Development of Metaphylaxis in Calcium Urolithiasis: A Restriction of Conventional Drug Therapy

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(Accepted October 28, 1993)

Between 1978 and 1992 (mean 9.2 years), metaphylaxis was introduced to 110 patients originally hospitalized for recurrent urinary calcium stones (mostly bilateral or multiple). Patients with hyperparathyroidism or with sponge kidney were excluded from the study. Until 1984, the condition had been treated mostly using conventional drug metaphylaxis (thiazides and allopurinol in 75% and 57%, respectively). After that year, there was a gradual decrease in the number of patients treated with thiazides (to 15%) and allopurinol (to 10%). This was associated with a steep rise in the proportion of patients treated with inhibitors (magnesium to 36% and citrates to 30%), or exclusively with non-medicamentous therapy (to 31%). These fundamental changes in approach have not reduced the effectiveness of metaphylaxis, and recurrence rates in individual years have not changed significantly either. Metaphylaxis was successful in 105 patients (95%) and the rate of recurrence has declined from 0.9 to 0.08 stones per year. The restriction of conventional drug metaphylaxis has entailed a marked decrease in the incidence of side effects of therapy and, consequently, a reduced need for follow-up tests and outpatient follow-up.

Introduction

Drug metaphylaxis of urolithiasis started to be gradually introduced into clinical practice in the late 1960s [1-4]. A key factor playing a part in this process was the detection of metabolic risk factors of stone formation. Administration of thiazides and allopurinol has been criticized in recent years on grounds of both treatment efficacy and adverse reactions observed during their long-term use [5-8]. These facts made scientists turn their attention to inhibitors [4, 9-12] and non-medicamentous therapy. The body of evidence documenting what is referred to as the “stone clinic effect” is growing. Its beneficial action is based on regular follow-up of the patient and compliance with dietary restrictions and high fluid intake [13-15]. The “stone clinic effect” was recommended to be tested in each patient with urolithiasis, especially on the first episode [8].

The authors of the present paper reviewed the course of metaphylaxis in patients with recurrent renal calcium stones, in an effort to establish whether or not it was possible to replace conventional drug therapy (hydrochlorothiazide and allopurinol) with inhibitors (magnesium and citrates) or with non-
medicamentous therapy (dietary and fluid intake regimen) alone. This study was designed to determine the impact of these changes in metaphylaxis, started in 1985, on recurrence rates and on the incidence of adverse reactions.

**Material and methods**

The study included a group of 110 patients with recurrent calcium urolithiasis who were on metabolic follow-up and had been treated in the period 1978-1992. Mean duration of therapy was 9.2 years (range, 4-14). Those enrolled into the study included all patients who had received preventive treatment at our Department for a period longer than the mean interval between recurrence episodes prior to start of therapy. The only subjects excluded were patients with primary hyperparathyroidism and with sponge kidney.

After obtaining special medical history and the first metabolic evaluation, patients with calcium stones are put on regular follow-up and receive treatment. Urine collection is made while the patients are on a low-calcium diet; it is followed by a test developed by Pak (a modification). The type of hypercalciuria found in each patient is a factor affecting only partially the therapeutic tactics to be employed. Pak's test is used mainly to exclude a disorder of calcium metabolism; it also serves to monitor the dynamics of Ca/Mg coefficients and fresh urine samples are used to determine the pH. Citraturia has been assessed only since 1985.

**Method of therapy**

Until 1984, the overwhelming majority of patients were on drug therapy according to the results of metabolic studies. After some time, this therapy was adjusted according to results of metabolic follow-up (initially at a six-month interval, later after one to two years). The patients were mostly on conventional drug therapy consisting of thiazides, 25-50 mg/day, allopurinol, 100-200 mg/day, and pyridoxin 60 mg/day; orthophosphates were administered only sporadically. From 1985 on, most of our patients have been recommended to start with specific dietary restrictions and fluid intake regimen, with drug therapy added usually six months later after metabolic follow-up. Then, as a rule, preference was given to magnesium or citrate supplementation if deficiency was found (magnesium oxide 400-1200 mg/day, Na + K citrate 4.0-6.0 g/day). This therapy was applied also in some patients originally treated by conventional therapy. Usually, thiazides were administered only in cases of persistent severe hypercalciuria (especially isolated hypercalciuria) and, also, in severe forms of urolithiasis. Thiazide administration was continued in part of patients benefiting from this therapy in the initial period. Allopurinol was reserved exclusively for patients with hyperuricaemia or, more rarely, hyperuricosuria persisting despite dietary restrictions, or where the diet could not be consistently adhered to (e.g., in diabetics).