

INTRAVESICAL PROSTAGLANDIN E₂ EFFECTIVENESS IN THE PREVENTION OF URINARY RETENTION AFTER TRANSVAGINAL RECONSTRUCTION OF THE PUBO-CERVICAL FASCIA AND SHORT ARM SLING ACCORDING TO LAHODNY: A PROSPECTIVE RANDOMIZED CLINICAL TRIAL

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SUMMARY: *Intravesical prostaglandin E₂ is effective in the recovery of spontaneous voiding after transvaginal reconstruction of the pubocervical fascia and short arm sling according to Lahodny. The aim of the study was to compare the effects of intravesical prostaglandin E₂ in the prevention of urinary retention after transvaginal reconstruction of the pubocervical fascia and short arm sling according to Lahodny. STUDY DESIGN: From November 1996 to June 1999 fifty women underwent the Lahodny procedure for moderate/severe cystocele and stress urinary incontinence. Women were randomly assigned to 1 of the 2 study groups: intravesical prostaglandin E₂ versus controls. Data obtained were analyzed with the Student t test and the Fisher exact test. RESULTS: Two patients of the treatment group had to be excluded from the study, one because of the wrong measurement of the post-voidal residual volume and another due to a fastidious burning sensation which appeared immediately after prostaglandin instillation and required the suspension of the treatment. No other side effects such as nausea, vomiting, diarrhea or hyperthermia were observed. Patients who underwent the prostaglandin E₂ treatment showed a recovery of spontaneous voiding after 7.9±6.7 days, whereas this interval was significantly longer in the control group, being 12.9±9.7 days (p=0.04, Two tailed Unpaired Student's T test). CONCLUSION: The effectiveness and the low associated morbidity mark the treatment with intravesical prostaglandin E₂ useful in the recovery of normal voiding after transvaginal pubocervical fascia reconstruction and short arm sling with the procedure according to Lahodny.*

INTRODUCTION

The slow recovery of spontaneous voiding after anterior colporrhaphy and transvaginal cystourethropexy represents a challenging problem both for patients and gynecologists. The need for prolonged post-operative bladder drainage results in patient distress, prolonged hospitalization, urinary infections and increased use of antibiotics.

There are several surgical techniques for anterior colporrhaphy, but they are not comparable because of the different anatomical structures affected by the procedure, as well as their ability to sustain the bladder neck and the urethra. The urethropexy procedure developed by Johann Lahodny (1) provides a good support for the bladder neck and the urethra, and thus is able to correct the stress urinary incontinence (SUI) due to hypermobility.

Various drugs acting on bladder and urethra contraction have been used in order to obtain a faster recovery of spontaneous voiding, but the results have not been satisfactory. The physiology of micturition is based on two mechanisms, namely the contraction of the detrusorial muscle fibers and the relaxation of the bladder neck and urethra muscle fibers (2). Cholinergic agonists cause bladder contraction through a direct inotropic effect on the detrusor muscle (3); however, drugs such as Bethanechol, induce bladder neck contraction at the same time. This side effect, associated with the rapid metabolic turnover of the drug, seriously limits its application in clinical practice (4). Alpha-lythic drugs are able to reduce urethral resistance, and thus can counteract the effect of cholinergic drugs on urethral tone (5). The combination of these two drugs

has not provided the expected results on bladder function. In the last two decades, several studies investigated the effects of prostaglandin E1, E2, F1 α and F2 α on bladder and urethra contraction, and on micturition (6-8). In particular, prostaglandin E2 efficacy on the recovery of spontaneous voiding has been demonstrated in patients with vaginal hysterectomy and cystourethropexy (6,7), and after retropubic colposuspension (8).

The aim of this study was to evaluate, in an open randomized prospective clinical trial, the efficacy of prostaglandin E2 on the recovery of spontaneous voiding after vaginal hysterectomy and pubocervical fascia reconstruction using a short arm sling as described by Lahodny.

PATIENTS AND METHODS

From November 1996 to June 1999, 50 women with anterior vaginal prolapse (II and III degree) were assessed in the Urogynecology Unit of the Maternal-Infantile Department, Lecco General Hospital and at the Gynecological Division of Valduce Hospital, Como.

