URODYNAMIC APPROACH TO FEMALE URINARY INCONTINENCE REFRACTORY TO TREATMENT WITH ANTICHOLINERGICS

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Summary.- OBJECTIVES: The administration of empirical anticholinergic treatment is widespread in women with urinary incontinence and has produced varied results. The objective of our paper is to determine the effectiveness of anticholinergics for the treatment of female urinary incontinence and to determine by urodynamic the possible causes that may explain the resistance to anticholinergics to obtain urodynamic predictors of success or failure.

METHODS: We evaluated 182 women over 14 years of age with urinary incontinence that had previously been treated with anticholinergics for at least three months. The patients underwent a complete medical history including clinical history, physical examination, and urodynamic and lower urinary tract video-radiologic studies. Statistical analysis was performed using SPSS 17.0 for Windows.

RESULTS: Clinical therapeutic efficacy was demonstrated in 39.6% of cases. Cystometric bladder capacity was decreased in 89.2% of patients that did not improve clinically with anticholinergics (p=0.01). Detrusor overactivity was urodynamically demonstrated in 51% of cases (p = 0.05) among patients without clinical improvement with anticholinergic treatment. This hyperactivity was demonstrated during early bladder filling (<100ml). Urodynamic stress urinary incontinence (SUI) was demonstrated in 26.5% of patients without clinical improvement after treatment (p=0.04). Lower urinary tract obstruction was urodynamically demonstrated in 20.6% of patients with no clinical improvement (p=0.05). Urodynamic data did not demonstrate a relationship between detrusor overactivity, a high-grade cystocele (37.4% of total), and irregular bladder morphology (11.5% of total).

CONCLUSIONS: It is important to conduct urodynamic study before starting anticholinergic treatment of females with urinary incontinence to identify therapeutic data of poor prognosis, such as SUI and lower urinary tract obstruction, thus optimizing the therapeutic efficacy of anticholinergics.

Keywords: Urinary incontinence. Anticholinergics. Urodynamics study.
Resumen.- OBJETIVO: Está muy difundida la aplicación del tratamiento anticolinérgico empírico en la incontinencia urinaria femenina con diferentes resultados. En nuestro trabajo se ha intentado conocer la eficacia de los anticolinérgicos en el tratamiento de la incontinencia urinaria femenina, así como determinar urodinámicamente las posibles causas que explican la resistencia al mismo e intentar obtener predictores urodinámicos de éxito o fracaso.

MÉTODOS: Se han evaluado 182 casos de mujeres, mayores de 14 años, con incontinencia urinaria, que habían sido tratadas con anticolinérgicos previamente durante al menos tres meses, a las que se les realizó historia clínica completa con anamnesis, exploración física, estudio urodinámico y videorradiológico del tracto urinario inferior. El análisis estadístico de los datos se realizó con el programa SPSS 17.0 para Windows.

RESULTADOS: Se demostró eficacia terapéutica clínica en el 39,6% de los casos. La capacidad vesical cistomanométrica estaba disminuida en el 89,2% de las pacientes que no mejoraron clínicamente con los anticolinérgicos (p=0.01). La hiperactividad del detrusor fue demostrada urodinámicamente en el 51% de los casos (p=0.05) entre las pacientes sin mejoría clínica con el tratamiento anticolinérgico. Esta hiperactividad se demostró precozmente en el llenado vesical (<100ml). Se demostró urodinámicamente IUE en el 26,5% de las pacientes sin mejoría clínica postratamiento (p=0.04). Se demostró urodinámicamente obstrucción del TUI en el 20,6% de los casos sin mejoria clínica (p=0.05). Los datos videourdinámicos no demostraron una relación entre la hiperactividad del detrusor, el cistocele de alto grado (37,4% del total) y la morfología vesical irregular (11,5% del total).

CONCLUSIONES: Es importante la realización de un estudio urodinámico previo al tratamiento anticolinérgico de la incontinencia urinaria femenina para identificar los datos de mal pronóstico terapéutico como son la incontinencia urinaria de esfuerzo y la obstrucción del tracto urinario inferior, optimizando así la eficacia terapéutica de los anticolinérgicos.

Palabras clave: Incontinencia urinaria. Anticolinérgicos. Estudio urodinámico.

