

Urinary Excretion of Renal Stone Following Prolonged Acetazolamide Therapy: A Case Report

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SUMMARY:

This article reports a case of urinary excretion of renal stone following prolonged acetazolamide therapy in otherwise healthy patient with Primary Open Angle Glaucoma (POAG).

KEYWORDS: *Acetazolamide, POAG, Renal stone*

INTRODUCTION

Acetazolamide is a systemic carbonic anhydrase inhibitor often used as adjunct when intraocular pressure (IOP) is not regulated with other ocular hypotensive agents in the treatment of Glaucoma.

Carbonic anhydrase inhibitors (CAI) are known to reduce aqueous humour production and lower IOP¹

Acetazolamide has been used to reduce IOP for over 140 years²

The oral administration has been found by several investigators to decrease markedly the urinary excretion of citrate in humans.^{3,4}

CASE REPORT

A 52 year old male patient on treatment for an established diagnosis of POAG for 9 years presented with history of urinary excretion of a stone (Fig1)

Medical history was remarkable of recurrent backache associated with passage of cloudy urine in the last 3 years. He had consistently used acetazolamide as adjunct therapy to topical beta adrenergic blockers (Betaxolol/Timolol) in the control of his IOP for 5 years.

He was subsequently referred to a physician where the genito-urinary system was investigated. The abdominal ultrasound scan was normal. Intravenous Urogram did not reveal any abnormality. (Fig2) Mid stream urinary microscopy, culture and sensitivity were normal.

Serum albumin, phosphate and calcium were all within normal limits. An analysis of the renal stone revealed a stone weighing 0.09g, with rough surface and off white in colour. It was a simple stone made up of calcium, oxalate and phosphate.

