SKILL AND TALENT

Botulinum toxin in the failure of high urinary diversion closure


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KEYWORDS
Botulinum toxin; Urinary diversion; Posterior urethral valves

Abstract
Introduction: The closure of urinary diversions performed on newly born infants has a notable failure percentage in patients with bladder disease. We present the use of botulinum toxin as a useful and minimally invasive alternative to treat these patients.

Materials and methods: We present two patients with a single kidney and with posterior urethral valves (PUV), in whom it was necessary to perform a ureterostomy due to chronic kidney disease. In both patients, the subsequent attempt to close the diversion failed. Aged 4 and 10 years respectively, they presented bladders commonly known as "dry bladders", with a low capacity (20 and 110 ml), bad adaptation (1.5 and 3.1 ml/cm H₂O) and high opening detrusor pressure. A 10 UI/kg botulinum toxin A puncture was applied in the detrusor on one and two occasions respectively, prior to the closure of the diversion.

Results: Neither of the patients suffered clinical or ecographic worsening after the closure of the diversion and their kidney function continued without change with respect to the first diversion after 1 and 4 years of follow-up respectively. One year after the surgical procedure, video urodynamics showed a significant improvement in bladder capacity (451 and 250 ml), in adaptation (20.4 and 81.9 ml/cm H₂O) and in the opening detrusor pressure.

Conclusions: The closure of high urinary diversions has a high failure percentage in infants with pathological high-pressure bladders. Botulinum toxin may be useful as bladder treatment prior to closure of the diversion, especially in patients with a single kidney.

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PALABRAS CLAVE
Toxina botulinica; Derivación urinaria; Valvas de uretra posterior

Toxina botulinica en el fracaso del cierre de derivaciones urinarias altas

Resumen
Introducción: El cierre de las derivaciones urinarias realizadas en la edad neonatal tiene un no despreciable porcentaje de fracasos en pacientes con patología vesical. Presentamos el uso de toxina botulinica como alternativa útil y mínimamente invasiva para el tratamiento en estos pacientes.

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Introduction

The urinary diversions at different levels of the urinary tract have been, for years, the treatment of choice in selected patients with pathologies involving high pressures in the upper urinary tract and that, either because of the patient’s age, the underlying disease, or the child’s general state, surgical correction of the problem was not possible. Today it remains an effective, useful and necessary treatment in selected cases, although its indications have decreased and minimally invasive treatments have occupied part of its space. The pathologies treated are as diverse as neurogenic bladder, posterior urethral valves (PUV), vesicoureteral reflux or high-grade Prune-Belly syndrome.

Some of the problems that we encountered at the time of performing definitive treatment, together with the closure of the diversion are the urodynamic changes that have occurred in these bladders {AQ: for edit}. Thus, we are faced with poorly compliant bladders, low capacities, and high opening detrusor pressure. Although these changes revert in most patients after the closure of the diversion, in those in whom it has remained opened for more years, or the underlying disease is PUV or neurogenic bladder, we found that up to 25% of the closures fail.

So far, bladder augmentation (enterocystoplasty or other technique) was the only option that allowed for the closure of the urinary diversion in these children, with the aim to improve their quality of life without compromising renal function. The use of botulinum toxin (BT) for the bladder treatment of patients with failure to close their urinary diversion is not described, although there exist prospective studies supporting its safety and usefulness in those bladders with abnormalities implying increased pressures on the urinary system. We propose the use of BT in two children with a single kidney with PUV to achieve permanent ureterostomy closure after a previous failure.

Materials and methods

The first patient, aged 4 years, was treated at another center with PUV neonatal endoscopic fulguration. During the follow-up, the functional absence of the right kidney with severe left ureterohydronephrosis and progressive renal failure was confirmed, so right nephrectomy and left ureterostomy were performed at 4 months of life. The postoperative development was satisfactory and renal function normalized. At 2 years of life, closure of the diversion was attempted unsuccessfully, as the patient went into renal failure with worsening of his ureterohydronephrosis. On arrival at our center, cystoscopy observing a good urethral caliber along its entire course was performed. In videourodynamic studies, a bladder capacity (BC) of 20 ml is observed, with a maximum detrusor pressure (MDP) of 28 cm H\textsubscript{2}O and an adaptation of 1.5 ml/cm H\textsubscript{2}O, with a vesicoureteral reflux to solitary left kidney and right ureteral remnant (Fig. 1).

The second patient, aged 9 years, was treated for PUV at neonatal age due to renal failure, with ultrasound images of left renal dysplasia and right severe ureterohydronephrosis, vesicostomy being performed. Given the poor clinical, ultrasound, analytical progress, and renal gammagraphy with left renal functional cancellation, we decided to perform right ureterostomy at 2 months of life. At 2 years of life, left nephrectomy, bladder augmentation with left ureter, and closure of the urinary diversion were indicated, failing a month after surgery as the patient went into uncontrollable renal failure and severe right ureterohydronephrosis. At the time of the assessment, he showed mild renal insufficiency, with a grades II–III right single kidney hydronephrosis. In the videourodynamics, the BC was 110 ml, with a MDP of 59 cm H\textsubscript{2}O, an adaptation of 3.1 ml/cm H\textsubscript{2}O, and a pressure of fluid loss (PFL) of 49 cm H\textsubscript{2}O.
Results

