Vaginal Viscoelasticity and Stress Urinary Incontinence: Therapeutic Application of an "Intelligent" Vaginal Device

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Abstract

An intravaginal device to prevent urinary incontinence was devised based on the notions of the 'viscoelasticity of the anterior vaginal' wall. As the anterior vaginal wall can be divided into segments with differing viscoelastic properties, this device is comprised of two parts: a rigid component to treat the urethral side, and a flexible ring-shaped component to exploit thee lastic properties of the anterior vaginal wall in its horizontal portion under the bladder. The resulting device has the potential to address each stage of bladder function in women: straining, bladder filling, and micturition. These specifications ensure that the device is effective and well tolerated by patients. This is hence a new therapeutic approach for the managementof female urinary incontinence. The high efficiency of the device is a validation of the physiological notion of differential viscoelastic properties of the pelvis (and the anterior vaginal wall) on either side of the vaginal cap.

Keywords: Stress urinary incontinence, Intravaginal device, Viscoelasticity.

Introduction

The difference in the dimensions and viscoelastic properties of the suburethral and subvesical segments of the anterior vaginal wall may underlie the mechanisms of stress urinary incontinence [1-3]. To confirm this hypothesis, modeling of the effect of abdominal pressure on the bladder was used to create a new intravaginal device that allows this difference in the viscoelastic properties to be recreated. The aim was to verify whether such as device would allow stress urinary incontinence (SUI) to be effectively mitigated. Confirmation of its efficacy would tend to support the hypothesis of 'differential viscoelastic properties'.

3.1 Effect of abdominal pressure on the bladder

The exerted abdominal pressure was represented by a handle-driven piston so as to identify the potential movements induced by the differences in elasticity. The bladder was represented by a deformable balloon, placed squarely over the underlying structures. The underlying structures were represented by two segments corresponding to the underlying structures on each side of the urethral-vesical junction. These two segments rest on posts, located at each end, so as to visualize the theoretical viscoelastic properties. The balloon was positioned in the middle, straddling the two segments that were also designated as being the front and the back. The experiment was performed on the forward segment that was rigid and non-deformable, and a rear segment that was flexible.

In the theoretical model (Figure 1), the hinged plate tilted backwards and forwards, as did the horizontal axis of the balloon when there was compression by the balloon on the two structures with differing elasticity's. The vertical arrows became asymmetric, which translated into a backward and downward displacement
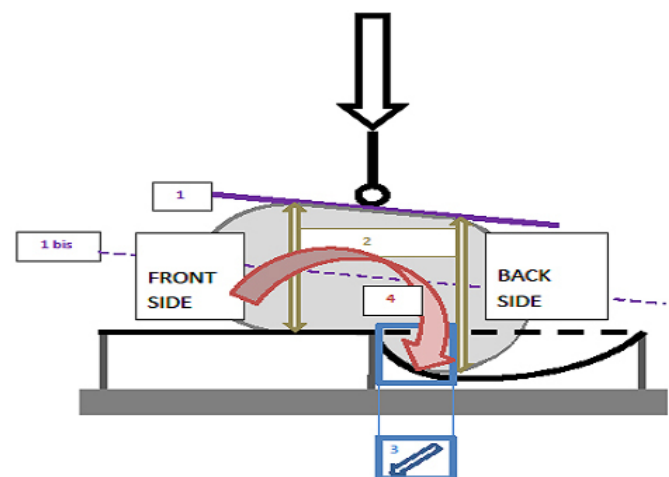
Figure 1: Effects of squashing the balloon on two segments with different elasticities

1: Switch of the hinged faceplate toward the more elastic rear portion. 1 bis: Identical horizontal switch of the balloon toward the rear. 2: Asymmetrical heights, higher for the more elastic rear side, lower for the front side. 3: Downward and rearward tilt of the resilient structure located against the central post (blue window); and downward and forward movementof the portion of the resilient structure located against the central post. 4: Movement of the fluid content of the balloon.

of the internal content of the balloon. The part of the flexible rear segment adjacent to the central post tilted downward and the backward, with a forward propulsive motion.

The increase in abdominal pressure with straining leads to an asymmetrical deformation of the bladder, and hence a downward and rearward displacement of the urine, as well as forward propulsion of the horizontal segment of the anterior vaginal walls (a downward and rearward tilt). This motion was visualized radiologically by placing clips and by opacification [4], and it is outlined in the various versions of the integral theory [5-7].

Conceptualization of the intravaginal device

If the difference in viscoelastic properties on both sides of the urethral-vesical junction and the vaginal cap is the underlying mechanism of an adaptation by the pelvis to the straining that blocks urinary incontinence, just the introduction of a device in the vagina that is flexible in the rear and rigid in the forward section should, by restoring this differential elasticity, validate the concept. Thus, the following process was undertaken: establishment of collaboration with the B. Braun Medical laboratory to produce a device that corresponds with the features stipulated by the concept, followed by engagement in a multicentric randomized phase III trial to objectively test and validate the efficacy of the theoretical concept and the device itself.

