



Nephrolithiasis With Topiramate in Nonambulatory Children and Young Adults in a Long-term Care Facility

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RATIONALE

- ◆ Nephrolithiasis in association with topiramate (TPM) therapy occurs in 1.5% of patients. This incidence is 2-4 times that expected in the background population and thought to be due to TPM's carbonic anhydrase inhibiting effect which decreases urinary citrate and prevents adequate urine acidification.
- ◆ Other well known risk factors for kidney stones include positive family history, race, recurrent urinary tract infections, renal anomalies, medications, diet & fluid intake, and physical inactivity.
- ◆ In nonambulatory individuals with epilepsy, additional risk factors exist. Immobilization itself leads to bone resorption resulting in hypercalcemia and hypercalciuria. Antiepileptic drugs may also contribute to osteopenia and hypercalciuria. To treat osteopenia, diets are often supplemented with calcium which may exacerbate hypercalciuria. Both hypercalciuria and hypocitraturia help precipitate calcium.
- ◆ We assessed the incidence and risk factors for nephrolithiasis with topiramate therapy at Hattie Larlham Center for Children with Disabilities, a long-term care facility for nonambulatory medically fragile children and young adults with severe mental retardation and developmental disabilities.

METHODS

- ◆ A retrospective chart review was performed of all individuals on TPM. Recorded parameters included sex, age, race, duration and dosage of topiramate, concomitant medications, radiological studies, diet (including calcium, Vit. D, sodium, protein, fluid intake), and other risk factors such as renal anomalies & urinary tract infections. Treatment and any complications were also recorded.

RESULTS

- ◆ Of the 126 individuals (ages 4-45 years) residing at Hattie Larlham, 23 (18%) were treated with TPM. Of these 23 individuals, 13 (56%) developed clinical evidence of stones. Their data is outlined as follows:

Risk Factors	Total	Cohort With Stones	Cohort Without Stones
N	23	13	10
Age (yrs)	13-35, mean 21.7	13-35, mean 23	13-27, mean 20
Sex	12F, 11M	5F, 8M	7F, 3M
Race	19W, 2B, 1Asian	11W, 1B, 1Asian	8W, 1B, 1W/Asian
TPM dose (mg/kg/day)	3.2-25.7, mean 7.4	3.2-25.7, mean 8	4.2-9.2, mean 6.7
TPM monotherapy	3/23	3/13	0/10
Fluid Intake (cc/kg/day)	31.8-64.3, mean 45.8	31.8-64.3, mean 44.8	37.6-53.3, mean 47.1
Mean Na Intake (meq/day)	58	49.3	68.7
Mean Ca Intake (mg/day)	1889	1829	1961
Mean Vit. D Intake (IU/day)	884.1	736.7	1064
Mean protein Intake (mg/kg/day)	1.3	1.4	1.3
Other Risk Factors	recurrent UTI: 8 horseshoe kidney: 1	recurrent UTI: 7 horseshoe kidney: 1	recurrent UTI: 1

- ◆ Age at onset of stones ranged from 11-29 years. Duration of TPM therapy before onset of stones averaged 48 months (range 1-84 months). Three of 13 patients were on TPM monotherapy. With the exception of two individuals who were on an oral diet, patients had a fixed fluid intake of 32-64 cc/kg/day. Total daily calcium intake including diet and supplementation varied between 1183-2742 mg (mean 1829 mg/day). No patients were on diuretics.
- ◆ All 13 patients had stone fragments in their urine. One had a horseshoe kidney without urinary outflow obstruction. Stones were analyzed in 3 patients; all were 90% calcium phosphate. Seven of 13 patients were weaned off TPM and 2 were treated with citrate supplementation. Two patients underwent lithotripsy for persistent stones. One failed lithotripsy and needed 2 percutaneous nephrostomies for stone removal. Urosepsis and retroperitoneal bleed requiring transfusion complicated lithotripsy in another.

CONCLUSIONS

- ◆ Incidence of nephrolithiasis with topiramate in our cohort was 56%, much higher than the 1.5% risk reported in the literature. In nonambulatory, neurologically impaired individuals, nephrolithiasis is a serious complication and may warrant surgical treatment as seen in our 2 patients.
- ◆ This population may be more vulnerable to nephrolithiasis with topiramate due to:
 - 1) bladder stasis from immobility and neurogenic bladder
 - 2) hypercalciuria from increased bone resorption, medications, and calcium supplementation
- ◆ Prospective studies measuring urinary chemistries including calcium & citrate and treatment with citrate supplementation will help substantiate our observations.

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