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URETHRAL INJECTION THERAPY. WHAT IS THE MECHANISM OF ACTION?

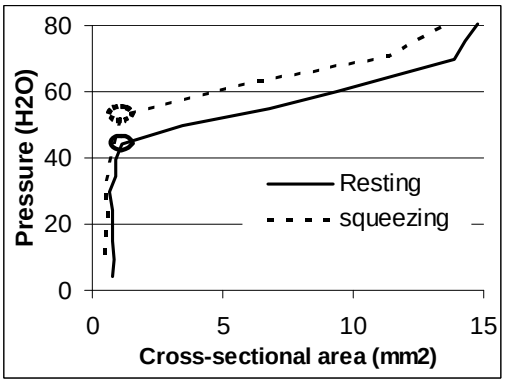
Hypothesis / aims of study

Although urethral injection therapy has been used for more than 100 years, the mechanism of action is unknown. It has been suggested that the effect of injection therapy was due to an obstructive or sealing effect [1]. None of these theories have been proven or can explain why the injection therapy has the same cure rate in different subgroups of stress incontinence patients [1]. Urethral pressure reflectometry (UPR) is a new reliable [2] method for simultaneous measurements of pressure and cross-sectional area (CA) in the female urethra [2]. Only a very thin polyurethane-bag (wall thickness 0.025mm) is placed in the urethra. The CA is measured with reflectometry (sound waves) and the pressure is applied to the polyurethane-bag by a pump. The pressure can be measured from 0-200 cmH2O and the CA from 0.4-16 mm². With this technique the opening pressure and the elastance (inverse of compliance) can be measured. In this study UPR was used to examine the influence of urethral injection therapy on the urethra.

Study design, materials and methods

15 patients with urodynamic stress incontinence (9) or both urodynamic stress incontinence and detrusor overactivity (6) were measured with UPR mean 94 days before and 101 days after urethral injection with Aquamid® (3) or Bulkamid® (12). None of the patients had other interventions between the two measurements. The UPR measurements with the patient resting were made as follows. The pressure was raised in steps of 5 cmH_2O from 0 cmH_2O until the polyurethane-bag was completely open. The procedure was repeated 3 times. The measurements while the patient squeezed were as follows. The pressure was raised in steps of 10 cmH_2O from 0 cmH_2O until the bag was completely open. The women were asked to squeeze during each pressure level and relax during the pauses. The whole procedure was repeated 2 times. A specially trained nurse instructed the patients to squeeze and watched if they did it correctly. From the UPR measurements the resting opening pressure, resting elastance, squeezing opening pressure and the squeezing elastance were obtained (fig. 1).The patient evaluated if the stress and urge symptoms were improved/cured, almost unchanged or worse at the post surgery measurement.
A sample of 15 subjects were needed to have a power of 90% to detect a significant difference (2 sided p-value 0.05), under the assumption that a change in the opening pressure of 5 cmH2O would be clinical relevant. This sample size calculation were made for the paired t-test but as the differences showed out to be non-parametric the Wilcoxon signed ranked test was used.

Figure 1. The figure shows a measurement before the injection therapy. The bottom trace was measured while the patient was resting. The upper dotted trace while the patient squeezed. The resting and the squeezing opening pressures are marked with circles on the respective traces. The elastances are the slopes of the horizontal part of the respective traces.



Results

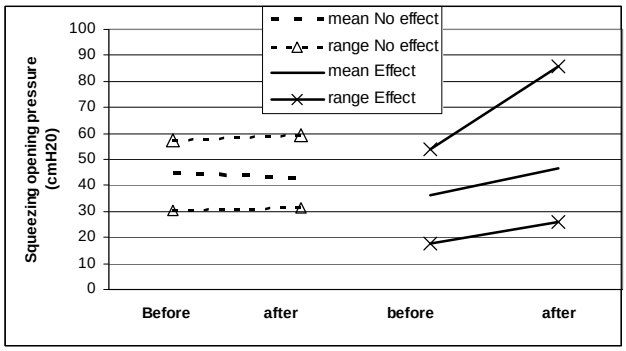
All the patients had stress symptoms before bulking, 10 were improved/cured after the injection therapy. 6 patients had urge symptoms none of them improved after the injection therapy. None became worse. Table 1 shows the results before and after the injection therapy. The patients had significantly higher squeezing opening pressure after the injection. The other parameters were unchanged.

Table 1.The table shows the mean values and the ranges for the different parameters.

Mean (range)	Before injection	After injection	P-value
Opening pressure relaxed (cmH2O)	32.5 (16-54)	31.7 (21-44)	0.9
Elastance relaxed (cmH2O/mm2)	1.6 (0.8-2.4)	1.5 (1.0-2.2)	0.4
Opening pressure squeeze (cmH2O)	38.9 (18-58)	44.3 (26-86)	0.01
Elastance squeeze (cmH2O/mm2)	1.9 (1.1-2.8)	1.9 (0.9-3.4)	0.8

The patients were divided into two groups based on their subjective assessments of effect on the stress symptom. One group of patients with effect (10) and one group without effect (5). The squeezing opening pressure increased significantly ($P<0.01$) more in the group of patients with effect (10.6 cmH2O) than in the group without effect (-1.6 cmH2O) figure 2.

Figure 2. The figure shows the squeezing opening pressure before and after the injection therapy. The dotted lines are the patients with no effect on the stress symptoms, the full lines are the patients with effect



Interpretation of results

The resting opening pressure and elastance did not change after the injection therapy, while the opening pressure during squeezing was significantly increased after the injection therapy and the patients with effect on the stress symptoms had significantly higher increase of the squeezing opening pressure than the patients without effect. These results suggest that the effect of the injection therapy is by increasing the strength of the urethral sphincter. A sphincter needs some central tissue volume in order to both compress the lumen in the continence phase and open while voiding [3]. The volume of this inner tissue determines the length of the muscle fibre. The power of the muscle increases when the muscle fibre is stretched until the muscle fibre is overstretched after which the power declines rapidly. The injected material might function as additional central tissue volume for the striated urethral sphincter and thereby increases the power.

Concluding message

The study suggests that the mechanism of action of urethral injection therapy is by increasing the strength of the urethral sphincter mechanism, which might explain why the injection therapy helps both patients with ISD and patients with hypermobility (1). One might expect that the optimal injection therapy would include the mid-urethra as the striated muscle is most widespread in this area. Assessments of the pelvic floor function before injection may have an predictive value.

References

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[2] Neurourol Urodyn (2005) 24; abstract 78,
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