Clinical effectiveness of Abobotulinumtoxin A (Dysport®) therapy in the treatment of idiopathic overactive bladder syndrome

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Abstract

Introduction: Idiopathic Overactive Bladder Syndrome (OAB) is a highly prevalent urological disease, with profound consequences on the patient's quality of life, The aim of the study was to analyze the feasibility and clinical efficiency of a new, minimally-invasive treatment method: the submucosal injecting of Botulinum toxin type A - Abobotulinumtoxin A.

Material and methods: Two female patients were included in the study, both with a long history of Idiopathic OAB. According to the study protocol, they were evaluated both subjectively (using questionnaires) and objectively using flow-charts and urodynamic studies. After the study drug was adminstered, the patients were periodically re-evaluated at 1, 3 and 6 months.

Results: The first patient had a favourable outcome after the treatment, with a decrease in frequency, together with an increase in total bladder capacity and a consecutive improvement in the quality of life. For the second patient, there was an increase in her post-void residual volume that needed clean intermitent catheterisation. The patient gradually recovered her spontaneus micturitions afterwards.

Conclusion: The use of Abobotulinumtoxin A in the treatment of Idiopathic OAB est a feasible method, with promising therapeutical results. Still, there is a need for further studies on larger patient groups.

Key words: Abobotulinumtoxin A, botulinum toxin type A, idiopathic overactive bladder,

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Introduction

Overactive Bladder Syndrome (OAB) is a highly prevalent urological condition, affecting both males and females at rates up to 11.8% in Western European countries and Canada [1]. It has considerable effects on patients' quality of life, with a profound psychological, social, sexual, hygienic and economical impact [1,2]. Clinically, Idiopathic OAB is characterized by urgency with or without urinary urge incontinence (UUI) while urodynamically, OAB is demonstrated by Idiopathic Detrusor Overactivity (IDO), a series of involuntary detrusor contractions that appear in the filling phase [3]. UUI affects 30% of OAB patients, with an increased prevalence in the elderly with multiple co-morbidities [2,4].

Management of Idiopathic OAB is foremost performed using anticholinergic medication, with good therapeutic outcomes but with bothersome side effects, often leading to poor compliance: dry mouth, constipation, blurred vision, urinary retention, etc. [5,6,7,8].

Intradetrusor Botulinum Toxin type A (BTX) injections is a revolutionary treatment method that is currently used for Neurologic Overactive Bladder under the form of the precursor toxin Onabotulinumtoxin A (Botox® - Allergan, Irvine, CA, USA). Its efficiency is supported by results of numerous clinical trials, resulting in formal recommendations for its use in the treatment of Neurologic OAB. The use of Onabotulinumtoxin A in Idiopathic OAB is currently performed for research purposes with promising results [5,9,10,11].

Using different production processes, other toxin precursors have been obtained, like Abobotulinumtoxin A (Dysport® - Ipsen, Slough, Berkshire, UK) that is currently indicated for treating various dystonia and for cosmetic purposes but with official urological recommendations still pending. In the case of Idiopathic OAB, reported results for Onabotulinumtoxin A are very promising, many trials demonstrating a clear efficiency when compared to placebo [5,6,7,8,12,13]. However, studies concerning the efficiency of Abobotulinumtoxin A for treating IDO are scarce and with small patient numbers [14,11].

The aim of our pilot study was to assess the feasibility and clinical efficiency of the Romanian available Abobotulinumtoxin A in a series of Idiopathic OAB patients with urodynamically demonstrated IDO.

Methods

Selection protocol

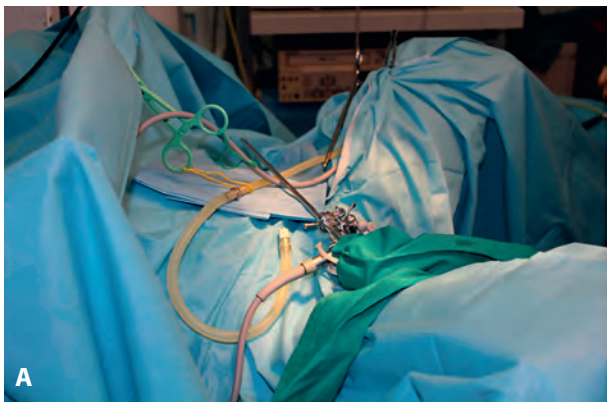
The study lot was selected from patients requesting urological consultations at the Clinic of Urology, Mureş County Hospital showing signs or symptoms of Idiopathic OAB. All patients over 18 years of age, diagnosed with Idiopathic OAB, that were either non-adherent (because of side-effects) or non-responsive to anticholinergic treatment were eligible for the trial. The final Idiopathic OAB diagnosis was set on urodynamics by the means of IDO. The main exclusion criteria were: a neurogenic bladder (Spina Bifida, Parkinson's disease and spinal trauma), a Post Void Residual volume (PVR) of 100 ml or more, the presence of Bladder Outlet Obstruction or detrusor underactivity by urodynamic study and the presence of urinary tract infection, lithiasis or malignancy of the urinary tract. Patients showing disorders of the neuromuscular junction (like amyotrophic lateral sclerosis) and dysphagia were also considered unsuitable for the study.

