

GABAPENTIN FOR OVERACTIVE BLADDER AND NOCTURIA AFTER ANTICHOLINERGIC FAILURE

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ABSTRACT

Introduction: We reviewed our experience with the use of gabapentin to treat symptoms of overactive bladder (OAB) and nocturia in patients who have failed conventional anticholinergic therapy.

Methods: Thirty-one patients referred to us with refractory (OAB) and/or nocturia were treated with oral gabapentin. All the patients had tried or remained on antimuscarinic drugs during treatment. Twenty-four of 31 complained of bothersome symptoms during day and night and the other seven had primary complaints of nocturia. Initial gabapentin doses ranged from 100-300 mg at bedtime. Dose was slowly titrated up to 3,000 mg based on patients' symptomatology and tolerability.

Results: The mean age was 51 years old (range 27-78). There were 13 men and 18 women. The median steady state dose chosen by the patient after initial titration was 600 mg/day. Fourteen of 31 patients reported subjective improvement of their frequency and 8 have been on the medication for over 12 months with persistent efficacy. For the 14 improved patients, mean frequency/24 hours decreased from 14.1 ± 2.2 to 10.0 ± 2.1 . Three patients with primary nocturia reported improvement from a mean of 4.0 ± 1.3 to 1.0 ± 0.3 episodes/night. Six patients stopped taking the drug within one month due to side effects mostly described as drowsiness or lethargy.

Conclusions: Fourteen of 31 patients with refractory (OAB) and nocturia improved with oral gabapentin. Gabapentin was generally well tolerated and can be considered in selective patients when conventional modalities have failed.

Key words: bladder; nocturia; urination disorders; prostate; neuromodulation

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INTRODUCTION

Gabapentin is approved as an anticonvulsant but it has significant pain control properties. It has been widely used in neurology for the treatment of peripheral neuropathic pain. In animal test systems designed to detect anticonvulsant activity, gabapentin prevents seizures similar to other marketed anticonvulsants (1,2). Gabapentin is structurally related to the neurotransmitter GABA (gamma-

aminobutyric acid) but it does not interact with GABA receptors, it is not converted metabolically into GABA or a GABA agonist, and it is not an inhibitor of GABA uptake or degradation (3).

The mechanism of gabapentin's action for neuropathic pain has not been fully elucidated but it appears to have inhibitory activity on afferent C-fibers nerve activity (4). Because of demonstrated clinical safety and efficacy over the past decade, gabapentin appears to have attractive properties for

consideration to treat refractory lower urinary tract symptoms. We have previously reported on the successful use of gabapentin in patients with interstitial cystitis (5). Up-regulation of bladder C-fiber afferent nerve function may also play a role in certain cases of urge incontinence, overactive bladder (OAB) and sensory urgency (6). Therefore, gabapentin is a rational drug to consider in cases of refractory (OAB).

We hereby reviewed our experience with gabapentin as a method of treating symptoms of (OAB) and nocturia in patients who have failed conventional anticholinergic therapy. Gabapentin is not FDA indicated for urologic dysfunction and the patients treated in this series were explained that this was an off label use of the drug.

MATERIALS AND METHODS

Thirty-one patients referred to our university urology clinic with refractory (OAB) and/or nocturia were treated with oral gabapentin. The mean age was 51 years old (range 27 - 78). Mean duration of symptoms was 6.3 years. There were 13 men and 18 women. Twelve of the women had multiple sclerosis and had neurogenic detrusor hyperreflexia. The other 6 women had mixed urge and stress incontinence with urge as the predominate component. In the 13 men, 7 have had prior transurethral resection of the prostate and 3 had microwaves of the prostate. Six patients smoked and none had more than social alcohol consumption.

Baseline evaluation included exclusion of urethral outlet obstruction. None of the men had bladder outlet obstruction as documented on pressure-flow videourodynamics. None of the patient had neurogenic detrusor-sphincter dyssynergia as noted on multichannel videourodynamics.

All the patients had tried oral tolterodine or oxybutynin for at least 8 weeks prior to their referral. During the gabapentin trial, the patients were instructed to not change any of their prior or present medications. Sixteen of the patients remained on their usual dosage of antimuscarinic drug during gabapentin therapy. None of the patients discontinued or modified antimuscarinic treatment.

