<table>
<thead>
<tr>
<th>Start</th>
<th>End</th>
<th>Topic</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00</td>
<td>09:10</td>
<td>Introducción</td>
<td>David Castro Diaz</td>
</tr>
<tr>
<td>09:10</td>
<td>09:35</td>
<td>Future targets for Pharmacological therapy of Urinary incontinence</td>
<td>Francisco Cruz</td>
</tr>
<tr>
<td>09:35</td>
<td>10:00</td>
<td>Female sexual dysfunction</td>
<td>Montse Espuna</td>
</tr>
<tr>
<td>10:00</td>
<td>10:30</td>
<td>How do I do it? Occult SUI and POP</td>
<td>Paulo Palma</td>
</tr>
<tr>
<td>10:30</td>
<td>11:00</td>
<td>Break</td>
<td>None</td>
</tr>
<tr>
<td>11:00</td>
<td>11:30</td>
<td>The failed sling</td>
<td>Teresa Mascarenhas</td>
</tr>
<tr>
<td>11:30</td>
<td>12:00</td>
<td>How I do it? Refractory OAB</td>
<td>David Castro Diaz</td>
</tr>
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<td></td>
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<td>Francisco Cruz</td>
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<td></td>
<td>Montse Espuna</td>
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<td></td>
<td>Teresa Mascarenhas</td>
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<td></td>
<td></td>
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<td>Paulo Palma</td>
</tr>
</tbody>
</table>

**Aims of course/workshop**

This meeting intends to provide an update on the recent advances in the field of Neurourology and Female Urology. Spanish and Portuguese speaking experts will discuss recent developments in Pharmacology of LUT, Female sexual dysfunction, Occult SUI, Failed mid-urethra sling and refractory OAB. Interaction and discussion with attendants will be encouraged. Target audience is Spanish/Portuguese speaking delegates.

**Educational Objectives**

To update on recent developments within the field of Neurourology & Urogynaecology
FEMALE SEXUAL DYSFUNCTION AND PELVIC FLOOR DISORDERS

MONTSE R. ESPUÑA PONS
Institut Ginecologia, Obstetricia, Neonatologia
HOSPITAL CLINIC UNIVERSIDAD DE BARCELONA

SEXUAL DISORDERS IN WOMEN WITH UROGYNAECOLOGICAL CONDITIONS

• Sexual health is a right for the healthy or sick individual human being.

SEXUAL DISORDER

Is defined as:

• “The various ways in which an individual is unable to participate in a sexual relationship as he or she would wish” (1).


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FEMALE SEXUAL DISORDER

Classification (major categories) of women sexual dysfunction.
Second International Consensus of Sexual Medicine (2003)*

1. Sexual desire / interest disorder
2. Arousal disorders (subtypes): subjective or genital sexual arousal disorder, combined subjective and genital sexual arousal disorder, persistent genital arousal disorder
3. Orgasmic disorder
4. Vaginismus (“vaginal spasm”)
5. Dyspareunia (pain disorder)

• …which causes personal distress.


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FEMALE SEXUAL DYSFUNCTION

Sexual dysfunction in women (EUROPE):

• N = 5,023 women (40 to 80 years)
• 32% at least one dysfunction

• Not consulted a physician 64%
• 76% lack of perception of problem


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• Less than 25% of men and women with a sexual problem had sought help for their sexual problem(s) from a health professional.
To estimate the prevalence of self-reported sexual problems (any, desire, arousal, and orgasm), accompanied by personal distress.

31,581 female respondents > 18 years from a households sampled from a national research panel representative of US women

The epidemiology of sexual dysfunctions.

- Sexual dysfunctions are highly prevalent in our society worldwide, and that the occurrence of sexual dysfunctions increases directly with age for both men and women.

- Personal distress about those symptoms appears to diminish as individuals become older.

FEMALE SEXUAL DYSFUNCTION:

In women with LUTS and PFD

M. España Pons

Sexual Disorders in Women with Urogynaecological Conditions

- In the context of urogynaecological clinical practice we have patients sexually active or inactive, with a self perceived “normal sexual life”, or with sexual disorders that may be related or not with their pelvic floor dysfunction (PFD).

- Emerging literature
  - Pelvic floor disorders negatively impact
    - Sexual activity
    - Sexual function

- Questions to be answered
  - Sexual function/activity affected more by one pelvic floor disorder than another?
  - Does sexual / activity function changes with treatment?
Sexual complaints, pelvic floor symptoms, and sexual distress in women over forty.

“...sexually related personal distress is significantly associated with dyspareunia, depressive symptoms, and decreased arousal during sexual activity”.


SEXUAL DISORDERS IN WOMEN WITH UROGYNAECOLOGICAL CONDITIONS

FEMALE SEXUAL DYSFUNCTION:

In women with LUTS

Several studies have found reduced sexual activity and function in women with urinary incontinence compared to continent women.


