected cases of acute limb ischaemia. In particular, patients with acute-on-chronic thrombosis, short duration of symptoms, non-reconstructable problems, distal occlusions, graft occlusions, arterial thrombosis following percutaneous transluminal angioplasty and no neurological deficit are mentioned as the most appropriate cases (5,6,9,10,11,18,19). Fibrinolytic agents provide significant potential in restoring circulation in these circumstances (8,11). Successful clearance of acute embolus and thrombosis occurs in 50-90% of cases (4,6). Emboli older than 72 hours, the results of local lysis are superior to those of embolectomy (15).

SK was chosen as it was easily obtainable and inexpensive compared with U and tPA. Lower clot lysis times have been reported for tPA than for SK in percutaneous thrombolysis, but overall lysis rates are similar and high cost of tPA is difficult to justify at present. There is probably an indication for tPA in patients who have received SK within the previous year as they are likely to have high antibody levels that will inactivate further doses and may cause anaphylaxis (3). The dose of 100.000 IU was selected because the literature suggested that this was unlikely to be associated with significant bleeding (3,7,8,9,11,19).

## REFERENCES

1. Barr H, Lancashire MJR, Torrie EPH, et al: Intraarterial thrombolytic therapy in the management of acute and chronic limb ischaemia. *Br J Surg* 78:284-287,1991.
2. Battey PM, Fulenwider JT, Smith III RB, et al: Intraarterial thrombolysis for acute limb ischaemia. *South Med J* 80:479-482,1987.
3. Beard JD, Nyamekye I, Earnshaw JJ, et al: Intraoperative streptokinase: a useful adjunct to balloon-catheter embolectomy. *Br J Surg* 80:21-24,1993.
4. Belkin M, Belkin B, Bucknam CA, et al: Intra-arterial fibrinolytic therapy. *Arch Surg* 121:769-773,1986.
5. Berni GA, Bandyk DF, Zierler RE, et al: Streptokinase treatment of acute arterial occlusion. *Ann Surg* 198:185-191,1983.
6. Browse DJ, Torrie EPH, Galland RB: Early results and 1-year follow-up after intra-arterial thrombolysis. *Br J Surg* 80:194-197,1993.
7. Cohen LH, Kaplan M, Bernhard VM: Intraoperative streptokinase. *Arch Surg* 121:708-715,1986.
8. Comerota AJ, White JV, Grosh JD: Intraoperative intra-arterial thrombolytic therapy for salvage of limbs in patients with distal arterial thrombosis. *Surg Gynecol Obstet* 169:283-289,1989.
9. Earnshaw JJ, Cosgrove C, Wilkins DC, et al: Acute limb ischaemia: the place of intravenous streptokinase. *Br J Surg* 77:1136-1139,1990.
10. Earnshaw JJ, Shaw JFL: Survey of the use of thrombolysis for acute limb ischaemia in the UK and Ireland. *Br J Surg* 77:1041-1042,1990.
11. Earnshaw JJ: Thrombolytic therapy in the management of acute limb ischaemia. *Br J Surg* 78:261-269,1991.
12. Earnshaw JJ, Scott DJA, Horrocks M, et al: Choice of agent for peripheral thrombolysis. *Br J Surg* 80:25-27,1993.
13. Graor RA, Risius B, Young JR, et al: Thrombolysis of peripheral arterial bypass grafts: Surgical thrombectomy compared with thrombolysis. *J Vasc Surg* 7:347-355,1988.
14. Hess H: Thrombolytic therapy in peripheral vascular disease. *Br J Surg* 77:1083-1084,1990.
15. Hess H, Mietaschk A, Brückl R: Peripheral arterial occlusions: A 6-year experience with local low-dose thrombolytic therapy. *Radiology* 163:753-758,1987.
16. Kakkasseril JS, Cranley JJ, Arbaugh JJ, et al: Efficacy of low-dose streptokinase in acute arterial occlusion and graft thrombosis. *Arch Surg* 120:427-429,1985.
17. Quiñones-Baldrich WJ, Baker JD, Busuttill RW, et al: Intraoperative infusion of lytic drugs for thrombotic complications of revascularization. *J Vasc Surg* 10:408-417,1989.
18. Rush DS, Gewertz BL, Lu CT, et al: Selective infusion of streptokinase for arterial thrombosis. *Surgery* 93:828-833,1983.

19. Taylor LM, Porter JM, Baur GM, et al: Intra-arterial streptokinase infusion for acute popliteal and tibial artery occlusion. *Am J Surg* 147:583-588,1984.
20. Walker WJ, Giddings EB: A protocol for the safe treatment of acute lower limb ischaemia with intra-arterial streptokinase and surgery. *Br J Surg* 75:1189-1192,1982.