The preoperative and postoperative assessment included:

- gynecological and urological anamnesis, including the clinical score of subjective SUI according to the Monza score (9) (Table I)
- pelvic examination, including vaginal prolapse classification according to Beecham (10)
- stress test for objective SUI grading, according to Ferrari (11) (Table II)
- urethrocystoscopy
- Q-tip test
- uroflowmetry including post-voiding residual volume evaluation
- cystomanometry in the supine

Table I - Subjective SUI score (Monza's Score)

	1 point	2 points
1) condition	coughing sneezing lifting weights running jumping	coition laughing climbing stairs walking
2) frequency	weekly	daily
3) quantity	<=1 pad/daily	>=2 pads/daily

multiply points as follow: 1-2 = mild; 4 = moderate; 8= severe

Table II - Objective SUI Score (Ferrari's Stress Test)

		patients position during coughing	
		supine	erect
bladder volume	250 ml	IV class, severe	III class, moderate
	400 ml	II class, mild	I class, very mild

position with saline infusion (at a filling rate of 100 ml/min) using a dual microtip catheter in the bladder and a single microtip catheter in the upper part of the vagina (Dantec Instruments).

- urethral pressure profilometry, at rest and during stress, in the supine position using a dual microtip catheter (Dantec Instruments) and 250 ml of isotonic saline solution in the bladder .

Hypermobility of the bladder neck was defined at the Q-tip test as the presence under stress of an angle >30° compared to the horizon, plus a rotation of >30° between the rest

position and that observed after the Valsalva maneuver.

After a clinical and urodynamic evaluation, all patients underwent vaginal hysterectomy with reconstitution of the pubocervical fascia and short arm sling according to Lahodny. Women with chronic urinary retention, pre-operative detrusor instability, bladder neuropathy, urinary tract infections (active or recurrent), asymptomatic bacteriuria, known allergy to prostaglandins or any other allergy were excluded from the study.

All surgical procedures were performed by the house staff of the

two Urogynecological units participating in this study. All patients received prophylactic cephazolin sodium (1 gram i.v.) 30 minutes before surgery. Antithromboembolic prophylaxis with low molecular weight heparin was administered the morning on which surgery was performed and then continued for 5 days. For two days after surgery a suprapubic catheter (Cistofix, Braun Melsungen - Germany) was left in place for continuous bladder drainage. Starting from the third day, the catheter was clamped for three hours, and the patient was invited to void with a full bladder. All patients were discharged on day 7; if a post-voided residual volume of > 50 ml was observed, the cystostomic catheter was left in place and the patient was requested to keep a diary in which she recorded the voided volume and the post-voided residual volume. Whenever the latter was < 50 ml, the patient was seen in the outpatient clinic for the removal of the catheter.

The patients were divided into two groups (prostaglandin treatment and controls) according to a computer-generated randomization table. The patients assigned to the prostaglandin group were treated with 1.5 mg of Dynoprostone (2 vials of Prostin E2, Pharmacia & Upjohn, Puurs, Belgium) starting 48 hours after surgery. The drug was diluted in 5 ml of saline solution and injected into the bladder through the catheter, which was then clamped for at least 1 hour. Prostaglandin treatment was administered once a day up to five consecutive days.

The terminology employed in the paper, unless otherwise stated, is in accordance with the guidelines approved by the International Continence Society.

Two-tail Fisher test and two-tail Student's T-test for independent group of data were employed, when appropriate, for the statistical analysis.

SURGICAL TECHNIQUE: Anterior median longitudinal colpotomy is performed and the lamina vasorum is reached by passing between the vaginal wall and the vaginal septum (pubo-cervical fascia). The lamina vasorum constitutes the inferior pre-vesical fascia which hosts the inferior vesical artery, vein and nerve; after its exposure, a blunt dissection is performed near the pubo-coccygeal portion of the levator muscle aponeurosis employing a Pean clamp, penetrating for ~8 cm in the direction of lamina membranacea, (tendineous arc of the endopelvic fascia). The space obtained after this procedure (spatium vesico-pelvinum) is delimited by the tendineous arc which constitutes the lateral and cranial border, and caudally by the vesical-uterine ligaments. The bladder wall between the lamina vasorum and lamina membranacea is covered by a fascial part called the lamina coniugans, which represents the median border of the spatium vesico-pelvinum, whereas the pubococcygeal muscle aponeurosis encloses it laterally.