Baseline assessment

After verbal consent was obtained, the anticholinergic agent, if taken, was withdrawn for at least two weeks before the intervention. Symptoms were assessed using the International Consultation on Incontinence Questionnaire – short form (ICIQ-SF) and the Overactive Bladder (OAB V8) Assessment Tool questionnaires. Also, a 3-day flow-chart (FVC) was completed. For each patient a complete urodynamic study was performed.

Injection technique

Abobotulinumtoxin A was administred in a dose of 500 U as trigone-sparing submucosal injections in the bladder wall during rigid cistoscopy. The initial content of the vial (Dysport® 500UI) was reconstituted with 20 ml saline in a 25UI/ml solution that was injected in equal amounts at 20 different sites. As rigid cistoscopy is minimally invasive, antibiotic prophylaxis using Norfloxacin 400 mg was performed.


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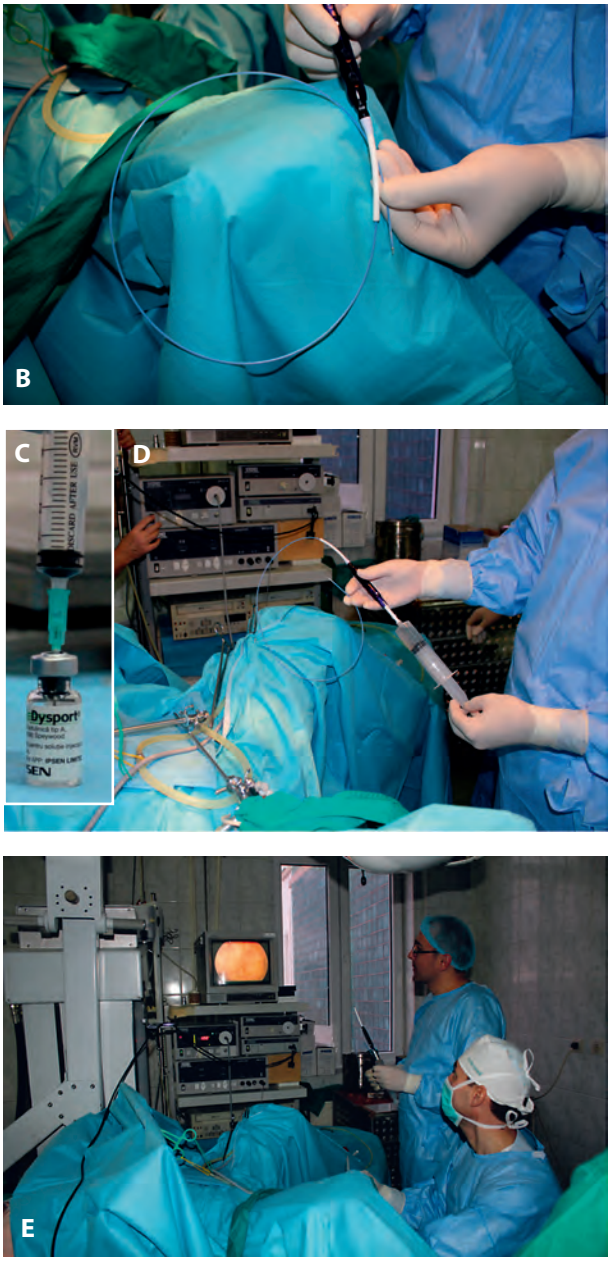


Fig. 1 The technique of the Abobotulinumtoxin A injections in the bladder wall: the patient is draped for cistoscopy (A), the injection needle is prepared (B), the product is reconstituted using saline (C), the solution is aspirated and the syringe is attached to the needle (D), the cistoscopy is performed meanwhile the product is injected (E).

Follow-up

For each patient, a systematic follow-up was performed at 1,3 and 6 months after the treatment. For each visit, the patient was assessed using the ICIQ-SF and OAB V8 questionnaires, a 3-day flow-void chart and an echography for evaluating the presence or quantity of Post Void Residual volume (PVR).

Results

We included a series of two patients into this pilot study. Both patients are females, aged 53 and 57, respectively.

The first patient had a long history of OAB and was treated using several anticholinergic drugs, which were gradually abandoned due to the disturbing side-effects. OAB symptoms were very intense (a majority of 5 point responses on the OAB-V8 questionnaire) but with no UUI. Concerning the patient's quality of life, OAB was considered responsible for a significant limitation in performing various sport activities but also in everyday life activities like shopping or going up the stairs.

According to protocol, a complete urodynamic study was performed. The patient presented a total bladder capacity of 207 ml, with an initial PVR of 43 ml. Urgency appeared at a capacity of 160 ml. During the filling phase, involuntary detrusor contractions appeared, confirming the diagnosis of OAB. The study drug was administered and it was well tolerated by the patient. There was no significant bleeding or pain after the procedure and the patient was discharged two days later.

