BOTULINUM TOxin IN THE TREATMENT OF Cystitis

LUCIA LUCAN1, DAN ENACHE2, BODO ORS ZSOMBOR2

1Clinical I of Obstetrics and Gynecology Cluj-Napoca
2Clinical Institute of Urology and Renal Transplantation Cluj-Napoca

Abstract

Objective. This study will follow the effectiveness of treatment of chronic cystitis in menopausal women, associated with overactive bladder syndrome, performed by endoscopic injection of botulinum toxin type A to patients who previously attended drug treatment and bladder instillational treatment but with persistence of clinical manifestations.

Materials and methods. We studied 43 patients, in menopause with chronic recurrent cystitis and overactive bladder. The data were statistically analyzed by descriptive analysis and linear regression. We used Chi-square, T-Student test. Treatment was performed by injecting botulinum toxin solution.

Results. The patients were divided in 2 groups. Group A, 22 patients underwent instillational treatment. Group B, 21 patients, underwent endovezical injection of botulinum toxin type A. 18 patients in group A after treatment showed an initial improvement of symptoms; after 3 months evaluation the improvement was in 63.63% and after 6 months only 54.54%. The B group after 2 weeks of treatment 85.71% had remission of symptoms.

Conclusions. Endoscopic treatment by injection of type A botulinum toxin in bladder mucosa represents a feasible therapeutic approach.

Keywords: overactive bladder syndrome, endovesical injection of botulinum toxin type A, chronic cystitis.

TRATAMENTUL CISTITEI CRONICE CU TOXINA BOTULINICĂ

Rezumat

Obiective. Studiul urmăreşte eficacitatea tratamentului cistitei cronice asociată cu sindromul vezicii hiperactive la femeile aflate la menopauză, cu toxina botulinică de tip A administrată prin injectare endoscopică, la paciente la care a existat persistenţa manifestărilor clinice după tratament medicamentos şi instilaţii vezicale.


Rezultate. Pacientele au fost împărţite în două grupuri. Grupul A, format din 22 de paciente, a urmat un tratament prin instilaţii vezicale. Grupul B, format din 21 de paciente, a urmat un tratament prin injectare endoscopică de toxină botulinică de tip A. După administrarea tratamentului, 18 paciente din grupul A au prezentat o îmbunătăţire în ceea ce priveşte simptomele; după 3 luni de evaluare îmbunătăţirea a fost resimţită de 63,63% dintre paciente, iar după 6 luni aceasta a ajuns la 54,54%. În grupul B, după 2 luni de tratament, 85,71% dintre paciente au resimţit îmbunătăţiri în ceea ce priveşte simptomele.

Concluzie. Tratamentul prin injectare endoscopică de toxină botulinică în mucoasa vezicii urinare reprezintă o alternativă terapeutică demnă de luat în seamă.

Cuvinte cheie: sindromul vezicii neurogene (hiperactive), injectare endovezicală de toxină botulinică de tip A, cistită cronică.
INTRODUCTION

Painful bladder syndrome overactive bladder, interstitial cystitis, are characterized by urgency with or without incontinence, usually associated with high urinary frequency and nocturia in the absence of infection. This affects all major aspects of quality of life: social, psychological, occupational, domestic, physical and sexual. Most cases of uncomplicated cystitis occur in women; each year approximately 10% of women recounts an episode of UTI annually and over 50% of the female population has at least one such infectious episode during their lifetime. Simple cystitis occasionally occurs in prepubertal girls; the incidence is increased in late adolescence and during two three decades of life.

MATERIALS AND METHODS

This study will follow short and medium-term evaluation of the effectiveness of treatment of chronic cystitis in menopausal women, associated with overactive bladder syndrome, performed by endoscopic injection of botulinum toxin type A to patients who previously attended drug treatment (antibiotic, inflammatory) and bladder instillational treatment but with persistence of clinical manifestations. The study was conducted on a total of 43 patients, aged between 42 and 65 in menopause, with chronic recurrent cystitis and overactive bladder in the period January 2004 - June 2008, in the Clinical Institute of Urology and Renal Transplant of Cluj Napoca and Gynecology I Clinic of Cluj Napoca after obtaining written informed consent of subjects to participate in the study. Patients who had undergone all stages of evaluation, a questionnaire assessment of symptoms, clinical examination, uroculture, ultrasound, uroflow-meters and cystoscopy to rule out other associated pathologies, the need was made urography and/or CT were introduced in the study. Follow up for the patients was performed at 2 weeks, 1 month, every 3 months to 1 year and consisted of a clinical examination, ultrasound evaluation questionnaire of symptoms and endoscopic reassessment after treatment.

The data collected were statistically analyzed by descriptive analysis and linear regression. The descriptive analysis highlighted differences between the groups. The main statistical methods used, were percentage expression, mean values with standard deviation.

Null hypothesis is used to define the significance of the difference. A statistical null hypothesis that denies the similarity between the two groups was used, the difference being a consequence of the therapeutic study. Correlation analysis was done by Chi-square calculation for qualitative values expressed as a percentage and T-Student test for quantitative values expressed as mean values with standard deviation. Simple linear regression using mean square error calculation was also used. We used the Epi-Info 3.5.3 statistical program from the Center for Control and Prevention USA disease.