In the first patient, 10 IU/kg of botulinum toxin were injected in the detrusor associating endoscopic treatment (STING) of the bilateral vesicoureteral reflux in the same procedure. Two months after the intervention, new videourodynamics, which observed an increase in bladder capacity up to 90 cc, with an adaptation of the detrusor of 2.6 ml/cm H$_2$O, with no reflux into the left ureter or uninhibited contractions was performed. Thus, we indicated the closure of the ureterostomy with double J reno-vesical stent placement that was removed at 3 weeks without complications. During the follow-up after 4 years, we found no worsening in ultrasound, gammmagraphic or analytical findings, currently remaining with a serum creatinine of 0.58 mg/dl. The child acquired control of the urinary sphincter at 5 years. The patient lived with IBC and antibiotic prophylaxis for 6 months until their withdrawal, and he suffered no urinary infections. Urodynamic studies performed periodically show good growth in bladder capacity with an improvement of the adaptation (Fig. 1). One year after the closure, the patient already had a BC of 183 ml, with an adaptation of 30.9 ml/cm H$_2$O, a MDP in the filling phase of 10 cm H$_2$O, and an opening detrusor pressure (ODP) of 20 cm H$_2$O, without vesicoureteral reflux (Fig. 2). The urodynamic changes remain today.

The second patient began treatment regimen with anti-cholinergics and a detrusor injection of 300 IU of botulinum toxin-A was performed, achieving a decrease in the MDP to 28 cm H$_2$O, with improved adaptation but with no increase in bladder capacity, so at 6 months, 300 IU of Botox$^a$ were re-injected. A program of intermittent bladder catheterization (IBC) was started three times/day, getting 100–150 ml of urine in each probing. The control videourodynamics presented a great improvement in BC (175 ml), adaptation (27.1 ml/cm H$_2$O) and ODP (18 cm H$_2$O), so we decided to close the ureterostomy. After the closure, the number of bladder catheterizations was sequentially reduced as there was no residue in post-void probing, currently keeping dry 1 year after the operation and with a single daily catheterization. The renal function has remained at the previous values (0.91 mg/dl), as well as ultrasound findings. The urodynamics 1 year after the closure shows a BC of 451 ml, an adaptation of 81.9 ml/cm H$_2$O, a MDP of 3 cm H$_2$O, and an ODP of 2 cm H$_2$O (Fig. 3).

Discussion

Urinary diversions remain one of the treatments of choice in a variety of pathologies despite the progress in recent years of minimally invasive and endourological techniques. Febrile urinary tract infections and increased serum creatinine levels in unweaned babies with neurogenic bladder, PUV, or severe bilateral vesicoureteral reflux are considered by many authors today as an indication for vesicostomy or bilateral ureterostomy that decompresses the upper urinary system. Secondarily, bladders treated like this will have urodynamic changes marked by a lower bladder capacity compared to the general population, despite the improvement in distensibility that occurs especially in patients with neurogenic bladder or PUV.

There are several studies examining the reversibility of these changes after the closure of the urinary diversion. About 90% of the patients will show a rapid increase in bladder capacity, with an improvement in distensibility and opening detrusor pressure that will allow us to maintain acceptable pressures in the upper urinary system. This percentage will be around 100% when the diversion is due to a high-grade vesicoureteral reflux. However, there is a group of patients whose bladders will not respond adequately to the closure, with bad adaptations and high opening detrusor pressure, causing damage to the kidney that will force us to associate other treatments or even to reopen the urinary diversion, as in the two cases presented. This is especially common in patients with neurogenic bladder and PUV, getting almost to the 25% failure rate. In addition, our patients had a high urinary diversion (ureterostomy) that was necessary to perform since the vesicostomy did not evolve appropriately, which leads us to believe that their urodynamic disorders were more severe.

Currently, we do not think that urinary diversions provide children or adolescents with an adequate quality of life, although they have done so in earlier stages of life. Therefore, the patients and their families come to us for solutions. Urinary continence is a need for them, feeling that without
it they cannot feel like their classmates or friends; consequently, that is our goal as well. Although these solutions must not jeopardize the patient’s urinary function, past failures should not be an obstacle to propose new options to our patients. In our cases, both children had a single kidney, so a poor progress after the ureterostomy closure was quickly reflected in its going into renal failure (monitored by the creatinine values in the blood), with the risk of not being reversible. However, both families demanded solutions to achieve continence and the disappearance of the ureterostomy. The therapeutic alternatives to the present are based on the use of anticholinergics and intermittent bladder catheterization, resorting to bladder augmentation for those cases in which these measures were not enough. The emergence of BT opens a new arsenal of treatment that can allow us to avoid enterocystoplasties and their medium- and long-term complications.8

We have not found references to the use of BT as a salvage treatment in the failures of the closures of high urinary diversions in the literature. However, it has been used for some years for the treatment of neurogenic bladder, in which it induces relaxation of the detrusor muscle through interaction at presynaptic level of cholinergic innervation, and has potential effects on the urothelial receptors.9 In our cases, the doses used, the puncture sites, and the solution employed are the same as those used in the neurogenic bladder, 10 IU/kg up to a maximum of 300 IU.10

BT-A has been used in many fields of medicine for years, so like other groups, we consider it a safe treatment.11,12 The side effects are mild and infrequent, although the production of antibodies against the toxin is described. This is more important in the cases of non-responder patients, and it may be among the possible causes of non-response. However, it seems that the current Botox® preparation minimizes the body’s immune response regarding the original one.12

The closure of the urinary diversions has a failure rate, especially in patients with severe bladder and infravesical pathology, which force us to associate it with other more
aggressive techniques if we want ‘‘undiversion’’ and, thus, to improve their quality of life. Therefore, we believe that BT could provide us with an easy, safe, reliable and little aggressive alternative for the bladder treatment of these cases.

Conflict of interest

The authors have no conflicts of interest to declare.

References