Diffusion of Epsilon Aminocaproic Acid to the Joints (34927)

ÅKE AHLBERG
(Introduced by I. M. Nilsson)
Department of Orthopaedic Surgery, and the Coagulation Laboratory, University of Lund, Malmö General Hospital, S-214 01 Malmö, Sweden

Okamoto *et al.* (1) were the first to demonstrate the antifibrinolytic effect of epsilon aminocaproic acid (E-ACA). This effect is due mainly to inhibition of the conversion of plasminogen to plasmin (2–4). The preparation has now been used for over 10 years in the treatment of various hemorrhagic conditions due to local or systemic fibrinolysis (5).

E-ACA has also been used in the treatment of haemorrhage in patients with coagulopathies, *e.g.*, joint bleedings in patients with hemophilia (6). The preparation has no effect on the actual coagulopathy, but it inhibits the local fibrinolysis in the joint capsule (7), which together with the systemic coagulation defect otherwise makes the bleeding still worse.

In addition to this antihemorrhagic effect E-ACA has an inhibiting action on various forms of experimental arthritis in animals (8, 9, 11). The effect can be explained by inhibition of the activation of plasminogen to plasmin, otherwise attacking the cartilage (12, 13).

The ability of E-ACA to diffuse to different organs and systems has been studied (14). Since the preparation is used in the treatment of joint bleeding in hemophilia and since it might prove valuable in the treatment of other joint diseases, such as degenerative and rheumatoid arthritis, it was considered worthwhile to find out whether it can diffuse to the synovial capsule and to the joint fluid.

Materials and Methods. The clinical series consisted of 16 patients admitted for operation of a ruptured meniscus of the knee joint. E-ACA was given iv in a dose of 0.1 g/kg body weight 1.3–16 hr before the operation. At operation all the synovial fluid was aspirated and a biopsy specimen was obtained from the synovial membrane. The specimens were frozen (without any additive) and sent to the research department of AB Kabi, Stockholm, for analysis. The specimens were thawed and weighed, after which they were homogenized in 1% picric acid. Denatured proteins were separated off and the amino acids were absorbed by a Dowex 50 X8 (H^+) ion exchanger. After washing with 0.5 *N* HCl and H_2O the amino acids were eluted with 1 *M* ammoniac. The eluate was evaporated, and the amino acids were separated electrophoretically and stained with ninhydrin. The stain was eluted with methanol and measured spectrophotometrically at 500 mμ. The content of the specimen was measured by comparison with a simultaneously analyzed standard.

Results. The results of the analyses are given in Fig. 1.

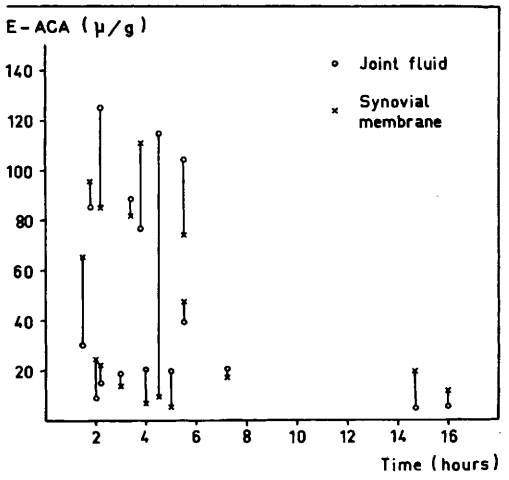

FIG. 1. Concentration of E-ACA in joint fluid and synovial membrane at different intervals after intravenous administration.

Discussion. The range of variation of the values found was wide. This may have been due in part to the lack of precision of the method and in part to differences in the severity of traumatic synovitis and in the amount of free fluid in the joint. The investigation showed that when E-ACA was given iv in a dose of 0.1 g/kg body weight the substance could be demonstrated in the joint capsule and the joint fluid within 80 min and that it was still demonstrable there up to 16 hr after the injection. McNicol *et al.* (15) recommended a plasma level of 130 μg/ml for control of the systemic fibrinolytic activity. Andersson *et al.* (14) reported that 100 μg/g tissue will produce 80% inhibition of the tissue activator activity. Such levels were observed in six of the present patients. Also, lower levels will produce a certain inhibition, but for the treatment to have a therapeutic effect, the dose should be repeated 4–6 times a day. The same dose can be used for administration orally or intravenously (15).

Summary. The concentration of E-ACA in the joint fluid and joint capsule was measured at different intervals after iv injection of the substance in a dose of 0.1 g/kg body weight in 16 patients undergoing operation because of a ruptured meniscus of the knee joint. It was found that E-ACA diffuses to both of the above-mentioned tissues and that some E-ACA can be demonstrated in the tissues for up to 16 hr after injection. A dose of 0.1 g/kg body weight 4–6 times a day orally or intravenously is recommended in the treatment of joint hemorrhages in patients with hemophilia.

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