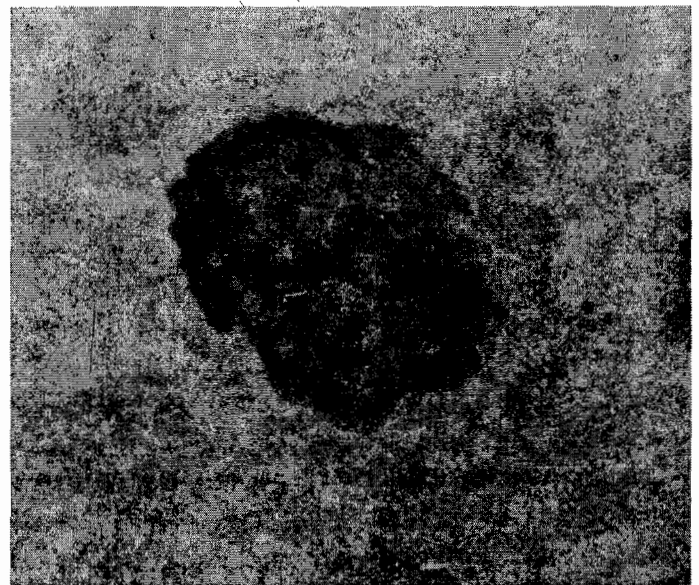


Figure 1: Excreted Urinary Stone

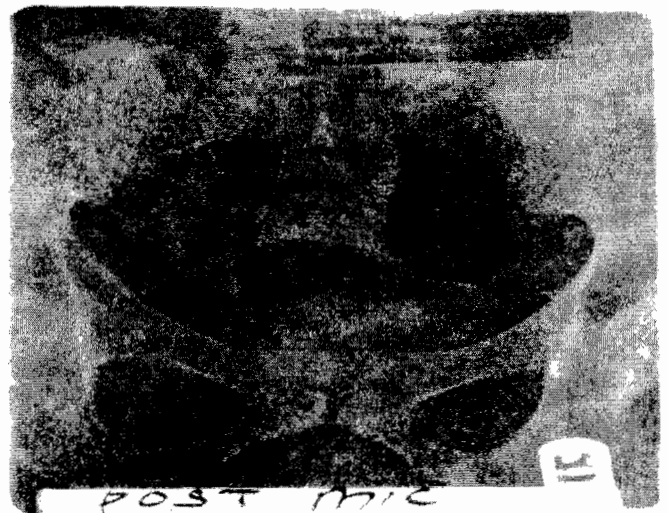


Figure 2: Normal Urogram

DISCUSSION

Carbonic anhydrase inhibitors are Sulfonamide derivatives that lower IOP by reducing aqueous humour production. They inhibit carbonic anhydrase, which is one of the enzymes that regulate aqueous humor formation¹. Side effects range from mild and annoying, to debilitation and life threatening complications.

Several complications have been known to arise from long term CAI therapy in the literature. Such complications reported are malaise complex, fatigue weight loss, depression, anorexia, loss of libido, paraesthesia of extremities, urolithiasis and life threatening blood dyscrasias (aplastic anaemia), anaphylactic reactions^{5,6}

CAI induces urolithiasis by reducing urine citrate excretion. Citrate normally chelates urinary calcium into a soluble complex and thus prevents stone formation⁴. When there is less citrate available to form this soluble complex, there is a nidus for stone formation⁷.

Acetazolamide reduces urinary citrate excretion more than the other CAI in controlled studies⁷. Calcific renal calculi formation had been documented in several case control studies with regular daily regimen of acetazolamide at 250mg thrice daily over 1 year. The rate of developing one or more stone per year was 11 times more than in control group⁷.

The bulk of the urinary stones that are of non-infectious origin are usually composed of calcium oxalate and/or phosphate as in our report. 70% of all renal stones observed in economically developed countries are calcium oxalate stones⁸.

It was also revealed in some studies that Potassium supplementation did not in any way alleviate the CAI side effect⁵.

The various systemic side effects have necessitated numerous investigators to search for topically active CAI with fewer side effect than the currently prescribed formulations.^{9,10} This led to the discovery of Dorzolamide, and Brinzolamide, which are gradually replacing the systemic formulations.

This is the first such reported case in our environment and it serves to remind Ophthalmologists that systemic CAI should be used only for short term control of IOP in glaucoma patient.

REFERENCES

- (1) Becker B: Decrease in Intraocular pressure in man by a carbonic anhydrase inhibitor, Diamox. *AM. J. Ophthalmol* 1954; 37:13
- (2) Maren TH. Carbonic anhydrase: Chemistry, Physiology and Inhibition. *Physiol Rev* 1967; 47:595
- (3) Gordon EE, Sheps SF: Effects of acetazolamide on citrate excretion and formation of renal calculi. *New. Eng. J. Med.* 1957; 256: 1215.
- (4) Constant MA; Becker B The effect of carbonic anhydrase inhibitor on urinary excretion of citrate by humans. *AM. J. Ophthalmol* 1960; 49: 929-34.
- (5) Epstein DL, Grant WM; Carbonic anhydrase inhibitor side effect: Serum Chemical Analysis *Arch Ophthalmol* 1977; 95: 1378
- (6) Epstein RJ Allen RC, Lunde MW; organic Impotence associated with carbonic anhydrase inhibitor therapy for glaucoma. *Ann. Ophthalmol* 1987;19:48
- (7) Kass M A et al Acetazolamide and Urolithiasis. *Ophthalmol* 1981;88:261
- (8) Trinchieri A. Epidemiology of urolithiasis. *Arch Ital Urol Androl* Sept 1996 ; 68(4); 203-49
- (9) Stein A; Pinke RP, Glabb KT et al The effect of topically administered carbonic anhydrase inhibitors on aqueous humor dynamics in rabbits. *Am. J. Ophthalmol* 1983; 95:772.
- (10) Kalina PH. Shetlar DJ. Lewis RA et al. 6-Amino-2-benzothiazole- Sulfonamide. The effect of topical carbonic anhydrase inhibitor on aqueous humor formation in the normal human eye *Ophthalmology* 1988;95:7772.