Urodynamic and clinical evaluation of postmenopausal women with stress urinary incontinence before and after cyclic estrogen therapy

V. R. V. Góes, M. G. F. Sartori, E. C. Baracat, G. Rodrigues de Lima, M. J. B. C. Girão

Gynecology Department, Federal University of São Paulo (Brazil)

Summary

Objective: The pupose of this study was to evaluate the effects of isolated cyclic estrogen therapy in menopausal women with stress urinary incontinence, and thus without the effects of progesterone.

Methods: Nineteen menopausal patients with stress urinary incontinence were selected and submitted to anamnesis and physical, gynecological and urodynamic examinations. The group was homogeneous in relation to parity, body mass index and degree of urogenital prolapse. All the patients received conjugated equine estrogens orally, at a dose of 0.625 mg, for 21 days each month. After three months the clinical and urodynamic evaluations in relation to urine loss, were performed again.

Results: Of the patients 57.9% were satisfied with the treatment. The urodynamic parameters remained unaltered in 36.85% of the patients.

Conclusion: Our results show that estrogen is important for stress urinary incontinence in postmenopause, specially in patients without cystocele or with cystocele of degree I or II.

Key words: Urinary incontinence; Estrogen replacement; Urodynamic.

Introduction

With the increase in life expectancy women are living around a third or more of their lives after menopause, and are therefore submitted to the prejudicial effects of estrogen deprivation for a substantial part of their lives. Of these effects those on the urinary tract, and in particular urinary incontinence stand out [1, 2].

The bladder and proximal urethra have endodermic origins, while the bladder trigone, formed from the mesonephric duct, has mesodermic origins [3]. Thus, the vagina and distal urethra originate from the urogenital sinus and therefore, steroids, and in particular estrogen receptors have been found in both [4].

Hormonal receptors have been identified in the lower urinary tract and in the pelvic musculature [3, 5], and the action of estrogens on the alphaadrenergic receptors found in the periurethral musculature, increase their number and sensitivity [6, 7].

There are various factors necessary for the maintenance of urinary continence, but prominent among them are the integrity of the urethral sphincter system, neck of the bladder and the proximal urethra [8].

The results of estrogen therapy on postmenopausal urogenital alterations are controversial, since the evaluation criteria, the types of hormones employed, the routes of administration and the dosages are widely varied [9, 10].

Thus various clinical studies have concluded that women with urinary symptoms such as dysuria, urgency and incontinence, when treated with estrogens present considerable improvement during the estrogen replacement [11, 12]. However, neither Wilson *et al.* [13] nor Cardozo [14] could confirm this finding.

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Through the use of urodynamic studies it is possible to obtain more objective diagnostic data which permit more adequate comparisons of the various treatments [14]. It has been observed that, with the advancement of age, there is a significant drop in the urethral closing pressure, a smaller bladder capacity and an increase in the postmicturition residue [15-17].

An increase in the urethral pressure profile after hormone replacement was observed in women treated either orally or vaginally with estrogens [18].

Sartori *et al.* [10] observed that oral estrogen and progesterone therapy, in post-menopausal women with stress urinary incontinence, promoted significant clinical improvement, as well as increasing the bladder capacity, the average urinary flow and the maximum closing pressure of the urethra.

In relation to the progesterones, Raz *et al.* [19] noted that their administration in female dogs caused stimulation of the beta-adrenergic receptors of the urethra and a consequent reduction in urethral pressure. However Rud [20] did not observe these alterations in humans.

Although the urodynamic results of hormone replacement in the treatment of stress urinary incontinence in postmenopause have not been uniform, the symptoms have improved in a great majority of studies [10, 18].

Therefore, various authors have sought to analyze the alterations that occur in the urethral mucosa and in the periurethral vascularization, musculature connective tissue after the use of steroid hormones, which could contribute to postmenopausal urinary continence [20].

Suguita *et al.* [21] observed that estrogen replacement in castrated rats, whether or not associated with progesterone, promoted metaplasia, hyperplasia and an increase in the thickness of the lower urinary tract epithelium.

The large periurethral blood vessels, disproportionate to the need to supply blood to the urethra, form a type of spongy body with an erectile function [22], through which intravascular pressure is transmitted mechanically to the urethra, obstructing it and impeding, in this way, the loss of urine. This vascular plexus is influenced by estrogen, which not only increases the passage of blood to the urethral cells, but also the arterial pulse [19]. However, progesterone reduces the effects observed with estrogens [23].

Endo *et al.* [24] observed that isolated estrogens increased the count of bladder and urethra blood vessels in castrated adult rats in relation to a group which only received placebo. However, association with progesterones also increased the number of blood vessels, although to a lesser extent.

Jármy-Di Bella *et al.* [25], used digitized color-Doppler velocimetry to study the periurethral blood vessels of fertile and postmenopausal women with and without stress urinary incontinence. They showed that the number of periurethral blood vessels, the systolic peak and diastolic minimum were less in the incontinent women after menopause, with a high incidence of a final diastole of zero, reflecting a high resistance to blood flow and therefore difficulty in carrying blood to the areas irrigated by these vessels.

Girão *et al.* [26] showed that estrogen replacement increased the number of periurethral blood vessels, systolic peak and diastolic minimum, with a tendency to reduce vascular resistance.

It has been shown that there are estrogen and androgen receptors in the skin fibroblasts which suggests that these collagen producing cells are susceptible to these hormones. On the other hand, a significant correlation was found between the quantity of collagen in the skin and the function of the urethral sphincter, confirming that estrogen therapy in postmenopause improves the urethral function due to an increase in the quantity of collagen in the urogenital tissues [27, 28].