MATERIAL AND METHODS

A retrospective study of 182 medical records of female patients greater than 14 years of age with UI was conducted in which the patients underwent a complete UDS and videocystography and were treated with anticholinergics for at least three months.

All UDS were performed following the protocol for urodynamics set by the International Continence Society (ICS) (Schafer et al., 2002) (2). A Medical Measurement SystemsSolar instrument was used to perform the UDS, and a General Electric machine was used to perform the videocystography. The urodynamic terminology used here follows the recommendations of the ICS, except when specified. We analyzed the following variables: demographics, symptoms, physical examination, video urodynamic tests, and response to treatment with anticholinergics. Prior to the completion of the UDS and videocystography, data were collected regarding the age, duration of symptom for which they sought consultation, type of urinary UI, sensation of urinary urgency, increased urinary frequency during the day and night, nocturia, and hypogastric pain. Patients who had a daytime urinary frequency of every two hours or greater (8 times a day) and nocturnal urinary frequency in those who got up to urinate at least two times during the night were considered to have increased urinary frequency during the day and night, respectively. Also noted was whether patients had a “feeling of vaginal...
bulge”, if they have had urinary tract infections (UTIs), and if they had constipation or voiding symptoms (i.e., voiding difficulty, decrease in urine flow, interrupted urine stream, and sensation of incomplete voiding). Regarding treatment with anticholinergics, the patient’s clinical response and whether a specific type of side effect was emphasized.

Statistical analysis of the data was performed using SPSS 17.0 for Windows. The statistical methods used included descriptive statistics of quantitative variables (DESCRIPTIVE procedure), descriptive statistics of qualitative variables (FREQUENCIES procedure), a Kolmogorov-Smirnov test (NPAR TESTS procedure), contingency tables for the relationship between qualitative variables (CROSSTABS procedure and chi square (χ²)), and an analysis of variance (ANOVA) (ONEWAY procedure, Snedecor’s F-distribution test, and Bonferroni test).

RESULTS

• AGE

Of the women in our study, 73.6% were > 55 years old, and 87.4% had > 1 year duration of symptoms. Approximately 23.6% of women were between 55 and 64 years old, 24.7% were between 65 and 74 years old, and 25.3% were > 75 years old.

• SYMPTOMS

Figure 1 shows the different types of UI of our series. Although 4.4% of the total patients did not attend consultation for UI, they did so for irritative voiding symptoms, and therefore, they were also included in this study (Figure 1).

Patients with irritative symptoms and symptoms of UUI or mixed UI, sense of urgency, and urinary frequency during the day and night were included under the OAB syndrome, which corresponded to 48.4% of the cases analyzed in our series. Most patients (89.6%) reported a feeling of urinary urgency. In addition, the majority of patients had symptoms of urinary frequency during the day or at night (76.9% and 62.6%, respectively). Symptoms are summarized in Figure 2.

• FLOWMETRY

Flowmetry was performed in all patients. No residual urine was observed in 81.3% of cases or was not considered significant (<20% of the voided volume) in 8.3% of cases. Thus, there was no significant residual urine in 89.6% of cases (Figure 3).

• CISTOMETRY

Of the 182 patients, 82.4% had decreased bladder capacity (<300 ml). Involuntary contractions (IC) of the detrusor were observed in 46.2% of cases, and 88.1% of cases had an amplitude between 0 and 49 cmH₂O. Regarding the bladder capacity at which the contractions began, the highest percentage (52.4%) of cases corresponded to between 0 and 100
ml, whereas the remaining 47.6% were greater than 100 ml. In 79.7% of cases, IC began at less than 200 ml, with the highest percentage (32.1%) occurring between 51 and 100 ml. Of the patients who had IC of the detrusor, 97.6% reported urge incontinence, and UI was observed during the filling phase in 81% of cases. Of the 182 cases in the series, it was shown that 20.9% had UI while coughing. There were no cases of diminished bladder compliance (all patients had normal bladder compliance below 30 cmH$_2$O). During the detrusor pressure/flowmetry test, 68.7% of the patients voided the bladder by abdominal press.

Lower urinary tract obstruction (LUTO) was observed in 16.5%, with AUR (average urethral resistance) values of $\geq 20$ cmH$_2$O during voiding. Regarding the involvement of detrusor isotonic contractility (negative values in $W_{80}$ - $W_{20}$ (contractility at 80% of voiding minus contractility at 20% of voiding)), it was observed that 23.1% of patients were affected.

