Induced precipitation of calcium-oxalate crystals and its prevention in laboratory animals

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Induced precipitation of Ca-oxalate crystals and the possibility of its prevention were studied in dogs. In the first phase of the experiments precipitation of Ca-oxalate crystals in canine renal tubules was induced by intraperitoneal administration of Na-glyoxylate. Preventive medication (lipoic acid, vitamin B₆, Milurit), applied in the second phase, resulted in a significant depression of induced precipitation. The successful experiments serve as a basis for clinical research aimed at a preventive medication of recurrent Ca-oxalate stone formation.

The primary task in the management of calcium oxalate calculosis is the elimination of the stone responsible for the symptoms. It is, however, of no lesser importance to protect the patient from subsequent calculous recurrences, an objective difficult to achieve.

First of all, the cause of stone formation has to be ascertained by all available means. If subrenal factors are involved in its aetiology, surgery for the elimination of the stone will have to be connected with the eradication of the responsible factor [1, 2, 3, 7]. Suspicion of prerenal or renal aetiological factors calls for the disclosure of the causes and consequences which are likely to be amenable to postoperative pharmacotherapeutic and dietary measures in the framework of a regular follow-up.

In order to make the follow-up studies of Ca-oxalate stone-formers more efficient, we sought to explore the pharmacotherapeutic possibilities of reducing the frequency of calculous recurrences. In this attempt we undertook serial experiments in dogs, using the method of Schneider [5, 6] with some modifications. In the first series of the experiments precipitation of Ca-oxalate crystals in the renal tubules was induced, and in the second it was sought to counteract this precipitation by preventive medication.

Material and methods

Forty-six dogs were divided into 9 groups. Six dogs, assigned to group I, served as controls. The other 8 groups were formed by 5 animals each. All animals were kept on mixed food.
For the production of Ca-oxalate precipitation, glyoxylate — the precursor of oxalate — was used in the form of its sodium salt. To the animals of group I, 100 mg/kg Na-glyoxylate was administered intraperitoneally in the morning and evening. On the next day the kidneys were removed under general anaesthesia. Slices of 5 mm thickness were excised from the cortical, medullary and papillary areas, the incision line being at right angles to the collecting tubules. The blocks were cut into sections of 25 to 30 μm thickness and, after the usual processing, stained with HE and examined by the polarization technique described by Romhányi et al. [4].

The animals of groups II–IX received preventive oral medication daily for a week. On the 7th day they were injected with 100 mg/kg Na-glyoxylate i.p. in the morning and evening. On the next day one kidney was removed and processed as in group I. After the intervention the animals continued on preventive medication for another week, at the end of which i.p. administration of Na-glyoxylate on two occasions was repeated. On the next day the remaining kidney was removed and after histological processing examined under polarized light.

Preventive medication included the following drugs:

- Group II: Lipoic acid 25 mg/day
- Group III: Vitamin B₁ 10 mg/day
- Group IV: Milurit (allopurinol) 100 mg/day
- Group V: Panthenol 2 x 100 mg/day
- Group VI: Vitamin B₁ 10 mg + lipoic acid 25 mg/day
- Group VII: Milurit 100 mg + Panthenol 200 mg/day
- Group VIII: Milurit 100 mg + Vitamin B₁ 10 mg + lipoic acid 25 mg/day
- Group IX: Milurit 100 mg + Vitamin B₁ 10 mg + lipoic acid 25 mg + Panthenol 200 mg/day

The microscopic sections of the animals which had been injected with Na-glyoxylate and of those which had been on preventive medication and injected with Na-glyoxylate afterwards, were studied under polarized light.

Readings of the Ca-oxalate crystal counts per mm² area were taken, evaluated within each group and also compared between the groups.

**Results**

The mean values of the crystal counts in the renal sections of the individual groups, evaluated on the basis of Student’s t-test, are represented in the histogram of Fig. 1.

The polarization microphotographs of some of the renal sections are shown in Figs 2, 3 and 4.

In an attempt to reduce Ca-oxalate crystallization, the drugs and/or combinations listed above were used. From the evaluation of the histogram and the mi-