The small fibrous sects present in the virtual space between lamina coniugans and the aponeurosis of the pubococcygeal muscle are removed by hand. The dissection maneuver causes the interruption of some of the inferior vesical nerve fibers.

The two lamina vasorum are brought together in the midline and sutured with 6-8 interrupted Vicryl sutures to eliminate the hiatus which caused the bladder and bladder

neck hernia. The urethrotendineous ligaments are then sutured on the midline below the bladder neck, followed by a partial suture of the posterior pubo-urethral ligaments which are easily identified after the suture of the lamina vasorum. A "short arm sling" is thus created, a structure which raises and sustains the urethro-vesical junction, repositioning it on the same level of the tendineous arc of the endopelvic fascia (12). Anterior colporrhaphy using interrupted 0 Vicryl suture concludes the operation.

RESULTS

Fifty patients were enrolled in the study; 25 received intravesical prostaglandins, whereas 25 constituted the control group. Twenty-six women reported stress urinary incontinence (SUI), whereas

stress incontinence was elicited in other 20 women after the stress test. Four women were subjectively and objectively continent. Preoperative clinical data and objective grading of genital prolapse, as well as subjective and objective grading of SUI are shown in Table 3 and 4 respectively. No significant difference was observed in the preoperative data or subjective SUI grading of the patients assigned to either group, while a higher number of continent patients were in class IV (Ferrari stress test) in the PGE2 group.

Two patients of the treatment group had to be excluded from the study, one because of the wrong measurement of the post-voidal residual volume and another due to a fastidious burning sensation which appeared immediately after prostaglandin instillation and required the suspension of the treatment.

Table III - Preoperative clinical data

	controls	PGE2	P value
N. pts.	25	23	
Age (Yrs ± SD)	61.6 ± 10.5	65.2 ± 7.6	0.17*
Parity (N. ± SD)	2.3 ± 0.7	2.4 ± 1.4	0.78*
Postmenopausal (N.)	21	21	0.37 ^
Body Mass Index (mean ± SD)	24 ± 1.5	24.3 ± 1.7	0.53*
Subjective SUI Score (mean ± SD)	1.5 ± 1.7	1.2 ± 1.6	1 *
Stress Test Class (mean)	3.2 ± 1.4	3.2± 1.5	1 *
Q-tip test at straining (mean ± SD; degrees)	52.5 ± 20.7	58.2 ± 24	0.57*
Cystocele II degree (n.)	12	11	0.60 ^
Cystocele III degree (n.)	13	12	0.60 ^

* Unpaired Student's T Test ; ^ Fisher's Exact Test

Table IV - Subjective and objective grading of SUI (preoperative, n°pts.)

grade	subjective SUI (MONZA SCORE)		objective SUI (FERRARI STRESS TEST)					
	controls	PGE2	neg	controls III	IV	neg	PGE2 III	IV
continent pts.	10	14	2	2	6	2	/	12
mild SUI	11	6	2	1	8	2	1	3
moderate SUI	3	3	/	/	3	/	1	2
severe SUI	1	/	/	/	1	/	/	/
total	25	23	4	3	18	4	2	17

Table V - Preoperative urodynamic data

	controls	PGE2	P value
Peak flow (ml/sec)	23.9 ± 9.8	21.8 ± 6	0.41
Mean flow (ml/sec)	10.7 ± 4.3	9.8 ± 3.2	0.42
Flow time (sec)	32.2 ± 15.8	38 ± 22.2	0.31
Urethral functional length (mm)	21.8 ± 4.8	22.6 ± 4.7	0.54
Max. urethral closure pressure (cm H ₂ O)	47.1 ± 22.9	37.6 ± 16.8	0.11

Unpaired Student's T Test. Values are mean ± SD

Table VI - Resumption of postoperative spontaneous voiding

	controls	PGE2	P value
removal of catheter (days)	12.9 ± 9.7	7.9 ± 6.7	0.04

Two-Tailed Unpaired Student's T Test; values are mean ± SD

Four other patients reported a mild burning sensation few minutes after prostaglandin administration, but it did not require the interruption of the study. No side effects such as nausea, vomit, diarrhea or hyperthermia were observed.