Figure 4 shows the different urodynamic findings of this patient series.

- **VIDEOCYSTOGRAPHY**

In 63.7% of the patients, a grade 1 cystocele at rest and a grade 2 or 3 in Valsalva (90.2%) was observed. The most common morphology was a smooth bladder (88.5%).

- **URODYNAMIC DIAGNOSES**

A diagnosis of sensory urgency, defined as a sensation of urinary urgency without IC of the detrusor with decreased bladder capacity and voiding by abdominal press, was reported for 29.7% of the patients. LUTO was observed in 16.5% of the cases. The highest percentage of patients, 84.6%, had normal or slightly decreased urinary flow (47.8% and 36.8% respectively) compared to those patients that clearly showed a decreased (3.3%) or greatly diminished (12.1%) urinary flow.

- **ANTICHOLINERGIC TREATMENT**

Data from our study showed limited therapeutic efficacy of anticholinergics. Only 39.6% of cases indicated positive results, whereas 56% reported no improvement after completion of the treatment. In addition, the treatment was discontinued in 4.4% of cases due to a lack of tolerance (Figure 5).

The association between the clinical improvements with anticholinergics variable with all other variables was analyzed.

A significant incidence of LUTO (20.6%, $p=0.05$) for patients who did not improve with anticholinergics was found. This could explain the presence of detrusor overactivity secondary to LUTO.

In our study, it was observed that patients who responded adequately to treatment with anticholinergic

![FIGURE 3. Residual urine.](image1)

![FIGURE 4. Urodynamics findings (% patients).](image2)
had a significantly higher bladder capacity (25%, \( p=0.01 \)) within the normal range compared to those who reported no improvement (10.8%). Furthermore, a statistically significant difference (\( p=0.05 \)) in IC of the detrusor between patients who improved with anticholinergics and those that did not (36.1% vs. 51%) was observed. Lastly, we observed a statistically significant reduction (\( p=0.009 \)) in the reproduction of the symptoms of UTIs in women for whom anticholinergics were effective (8.3% vs. 23.5%).

All of these data may be related to therapeutic efficacy of anticholinergics. The relationship between the effectiveness of anticholinergic therapy and urodynamic demonstration of SUI was statistically significant (\( p=0.04 \)); e.g., SUI was observed in 26.5% of patients that did not improve with treatment compared to 13.9% that noticed improvement with anticholinergics (Figure 6).

The best results of the series (49.6% of clinical improvement with anticholinergics) were obtained in
those patients in whom urodynamic reproducibility of UI symptoms or lower urinary tract obstruction were not observed (i.e., patients whose main symptoms were “irritative”). In contrast, the worst results (94.7% with non-therapeutic effects) were obtained in those patients where UI was demonstrated urodynamically without being associated with sensory urgency (i.e., patients with SUI). Another group that showed high resistance to treatment (72%) was that of patients in whom UI was not demonstrated during the urodynamic study but a lower urinary tract obstruction was observed (Figure 7).

Anticholinergic side effects after treatment were not registered in 58.2% of cases in our study. Side effects reported by patients were mild and consisted of constipation and dry mouth in 36.3% and 1.1% of cases, respectively. Treatment was discontinued due to side effects in 4.4% of the cases (Figure 8).

**DISCUSSION**

In our study, patients with UUI or mixed UI comprised 85.2% of the total cases. According to the associated symptoms, sense of urgency, daytime urinary frequency, and nocturnal urinary frequency was observed in 89.6%, 76.9%, and 62.6% of cases, respectively. The patients with the aforementioned symptoms were included in the OAB group, which corresponded to 48.4% of patients in our series. These symptoms usually suggest the existence of involuntary contractions of the detrusor. The diagnosis of OAB is usually performed by the patient’s clinical status, although we need to consider that detrusor overactivity can only be observed by performing a urodynamic study (Abrams et al. 2002) (4) and that the results are not always correlated.