In initial empirical antibiotic therapy fluoroquinolones provides an excellent spectrum in most cases and the duration of administration is 7 days. When bacterial susceptibility data are available modifications are made. Associated antibiotic treatment with NSAIDs, preferably administered orally or rectal suppository form can remove or diminish some symptoms and signs of inflammation.

Together with drug treatment, intravesical instillation is carried out for 10 days using a silver nitrate solution associated with Heparin 25,000 IU % alternating with dexamethasone 8 mg / 2 ml with 4.2% sodium bicarbonate. To view and evaluate the lower urinary tract lesions cystoscopy was used.

The method of treatment is performed by injecting botulinum toxin solution in 20 to 30 points covering the entire surface of detrusor, avoiding the bladder trigone area and 1 cm around the ureteric orifices. The bladder is filled with 100 ml saline. The injection solution is prepared as follows: 100 IU Botulinum toxin is diluted in 8ml 9% saline, then 4 of the 8 ml are withdrawn into a syringe of 20 ml and diluted with another 11 ml of saline resulting in a total of 15 ml; the same is done with the other 4 ml.

RESULTS

The 43 patients included were divided according to the treatment followed in 2 groups. Group A, 22 patients underwent instillational treatment and those in group B with 21 patients, underwent endovesical injection of botulinum toxin type A. All patients had negative urinalysis before they had submucous injection of botulinum toxin type A. A total of 8 patients who underwent endoscopic treatment with submucous injection of botulinum toxin, had vesico-ureteral reflux which was previously treated. Atrophic mucosa was found at postmenopausal patients which imposed hormonal therapy with estrogen. We used questionnaires to quantify and evaluate the quality of life score (Table I, Table II).

Table I. Quality of life evaluation.

<table>
<thead>
<tr>
<th>Symptom score</th>
<th>Quality of life score</th>
</tr>
</thead>
<tbody>
<tr>
<td>At urgency is it difficult to hold in your urine?</td>
<td>How much does this affect you?</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
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<tr>
<td>1</td>
<td>1</td>
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<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Do you have a problem with going to the bathroom often during the day?</td>
<td>How much does this affect you?</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
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<tr>
<td>1</td>
<td>1</td>
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<tr>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Do you wake up during the night to go to the bathroom?</td>
<td>How much does this affect you?</td>
</tr>
<tr>
<td>0</td>
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<tr>
<td>1</td>
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<td>2</td>
<td>2</td>
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<tr>
<td>3</td>
<td>3</td>
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<tr>
<td>Do you have urine leaks?</td>
<td>How much does this affect you?</td>
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<tr>
<td>0</td>
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<td>1</td>
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Adress for correspondence: lucanlucia@yahoo.com
Patients in group A after treatment showed an initial improvement of symptoms (Figure 1). At 3 months evaluation the favorable results were 63.63 %. At 6 months evaluation the number of patients with favorable results was reduced; thus only 54.54% had significant remissions of symptoms. Patients from group B after 2 weeks of treatment 85.71% had remission of symptoms. As a side effect we found incomplete urine retention evidenced by ultrasound measurement of post-micturition residues which under treatment disappeared at 1 month. One patient required re-injection of botulinum toxin because of persistent clinical signs.

Linear projection of symptom score marks clearly the difference between the two groups at 12 months (Figure 2). The quality of life score had a similar development of symptoms and the recurrence of clinical symptoms is reflected in the quality of life of these patients. Linear representation of the quality of life score of patients in group B shows, while maintaining the favorable effect of treatment, the difference is minimal between the two assessments. From the initial assessment it can be considered that these patients are cured. But the patients from group A show a deterioration in the quality of life with a recurrence of symptoms.

An objective method to diagnose overactive bladder represented by the uroflow-metry brings data that can be quantified and compared. We can make a differential diagnosis with pathology (eg Bladder outlet obstruction. In the case of an overactive bladder maximum bladder capacity is much reduced from normal. Under various treatments this can be improved even to reach normal levels. The average volume at patients with an overactive bladder from study was 267 ml (± DevSt 3). At 6 months following treatment the average volume showed a rise both for patients in group A but significantly from those in group B.

Bladder detrusor hyperreactivity and uninhibited bladder contractions may be recorded by uroflow-meters during bladder filling phase. Uroflow-metry is an objective method for assessing overactive bladder syndrome. If the female bladder normally has a capacity of up to 500-600 ml, for patients with overactive bladder the average was only 267 ml (± DevSt 3) (Figure 3). Uninhibited bladder contractions corresponding to OAB manifestations appear suddenly at an increased pressure in the bladder, so the initial assessment mean detrusor pressure was 63.4 m H2O registration (DevSt±2) (Figure 4).
Overactive bladder syndrome untreated or undiagnosed can properly engage, in economic terms, high costs for both the health system and for the patients.

**References**