The device comprised an insertion tube that allows the device to be inserted just like a tampon. This was composed of a flexible ring that fits into the deep part of the vagina, and a stiff 2 cm ring-shaped part that fits under the urethra. The shape of the flexible ring was chosen so as to not compromise blocking the impact of the elasticity under the bladder. Out of necessity, the dimensions of this ring exceed those of the rigid part so as to correspond to the different dimensions of the vaginal segments [2].

Thus, upon straining, the weight of the urine was directed toward the horizontal segment of the anterior vaginal wall, and propels it towards the down and forwards, thus engaging the flexible ring. The first consequence of this motion on the ring was a levered action linked to the difference is size of the rigid versus the flexible part (Figure 2). Thus, the rigid part elevated and compressed the urethra along its entire functional length, with a maximal effect at its end, recreating an angle as described in the integral theory. When the lever effect blocked the lower end of the device, the differential elasticity created a spring action (Figure 3) that then specifically supported the vaginal cap and the bladder neck, in keeping with the "hammock" theory [8], thereby avoiding vesicalization (funneling action) of the urethra. The suppression of this vesicalization of the urethra suppresses activation by the urine of receptors located at the level of the bladder neck that are normally activated to initiate the detrusor contraction. According to the integral theory, abnormal activation therefore leads to incontinence urge. It should be noted that the spring action is activated after the lever action, thus requiring application of a more substantial force, which could thereby reduce the effectiveness in regard to incontinence urge symptoms. The device hence has a dynamic action, only acting with straining which, unlike other devices, avoids permanent deformation of tissues that could potentially cause pain and discomfort.

On the other hand, with pelvic contractions initiated during micturition, the base of the bladder was raised upward and forward during the voluntary pelvic contractions, while with downward straining it was lowered [9]. The urethrovesical angle measured to be 110° +/- 20° is then increased up to 150° [10]. Thus, with pelvic thrusts at the same time as micturition, the spring action was inverted, and cancelled out, thereby facilitating micturition.

Conceptualized as such, the device was tested by a multicentric randomized trial [11] with the aim of establishing whether it is highly efficacious in regard to stress urinary incontinence, as well as in regard to mixed incontinence urges, the absence of dysuria,
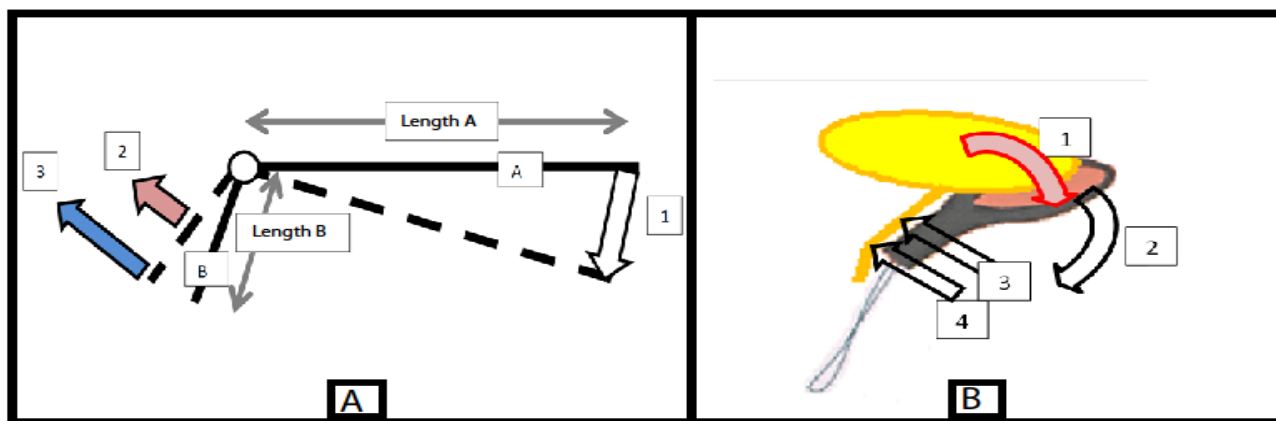
Figure 2: Mechanism of the lever

A: The lever's mechanism

A: Large arm of the lever. B: Small arm of the lever. 1: Pressure exerted on the lever. 2: Movement of the small arm of the lever arm (corresponding to the pressure on the vertical portion of the anterior vagina). 3: Movement up the small arm of the lever arm (corresponding to the pressure exerted on the middle 1/3 - lower 1/3 of the urethra). Ratio of length A / length B: effectiveness of the leverage