Twenty-four of 31 complained of bothersome symptoms during day and night and the other seven had primary complaints of nocturia. Initial gabapentin (Pfizer, New York, USA) doses ranged from 100 mg or 300 mg at bedtime. Dose was slowly titrated up to 3,000 mg based on patients' symptomatology, all taken at bedtime.

After a routine history and physical examination, including a measurement of bladder diary, the patients were started on gabapentin.

Micturition frequency was measured after 12 weeks and additional follow-up of up to 12 months was available in ten of the 14 patients who reported improvement.

Data Analysis: All values are presented as mean \pm standard error. Statistical analyses and comparisons between groups were performed using student t-test. A probability level of < 0.05 was accepted as significant.

RESULTS

No patient had a history of seizures or convulsions, nor had any ever been treated with an anticonvulsant or antiepileptic agent. The mean dose of gabapentin was 600 mg/day (range 100 - 3,000 mg). Fourteen of 31 patients reported subjective improvement of their frequency and 8 have been on the medication for over 12 months with persistent efficacy (Table-1). For the 14 improved patients, mean frequency/24 hours decreased from 14.1 ± 2.2

Table 1 – Bladder diary of patients who did or did not improve in frequency and nocturia groups.

	Baseline	12 weeks
Frequency (n = 31)		
Improved (n = 11)	14.1 \pm 2.2	10.0 \pm 2.1*
No improvement (n = 20)	13.6 \pm 1.9	12.5 \pm 3.1
Nocturia (n = 7)		
Improved (n = 3)	4.0 \pm 1.3	1.0 \pm 0.3**
No improvement (n = 4)	4.3 \pm 1.3	4.0 \pm 1.0

* $p = 0.01$; ** $p = 0.03$

to 10.0 ± 2.1 . Three patients with primary nocturia reported improvement from a mean of 4.0 ± 1.3 to 1.0 ± 0.3 episodes/night.

Gabapentin was well tolerated with only six patients stopping the drug within one month due to side effects mostly described as drowsiness or lethargy.

The side effects were transient and resolved promptly after the gabapentin was discontinued. Three of the patients who improved also reported lethargy but described them as tolerable and continued with the medication.

COMMENTS

Gabapentin has been widely used in the neurologic field for the treatment of focal neuropathic pain. Pain resulting from diffuse and focal neuropathies, such as painful diabetic neuropathy and post herpetic neuralgia, is a common but difficult clinical problem to manage (1). Neuropathy occurs in more than 50% of patients with diabetes who have been hyperglycemic for more than 15 years (7). Unfortunately, drug treatment for neuropathic pain is often unsatisfactory, as demonstrated by the large number of drugs that patients will have taken in an attempt to seek pain relief.

Rowbotham et al (1) and Backonja et al. (2), reported 2 clinical series on gabapentin for chronic neuralgic pain. Gabapentin was titrated from 900 mg/d to 3,600 mg/d or the maximally tolerated dosage over 8 weeks. Both studies demonstrated significant and clinically substantive amelioration of daily pain severity and improvement in important secondary end points, including sleep interference scores and quality-of-life measures.

Gabapentin was well tolerated, with similar numbers of treated and placebo patients withdrawing because of adverse effects (8% in gabapentin group and 6% in placebo group), Table-1.

The most common adverse effects were dizziness and drowsiness. Gabapentin may be a safer drug choice for the older patient who is prone to orthostatic hypotension and cardiac arrhythmias.

Gabapentin has been used in urology for the treatment in patients with refractory interstitial cystitis

(5). In that study ten of 21 interstitial cystitis patients reported subjective improvement of their pain. Why did we consider using gabapentin to treat refractory (OAB)? We hypothesize that certain cases of (OAB) may share a similar pathophysiology of up-regulation of afferent C-fiber sensory neurons as in interstitial cystitis (6) stimulated us to consider using gabapentin for (OAB) and nocturia. Overall 14 of 31 (45%) of patients reported improvement. It was rewarding to see that gabapentin was able to help certain cases of nocturia, which has been a difficult symptom for oral antimuscarinic agents to help. There did not appear to be a difference in efficacy in patients with or without multiple sclerosis.

CONCLUSIONS

Although only 14 of 31 patients improved with oral gabapentin, one should consider that these were patients with refractory (OAB) and nocturia. Gabapentin was generally well tolerated and can be considered in selective patients with (OAB) when conventional modalities have failed.

Dr. Michael B. Chancellor is consultant and investigator with Pfizer.

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