At initial follow-up, the patient reported a significant decrease in frequency, as reflected by the flow-charts. After a start with around 12 micturitions daily of 100-120 ml each, the patient reached an average of 6-8 micturitions per day of about 200 ml each. Concerning the quality of life, favorable results were obtained resulting both in an improved work schedule and implication in more time-consuming leisure activities.

The second patient also has a long history of OAB that was also treated using anticholinergic drugs. The patient presented with urinary incontinence and was treated using a trans-obturatory sling in another clinical setting, treatment that proved to be ineffective. At presentation in our clinic, the patient presented a severe UUI that had important consequences on her quality of life, according to the ICIQ-SF and OAB-V8 questionnaires. At urodynamics, a total bladder capacity of 231 ml was found, together with a PVR of 30 ml. Involuntary detrusor contractions also appeared during the filing phase, confirming the OAB diagnosis. The study drug was administered and was initially well tolerated by the patient. Several days after the drug administration the patient presented with significant bladder pain that was treated using conventional analgetic therapy. The patient developed urinary retention a month after the intervention, with a PVR of 200 ml.

According to protocol, this was managed using clean intermittent catheterization, the patient gradually recovering normal micturitions together with a gradual decrease in PVR.

Discussion

We performed a pilot study in order to assess the feasibility and clinical efficiency of a new, minimally invasive method for treating OAB, a frequent urinary condition with important consequences on the patients' quality of life. The results of this pilot study show that this technique is feasible, together with the need for larger case series in order to obtain a clear image upon the role of Abobotulinumtoxin A in the treatment of Idiopathic OAB.

Sahai et al, in their study dedicated to the use of Onabotulinumtoxin A in Idiopathic OAB demonstrated a significant increase in total cystometric capacity (+144,69ml and +95,71ml at 4 and 12 weeks, respectively) when compared to placebo [13]. Urgency was reduced after 4 weeks of treatment in the BTX A group while there was an increase in the PVR at 4 weeks that gradually decreased and became insignificant at 12 [13].

Okamura et al performed a similar study using Onabotulinumtoxin A and reported results similar to those of Sahai et al, with improvements in frequency, urgency, UUI, and urodynamically-proven IDO. They also reported an initial increase in PVR for several patients, one of them requiring clean intermittent catheterization afterwards [4].

Concerning the adequate dose of Onabotulinumtoxin A, Dmochowski et al found similar therapeutical effects when using doses of 100 U or greater in the management of Idiopathic OAB. However, increased doses were related to increasing PVR ratios. The rates of clean intermittent catheterization were also dose-dependent [7].

A serious concern when administrating BTX-A is the site of injection together with the complications that may emerge. Manecksha et al explored the rates of side effects (the theoretical vesicoureteric reflux) when administrating Abobotulinumtoxin A according to the trigone-sparing and trigone-including techniques [14]. Their study showed improved performance rates in the trigone-including group when compared to the trigone-sparing one, with no cases of subsequent vesicoureteric reflux [14].

Although the literature studies on the use of Abobotulinumtoxin A in the treatment of OAB are scarce, we consider that our results are promising and a full-scale clinical trial could be initiated.

Conclusion

Abobotulinumtoxin A is a new, promising and feasible treatment method for Idiopathic OAB Syndrome with good results both locally and on the patient's quality of life. However, there is a need for further studies on larger patient groups.

Acknowledgements:

„This paper is partially supported by the Sectorial Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/89/1.5/S/64153".

This study was partially supported by a research grant offered by the Târgu-Mureş University of Medicine and Pharmacy.

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Rezumat

Introducere: Sindromul de Vezică Hiperactivă Idiopatică (OAB) este o boală urologică cu prevalenţă mare, cu implicaţii profunde asupra calităţii vieţii pacientului. Scopul studiului a fost de a analiza fezabilitatea şi eficienţa clinică a unei metode noi de tratament minim invaziv al OAB idiopatice: administrarea intradetrusoriană de toxină botulinică de tip A - Abobotulinumtoxin A.
Materiale şi metode: Au fost incluse în studiu două paciente, ambele cu antecedente de OAB Idiopatică. Conform protocolului de studiu, ambele au fost evaluate atât din punct de vedere al simptomatologiei (prin chestionare) cât şi obiectiv prin intermediul calendarului micţional şi a studiului urodinamic. După administrarea medicamentului de studiu, acestea au fost reevaluate periodic la 1, 3 şi 6 luni.
Rezultate: Prima pacientă a prezentat o evoluţie favorabilă în urma tratamentului, cu scăderea frecvenţei micţiunilor concomitent cu creşterea capacităţii vezicale şi îmbunătăţirea consecutivă a calităţii vieţii. În cazul celei de-a doua paciente s-a înregistrat iniţial o creştere a reziduului postmicţional, fiind necesară efectuarea autocateterizării intermitente, aceasta reluându-şi treptat micţiunile spontane.
Concluzii: Utilizarea Abobotulinumtoxin A în tratamentul OAB Idiopatice este o metodă fezabilă, cu rezultate terapeutice promiţătoare. Totuşi, este necesară efectuarea de studii ulterioare, pe loturi mai mari de pacienţi.

Cuvinte cheie: Abobotulinumtoxin A, toxina botulnică de tip A, vezică hiperactivă idiopatică