Patients who underwent the PGE2 treatment showed a recovery of spontaneous voiding after 7.9 ± 6.7 days, whereas this interval was significantly longer in the patients belonging to the control group, being 12.9 ± 9.7 days ($p=0.04$, Two tailed Unpaired Student's T Test).

DISCUSSION

The technique proposed by Johann Lahodny is normally characterized by a slow recovery of spontaneous voiding, as already reported by the original paper (1). This fact could be justified by the surgical procedure itself, which requires large detachments that may cause the lesion of some of the inferior vesical nerve fibers.

Baudino (13) observed a high prevalence of post-operative urinary retention after Lahodny's procedure, with a recovery of normal voiding after 12.5 days, data comparable to those obtained in the present study (12.9 days). These data also confirm that Lahodny's technique can cause more prolonged urinary retention than the well-known Kelly-Kennedy cystourethropexy (6,7), where recovery of spontaneous voiding usually occurs at 6-8 days after surgery. Furthermore, this evidence supports the need for drugs which can prevent or treat post-operative urinary retention.

Several studies have demonstrated that prostaglandin E2 can cause the contraction of the longitudinal

vesical muscles (14,15,16,17) and a relaxation of the circular urethral muscle fibers (18), unlike what has been observed for other prostaglandins such as $F2\alpha$ (19), that causes a contraction of the urethral muscles. Thus these physiologic data prompted various investigators to assess the efficacy of different prostaglandins in patients with urinary retention. Jaschevatzky (20) observed an increase in detrusor pressure of 40% using intravesical instillation of $PGF2\alpha$ in women who underwent vaginal hysterectomy.

Koonings (8) demonstrated the efficacy of the early administration of 10 mg PGE2 in reducing urinary retention after retropubic colposuspension, without any major side effects.

Scalambrino et al (6) obtained a significant shortening of the recovery time in patients with anterior colporrhaphy after an early intravesical administration of 1.5 mg of dynoprostone (PGE2) diluted in 50 ml of saline solution. These data were also supported by Bergman et al (7), who observed a significant improvement in spontaneous voiding after treatment with 3 mg PGE2 in women with anterior and posterior colporrhaphy. Interestingly, the study by Wagner et al (21) suggested that the time of prostaglandin administration could play a role in its efficacy, which was markedly decreased when the treatment was delayed (6-7 postoperative days).

At the present time there are no data on the use of PGE2 to facilitate the recovery of spontaneous voiding after the Lahodny procedure. In this randomized study on patients with vaginal hysterectomy followed by vaginal reconstruction according to Lahodny, intravesical PGE2 administration significantly improved

the recovery of spontaneous voiding, with a reduction of approximately 40%. Intravesical PGE2 instillation was preferred, since the presence of a suprapubic catheter already in place allowed the administration of the drug with minimal discomfort for the patients.

The therapeutic effect of PGE2 could be due to the stimulation of the sensory terminations present in the epithelium of the urinary tract, which in turn could cause a reflex contraction of the bladder detrusor muscle. In vitro and in vivo data have demonstrated that the efficacy of PGE2 is concentration-dependent (19,22), and therefore we diluted the drug in a final volume smaller than those previously reported (6,7,8) in order to improve its efficacy. However, we could not perform a direct comparison of two different final volumes because of the number

of patients enrolled, and further studies will be necessary to confirm this hypothesis.

In summary, the data obtained in this group of patients support the efficacy of an early administration of PGE2 even in case of Lahodny's procedure. In fact, as previously demonstrated by two different groups (21), late administration of the drug is associated to low efficacy, since an over-distension of the bladder muscular fibers is already present. A prophylactic administration of PGE2 should thus be recommended 24-48 hours after surgery, before an irreversible distension of the muscular fibers takes place. PGE2 treatment could represent an important tool in the management of postoperative urinary retention, even after surgical procedures which require large bladder detachments.

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