Thrombolysis by ultrasound

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Summary

1. A new method of destroying thrombi in blood vessels by ultrasound and simultaneously removing them is reported.

2. Experiments were performed in twenty dogs with artificial thrombi in the iliac and femoral arteries and veins. The length of the thrombi ranged from 4 to 5 cm and the age from 12 h to 10 days. The unit used consisted of a generator, a frequency counter, an ultrasonic transducer with the hollow waveguide and a vacuum pump. For protection of the vessel wall the guide is surrounded by a plastic tube. The ultrasonic frequency is 26.5 kHz, the amplitude 25–30 μm. The time needed to destroy the thrombus by ultrasound and suck out the thrombotic material ranged from 2.5 to 5 min.

3. To check side effects, experiments were performed in forty-four dogs. No significant changes were seen in the fibrinolytic system or microscopic structure of the vessel wall after ultrasound.

Key words: experimental thrombosis, thrombolysis, ultrasound.

Introduction

The therapy of thrombosis in peripheral arteries and veins has made good progress in recent years with development of vascular surgery and commencement of fibrinolytic therapy; there are, however, limitations in its application on account of contraindications.

We report on a new method which is able to destroy thrombi in dogs and remove the thrombi at the same time. The starting point in our experiments was the observation that the viscosity of liquids can be reduced by ultrasound, and the investigations by Hamrick & Cleary (1969) of the breakdown of macromolecules in ultrasonic fields. Preliminary experiments had shown that thrombi up to a certain age gained from deceased patients could be destroyed by their contact with a longitudinally vibrating rod of an ultrasonic frequency of 25 kHz and an amplitude of 25 μm.

Methods

Procedure

The technical unit consists of a generator, a frequency counter, an attenuator, the waveguide with transducer and the vacuum pump. The high-frequency tension produced in the generator reaches via an adjustable attenuator the piezoceramic ultrasonic transducer to which the waveguide is attached. The dissolved thrombus can be sucked out through the hollow waveguide and a central channel in the transducer. A vacuum pump generates the required suction. The waveguide is in a plastic tube to protect the blood vessel wall from possible temperature increase. During the irradiation sodium chloride solution (9 g/l) flows via a tube branch continually between the tube and the waveguide. If necessary, a contrast medium can be injected through this branch in order to localize the thrombus as well as to check the position of the waveguide in the blood vessel. The most recently developed waveguides are 21, 29, 35 and 47 cm long; the outer diameter is 2 mm, the inner diameter 1.4 mm and the reduced aperture diameter 0.4 mm. The frequency of the ultrasound is 26.8 kHz, the amplitude 25 μm.

After completion of experiments in vitro (Sobbe, Stumpff, Trübestein, Figge & Kozuscheck, 1974) the following experiments in vivo were performed.
In fifteen anaesthetized mongrel dogs the iliac or femoral vein was ligated unilaterally at a length of about 4 cm; then for coagulation activation thrombokinase was injected into the blood column. After removing the ligatures in five dogs after 1–2 h and in ten dogs after 1–10 days, angiographically demonstrated thrombi were irradiated by ultrasound. To do this the waveguide was inserted through a small incision in the femoral vein and under X-ray control pushed up to the distal end of the thrombus. The irradiation was performed intermittently, whereby after 1 min irradiation there followed a pause of 15 s. The destroyed thrombotic material was sucked out through the hollow waveguide during the irradiation. In a similar way thrombi up to an age of 36 h were removed from the iliac or femoral artery of five dogs. The waveguides were inserted through a small incision in the femoral artery and pushed forward to the distal end of the thrombus.

Side effects

Five dogs were irradiated with the intravascularly situated waveguide for 0.5, 1, 2, 3, 4, 5 and 10 min with a break of 15 min between each period. After each period a blood sample was taken. The variables measured were factors I, II, V, VII, VIII and X, antithrombin II/III, the thrombin time, the euglobulin lysis time and the thrombelastograph. In a separate experiment lactate dehydrogenase, bilirubin and haemoglobin were measured before and after an irradiation period of 20 min in fifteen dogs.

In eighteen dogs the waveguide was put into the iliac vein and ultrasonic irradiation performed for a total of 15 min. After 1, 3, 5, 9, 15, 21 and 28 days the intravital formalin-fixed blood vessel was surgically removed and examined.

Lung scans were performed in six dogs after successful ultrasonic thrombolysis of ilio-femoral thrombosis and additionally pulmonary angiograms were carried out in four of these dogs.

Results

The thrombi in the twenty dogs were able to be destroyed and the thrombotic material completely sucked out as demonstrated by angiography. The total irradiation period was between 2.5 and 5.5 min depending upon the age of the thrombus. The coagulation factors and other variables measured showed no change with a total irradiation period of 20–25.5 min apart from an effect due to dilution by infowing saline and removal of blood for examination. The histological examinations of the vein wall showed lesions of the endothelium in the first days. After 15 days the changes of the endothelium had completely resolved. There was also no damage to the venous valves (Trübestein, Cremer, Stumpff & Figge, 1975). The lung scans and the pulmonary angiograms before and after thrombolysis showed no significant differences.

Discussion

The great advantage of this new method as opposed to other procedures (thrombectomy and fibrinolytic therapy) is that it is relatively easy to perform. The time needed for the treatment is short and is usually between 20 and 30 min. Embolism during this procedure is negligible because the thrombotic material is destroyed and sucked out at the same time. Another advantage of thrombolysis by ultrasound is that it can be performed several times on the same patient without having any limiting effect on a later surgical or fibrinolytic treatment. A disadvantage at the present state of development is that the method is limited to occlusions which are not older than 10 days and the insufficient flexibility of the present waveguides for very curved vessels.

In conclusion we can state that it is possible to destroy and suck out simultaneously venous and arterial thrombi in the dog by the use of ultrasound. No significant side effects have been observed so that the application of the percutaneous technique of Seldinger (1953) to ultrasonic clot lysis appears feasible.

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References