B: Levering effect of the device

1: Action of the urine weight. 2: Switch of the Diveen® ring. 3: Effect of the lever on the rigid lever part which compresses the urethra along its operative length (2 cm). 4: Maximal effect at the middle 1 / 3- lower 1/3 of the urethra (the point of continence linked to the action of the pubo-urethral ligaments in the integral theory of Ulmsten)
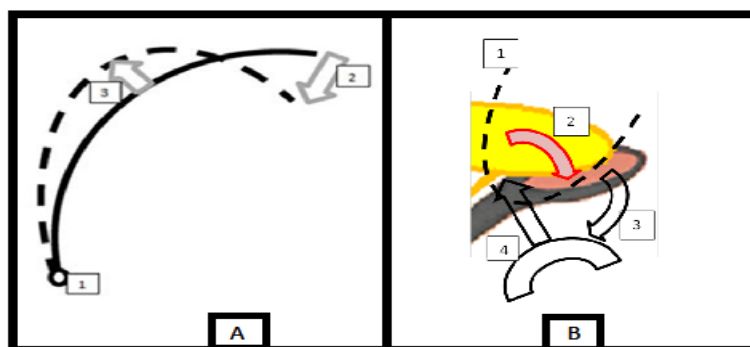
Figure 3: Spring mechanism and overactive bladder treatment

A: Mechanism of the spring

1: Fixed point. 2: Pressure exerted on the spring. 3: Deformation of the middle of the spring in response to the exerted pressure

B: Effect on the vaginal cap for treating incontinence urge

1: The vaginal cap and its attachment to the tendon bows. 2: Action of the weight of the urine on the ring portion. 3: Switch of the Diveen® ring. 4: Spring effect toward the bladder neck, compressed by the bottom, and driven by the movement of the urine and bladder between the two branches of the ring

and tolerance of the device.

Methods

Study design

A multicentric, randomized, controlled phase III trial was initiated. The recruiting doctors were gynecologists, urologists, or rehabilitation doctors engaged in either private or public hospital practice. In order to optimize the objectivity of the study, the number of patients recruited was limited to seven per doctor, so as not to alter the outcomes of the study due to an excessive imbalance in the ratio of patients/recruiting doctor.

For the designer of the device, the main aim of the study was to generate the different viscoelastic properties of the segments of the anterior vaginal wall on both sides of the vaginal cap. If the device based on this theory proved to be objectively effective, it would provide a strong argument in support of this new physiological hypothesis. This aim was not disclosed to either the laboratory manufacturing the device or to the doctors recruiting for the study. For the recruiters, management of SUI with the intravaginal device would provide an alternative to surgery, although there was a lack of a significant level of testing. The aim was hence to specifically assess efficacy, tolerability, and acceptability of the 75NC007 intravaginal device for treatment of stress urinary incontinence (SUI).

The multicentric trial

Following a period of therapeutic withdrawal with no treatment, allowing a baseline assessment to be made, the women with SUI were randomly assigned to a treatment or a control (i.e. no treatment) group. The main criterion was the reduction of the incontinence episode frequency (IEF), according to the hourly urination diary, relative to the initial value. The secondary criteria were variation in the USP (Urinary Symptoms Profile) score, the pad test over 24 h, and scores derived from the Contilife questionnaire relative to the baseline assessment. The analysis was performed on the Intention-to-treat mode and on the protocol mode.

Results

Fifty-five patients were included and analyzed (26 controls and 29 treated). The variations in the IEF, SUI, USP, and overactive bladder (OAB) subscores were larger for the treated group than for the control group (-31.7 ± 65.1% vs. -7.6 ± 24.5%, p=0.002, -2.4 ± 2.6 vs. 0.2 ± 2.2, p=0.004, and -1.5 ± 2.8 vs. 0.2 ± 1.8, p=0.016, respectively). The USP subscores were slightly lower for the treatment group. The Contilife scores were slightly better for the treatment group. The variations in the 24 h pad test did not differ between the two groups. There were no severe adverse side effects over the entire course of the study.

Discussion

The multicentric randomized study demonstrated a significant level of efficaciousness of the device. It has been commercially available since June of 2016, under the brand-name Diveen˚. The ability of this novel therapeutic intravaginal device to cure female stress urinary incontinence and mixed incontinence appears to be based on selective alteration of the viscoelastic properties of the anterior vaginal wall.

This "intelligent" device works in a dynamic way, closing the urethra during involuntary stress, and allowing it to open during micturition; its movements and deformations adapt to the various real life stages of bladder functioning in women. By avoiding permanent deformation of the tissues, the device does not generate discomfort or pain.

This new therapeutic tool is effective, is self-managed by the patients, and no significant secondary effects were noted [11]. Thus, it is well suited to complement currently available treatments (e.g. surgery, electrostimulation, rehabilitation, etc.). The efficacy of the device has validated the principal of restoration of the differential in the viscoelastic properties of the tissues on both side of the vaginal cap.

Aside from the therapeutic aspect, the physiological and pathophysiological theories of stress urinary incontinence must now, therefore, incorporate the underlying mechanism of

the difference in viscoelastic properties of the segments of the anterior vaginal wall on both sides of the vaginal cap.

Conclusion

The 75NC007 intravaginal device provides safe, non-invasive, and effective treatment of SUI in women.

Acknowledgements

We thank all of the B. Braun Medical laboratory team for having faith in this project and for their collaboration over the years to develop this device.

Conflict of interest

The development of this device in collaboration with the B. Braun laboratory presents an undeniable and unavoidable conflict of interest. No personal participation in the multicentric trial.

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