Analysis of the quantity of muscle fibers and collagen on the urethral musculature of castrated rats that receive estrogen, medroxyprogesterone acetate or both, has shown that isolated estrogen replacement favors a reduction in infiltrated collagen in the muscles. However, it induces a significant increase in the muscle fibers while progesterone does the opposite. Thus, the administration of progesterone does not appear to be ideal for improving the muscle layer of the urethra during hypoestrogenism [29].

As there are still questions regarding hormone replacement for the treatment of stress urinary incontinence, the present study was performed to evaluate the effects of isolated cyclic estrogen therapy in menopausal women with stress urinary incontinence, and thus without the effects of progesterones.

Materials and Methods

Nineteen menopausal patients with stress urinary incontinence were selected and submitted to anamnesis and physical, gynecological and urodynamic examinations.

The study did not include women with urinary infections, neurological illnesses, kidney diseases, serious hepatic diseases, severe arterial hypertension, immunological illnesses or any women who presented contraindications to the use of estrogens, such as hormone dependent cancer or prior thromboembolic diseases.

Included in the study were patients with a history of more than a year of stress urinary incontinence, who were not using hormone replacement. The group was homogeneous in relation to parity, body mass index and degree of urogenital prolapse.

All the patients received conjugated equine estrogens orally, at a dose of 0.625 mg, for 21 days each month. After three months the clinical and urodynamic evaluations in relation to urine loss, were performed again.

The subjective evaluation, performed by the patients, was counted as a cure when there were no more episodes of urine loss; as a marked improvement when urine loss continued, although more rarely, and the patient was satisfied with the treatment and was not interested in other therapies; as an improvement when there was a reduction in the episodes of urine loss but not sufficient to satisfy the patient; and as unaltered when there was no improvement whatsoever.

The objective evaluation was performed by a urodynamic examination.

The standard t-test was employed for statistical analysis with p set at 0.05 or 5%.

Results

Of the patients 57.9% were satisfied with the treatment, reporting either a cure or a marked improvement (Figure 1). There were, however, no significant alterations in the urodynamic data (Table 1).

Nevertheless, four (21.05%) of the women were no longer loosing urine in the urodynamic evaluation performed after three months and in eight (42.10%) loss continued but with a greater bladder volume. The urodynamic parameters remained unaltered in 36.85% of the patients (Table 2).

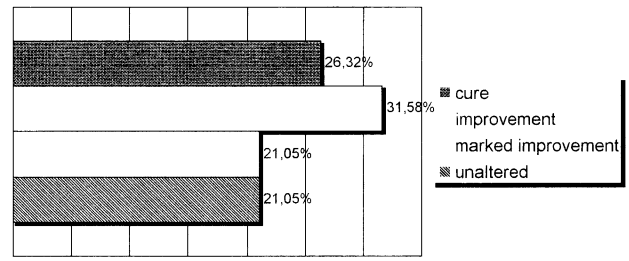

Figure 1. — Subjective evaluation of urine loss three months after treatment.

Table 1. — *Urodynamic data before and three months after cyclic estrogen treatment.*

Urodynamic data	Before	After
Post-micturition residue	8.6 ml	10.5 ml
Bladder capacity at first desire to void	132.5 ml	178.9 ml
Maximum cystometic capacity	413.2 ml	413.2 ml
Maximum urethral closing pressure	51.9 cmH_2O	52.4 cmH_2O
Functional length of the urethra	2.0 cm	2.3 cm
Maximum urinary flow	24.8 ml/s	27.5 ml/s
Average urinary flow	14.6 ml/s	15.9 ml/s

Table 2. — *Bladder volume (ml) at the moment of urine loss, before and after cyclic estrogen treatment.*

Patient number	Before	After
1	200	300
2	200	200
3	No loss	No loss
4	350	No loss
5	200	No loss
6	200	400
7	300	400
8	No loss	No loss
9	No loss	No loss
10	No loss	450
11	No loss	No loss
12	200	200
13	No loss	No loss
14	No loss	No loss
15	250	500
16	300	450
17	500	300
18	200	200
19	200	No loss

Discussion

As urinary incontinence in postmenopause can be caused or aggravated by hypoestrogenism, this study sought to investigate the role of estrogens in its treatment. To this end the effects of cyclical estrogen replacement in postmenopausal women with stress urinary incontinence were evaluated, both through subjective data reported by the patients, and through objective data collected during urodynamic examinations.

Our results showed that 57.9% of the patients were satisfied after the hormone therapy, and did not want other forms of therapy. However, 42.1% judged their situation to be only a little better or unaltered following the hormone therapy.

These findings are in agreement with those of various other studies [9-12] which have clearly shown the beneficial effects of estrogen therapy on incontinent women in the post-menopause.

The urodynamic results reflected clinical improvement. In 24.05% of the women urine loss was no longer observed during cystometry. In 42.10% of the cases, loss did occur but only with a bladder volume greater than that before the start of treatment (Table 2). Thus a group of women themselves to be cured or improved, but continue to have objective urine loss although with a greater bladder volume. These data suggest that such patients feel that they are cured because they do not reach their new bladder volume during their daily routine and therefore no longer present episodes of urine loss.

The treatment did not result in any statistically significant difference in the urethral profile. These results are in agreement with those in the literature [18].

In relation to the functional length of the urethra, it was not possible to show any alterations after three months of hormone treatment, similar to other studies [10, 15].

Our results show that estrogen is important for stress urinary incontinence in postmenopause, specially in patients without cystocele or with cystocele of degree I or II.

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Address reprint requests to:
M. F. SARTORI, M.D.
Av. Onze de Junho, 1006, apt. 51
Vila Clementino
04041-003 São Paulo, SP (Brasil)