42

Antonio Carbone G. P. [1], Parascani R. [2], Morello P. [2], Tubaro A. [2], Di Crosta G. [2]
1. La Sapienza University, 2 University of Rome, Italy

THE USE OF GABAPENTINE IN THE TREATMENT OF NEUROGENIC DETRUSOR OVERACTIVITY: PRELIMINARY URODYNAMIC AND CLINICAL RESULTS.

Aims of Study

Detrusor overactivity is often associated with symptoms of overactive bladder, namely frequency, urgency and urge incontinence. Both neurogenic and myogenic causes of involuntary detrusor contractions (IDCs) have been identified (DeGroat 1993, Elbadawi 1993). Among the various hypotheses to explain the pathophysiology of detrusor overactivity, hyperactivation of bladder receptors resulting into an increased afferent input in the spinal cord, where the sacral reflex controlling detrusor activity is integrated, has been proposed. Consequently, modulation of bladder receptor activity and/or of the sacral reflex has been considered as a possible approach to control involuntary detrusor contractions (IDCs). Various drug, such as antiepileptic agents, are known to modulate excitability of C and Aδ fibres which mediate the micturition and the excitability of reflex centre in the spinal cord. In this study we investigated the effect of gabapentine, an anticonvulsive agent which proved to be effective in the management of depression, on paroxysmal activity of C and Aδ fibres in patients with neurogenica detrusor overactivity.

Methods

Fifteen patients, 14 males and 1 female, of 45 to 76 years of age (median 63), were enrolled in the study after neurogenical detrusor overactivity was diagnosed on pressure-flow study and the informed consent was signed. Five patients suffered multiple infarction encephalopathy, 3 patients had Parkinson disease, 2 patients had multisystemic atrophy, 2 patients had multiple sclerosis (without clinical or radiologic evidence of spinal cord lesion), 4 patients had post-infectious myelitis. The diagnostic workup included, history, general and neurologic physical examination, voiding diary, International Prostate Symptom Score (IPSS), urinalysis and urine culture, renal, vesical and prostatic ultrasonography, uroflowmetry (in duplicate, 45 minutes apart) and pressure-flow study with concentric needle electromyography of the pelvic floor. Room temperature saline was used for water cystometry and a filling rate of 30 ml min was adopted. All patients were evaluated at baseline and after 21 days of treatment with gabapentine (900 mg/day per os).

Results

A significant subjective improvement of overactive bladder symptoms was reported by all patients. The following change in overactive detrusor severity was observed.

	Pre	Post	*p<
IPSS	14.8	8.8	0,023
Cystometric capacity (mls)	342 ± 99	430 ± 98	0.05
PdetQmax (cmH2O)	47,74 ± 20	36 ± 12	0.05
IDCs	15/15	11/15	
Volume at 1st IDC (mls)**	217,2 ± 120	318,7 ± 70,5	0.05
Max IDC amplitude (cmH2O)**	42,4 ± 17	49±16	n.s.

*Student's t-test, **mean values in 11 patients with IDCs after gabapentine treatment

Conclusions

C and Aδ fibres can be activated by stretching of the receptors located at the submucosal and detrusor level. The afferent input caused by bladder distension is of importance for the micturition reflex integrated at the S3-S4 level. Detrusor overactivity in neurogenic patients is considered to be dependent upon hyper excitability of the spinal reflex centre in the absence of the inhibitory output from sovrapontine structures. Modulation of such hyper excitability can be obtained by reducing the afferent input or by reducing the excitability of the reflex centre; both effects could possibly be induced by gabapentine. In our series, gabapentine treatment produced a significant increase of maximum cystometric capacity. Numerous studies have shown that gabapentine is effective in reducing the neural trigger by acting on calcium type of the L Type which are present on both C and Aδ fibres (Yoshimura. 2001, Marais. 2001, Sergeant. 2001). The described mechanism could be responsible for the observed changes in cystometric parameters as well as of the reduction of proprioceptive sensibility. Further to the modification of afferent input from the periphery, a decrease in spinal excitability secondary to gabapentine effect on wide-dynamic range neurones which

integrate the sensory input in the spinal cord segment thus reducing the reflex activity of the detrusor (**Sutton. 2001**; Stanfa. 1997; Wang. 1999; Marais 2001; Bertrand. 2001; Sasaki. 2001). Maneuf (2001) observed how gabapentine can inhibit the release of substance P from the trigeminal nucleus in the rat which is responsible for an additional anti-hyperalgesic and allodinic effect of the drug. Gabapentine has an oral bioavailability of 60% and does not induce significant side effects ad dosages of 2-4 grams/day or lower. The results of this study suggest a significant improvement of urodynamic parameters of patients receiving gabapentine treatment and particularly cystometric capacity and detrusor overactivity. These results suggest the possibility to reduce detrusor overactivity by modulating the afferent input from the bladder and the excitability of the sacral reflex centre. These results support the need for further investigation on larger patient series including also non-neurogenic detrusor overactivity and long term treatment. Further exploratory work including the evaluation of the H-reflex in patients receiving gabapentine treatment is warranted to explore the impact of such treatment of micturition pathophysiology.

References

1. Andersson K-E. Advances in the pharmacological control of the bladder. Exp Physiol 1999; 84(1):195-213