Previous urinary tract infections are considered to be a frequent cause of UI in several female UI classifications (Sierra Moreno et al., 2007) (5); however, this factor was absent in 90.7% of cases in our series. A lower UTI is the main suspect in the differential diagnosis of women with daytime and nighttime urinary frequency and urgency. By definition, the diagnosis of OAB excludes the existence of UTI (Abrams, et al., 2002) (1). Previous studies have demonstrated a relationship between detrusor overactivity and the existence of significant bacteriuria. Cystitis found in routine bacterial cultures (>10^5 colonies /ml) was demonstrated in 6% of patients with involuntary contractions (IC) of the detrusor that had been subjected to a control UUI cystometry; this finding corresponded to 1% of the total (Moore et al., 2000) (6) and was consistent with other studies (Bhatia & Bergman, 1986) (7) (Choe, Lee, & Seo, 2007) (8).

Khasriya et al. (2008) (9) studied the prevalence of bacteriuria in women with irritative bladder symptoms according to the described microbiological thresholds. These authors reported a significant increase in bacteriuria by using a lower threshold (>10^2 colonies/ml; 30%) compared to the traditional microbiological cutoff (>10^5 colonies/ml; 12%) (Khasriya, et al. 2008) (9). Further studies are needed to substantiate these findings because currently, there are no action protocols for the management of bacteriuria with a low number of colonies (Rahn et al, 2005) (10). The role of low-count bacteriuria in women with UI and/or sense of urgency and increased urinary frequency without dysuria requires further clarification. To date, there is only one published study that corroborates the theory that bacteriuria with low colony counts was prevalent in women with OAB, as cited above (Khasriya, et al., 2008) (9).

In addition to UDS, there are other methods to diagnose detrusor overactivity. Some authors relate the presence of pelvic prolapse with the finding of detrusor overactivity. De Boer et al. (2010) (11) concluded that the presence of a prolapse could be considered a risk factor for OAB. In our series, a predominance of small cystocele (grade 1 cystocele at rest in 64% of cases and grade 2 with Valsalva in
urgency was defined as the urge to urinate small amounts of urine, which has its origin in the stimulation of afferent sensory pathways (Abrams, Cardozo, Fall, et al., 2002) (4). Clinically, sensory urgency is usually associated with other functional symptoms of the lower urinary tract, such as increased urinary frequency (and may even be a cause of UI), difficulty voiding, and suprapubic or hypogastric discomfort that are relieved by urination (Virseda et al, 2002) (14). The diagnosis of sensory urgency is urodynamic and is conducted by performing a cystometry. A differential diagnosis with motor urgency must be established because both motor and non-motor urgency have similar clinical symptoms (Robinson & Shea, 2002) (15). In cases of sensory urgency, should not have been prescribed the anticholinergic, so this is a factor of poor prognosis in the decision tree.

In our study, the urodynamic diagnosis of obstruction in the case of no response to anticholinergics may explain the persistence of detrusor overactivity. A previous urodynamic diagnosis of obstruction would have avoided prescribing the drug and instead advised the therapeutic removal of the obstruction. It would be interesting to study how many patients from those with involuntary detrusor contractions correspond to lower urinary tract obstruction, which will be considered for future revisions.

Although it is known that anticholinergics act during the bladder-filling phase, some authors consider that the use of anticholinergics may produce an increase of residual volume as a side effect. This has been reported in the literature mainly with the use of oxybutynin, but it is also referenced with the use of other anticholinergic drugs. In our study, treatment with anticholinergics was not associated with significant residual urine in 89.6% of cases. Accordingly, the therapeutic criterion for avoiding the recommendation of anticholinergic therapy in patients with risk of post-void residual could be reviewed. On the other hand, the absence of residual urine rules out the presence of overflow incontinence.

The best answer would be in patients who not reproduce the symptom of incontinence and had no other risk factors for treatment failure, such as stress urinary incontinence, lower urinary tract obstruction, sensory urgency and reduced bladder capacity.

CONCLUSIONS

It has been shown that a frequent cause of therapeutic failure of anticholinergics, is the absence of an indication based on the pathophysiology of symptoms presented by patients and is therefore required an etiopathogenic approach to treatment.
It is essential to conduct an urodynamic study prior to the anticholinergic treatment of urinary incontinence in women, so as to be able to recognize wrong therapeutic prognosis data such as effort-related urinary incontinence and lower urinary tract obstruction. This way, the therapeutic efficacy of anticholinergics would increase notably.

REFERENCES AND RECOMMENDED READINGS
(*of special interest, **of outstanding interest)