Results of a cross-sectional study

“Sexual dysfunction is common in women with LUTS and UI”. Salonia A et al. European Urology 2004; 45: 642-8;

216 patients with LUTS and 102 age-matched women assessed for yearly routine gynaecological evaluation and without urinary symptoms enrolled as cross-sectional CONTROLS.

Results of a cross-sectional study

“Sexual dysfunction is common in women with LUTS and UI” (1).

investigated in accordance with the Female Sexual Function Index (FSFI). (2)

Association of LUTS and Sexual dysfunction : 99 / 216 (46%)  

<table>
<thead>
<tr>
<th>Author</th>
<th>Method- questionnaire</th>
<th>N</th>
<th>LUTS – UI FSFI score for domain</th>
<th>Control FSFI score for domain</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salonia 2004</td>
<td>SFSI (higher score better SF)</td>
<td>216 LUTS 102 controls</td>
<td>Desire: 2.8 arousal: 2.8 Lubrication: 3.2 Orgasm: 4.1 Satisfaction: 2.7 Sexual pain: 1.8</td>
<td>Desire: 3.2 arousal: 3.6 Lubrication: 4.4 Orgasm: 4.4 Satisfaction: 4.0 Sexual pain: 4.0</td>
<td>0.01 0.01 0.01</td>
</tr>
</tbody>
</table>

(1) Salonia A et al. European Urology 2004; 45: 642-8;  
(2) Rosen et al J Sex Marital Ther 2000

Patients reported that sexual fantasies were frequently associated with the fear of having an UI episode during intimacy, thus resulting in sexual anxiety

(1) Salonia A et al. European Urology 2004; 45: 642-8

47 % of women with low sexual desire, also complained of a long history of SUI*
FEMALE SEXUAL DYSFUNCTION:

urinary leakage during sexual activity

Coital urinary incontinence

Impact on QoL of coital incontinence

- Women with coital urinary incontinence had a higher scores (worse QoL) in all dimensions of KHQ

N=633 women seeking treatment for UI.
(36.2%) of women were at risk

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Method</th>
<th>N</th>
<th>Patients</th>
<th>Coital UI</th>
<th>What stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hilton 1988</td>
<td>Questionnaire</td>
<td>324</td>
<td>urologic clinic</td>
<td>24%</td>
<td>lower penetration, 25% orgasm</td>
</tr>
<tr>
<td>Lam 1992</td>
<td>Questionnaire</td>
<td>441</td>
<td>with UI</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>Vierhout 1993</td>
<td>Questionnaire</td>
<td>196</td>
<td>gynecologic clinic</td>
<td>34%</td>
<td>75% penetration, 56% orgasm</td>
</tr>
<tr>
<td>Norgard 1995</td>
<td>Medical examination</td>
<td>224</td>
<td>annual gynecologic examination</td>
<td>77% had UI, 50% coital</td>
<td></td>
</tr>
<tr>
<td>Morin 1999</td>
<td>Retrospective</td>
<td>2153</td>
<td>urologic clinic</td>
<td>10.6%</td>
<td>80% penetration, 20% orgasm</td>
</tr>
<tr>
<td>Burrows 2004</td>
<td>Retrospective</td>
<td>330</td>
<td>urologic clinic</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Lindbladh 2006</td>
<td>Prospective</td>
<td>90</td>
<td>urologic clinic</td>
<td>32%</td>
<td></td>
</tr>
</tbody>
</table>

* Only 22 (10%) of 228 women with coital UI complained without direct question

Sexual function: pelvic organ prolapse

- It has been shown that women seeking treatment for advanced prolapse, their body image is decreased and they have lower quality of life scores.
The effect of SUI surgery on the sexual function

M. Espuna Pons

FEMALE SEXUAL DYSFUNCTION

The effect of pelvic surgery:

Anatomic
- Shortening of the vagina
- Reduction of vaginal length
- Etc.

Psychological
- Fear of damage to internal organs
- Partner’s apprehension
- All women who are going to have pelvic surgery are worried about the effect on sexual function

Assessment of sexual function with QUESTIONNAIRES:

A new instrument to measure sexual function in women with urinary incontinence or pelvic organ prolapse

Rebecca G. Rogers, MD; Dorothy Kammen-Drak; HB; Analia Villanueva, MD; Kimberly Cass, MD; and Clifford Qualls, PhD

Abqirypae, New Mexico, and Summ, Texas


Effect of surgery for SUI on the sexual function: comparative studies

<table>
<thead>
<tr>
<th>Author</th>
<th>procedure</th>
<th>No patients</th>
<th>questionnaire</th>
<th>Results *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jha 2007</td>
<td>TVT/TVT-OT</td>
<td>54</td>
<td>PISQ</td>
<td>Same improvement</td>
</tr>
<tr>
<td>Murphy 2008</td>
<td>TVT/TVT-O</td>
<td>237</td>
<td>PISQ-12</td>
<td>No differences</td>
</tr>
<tr>
<td>Pace 2008</td>
<td>TVT-TOT</td>
<td>108</td>
<td>FSFI</td>
<td>Same improvement</td>
</tr>
<tr>
<td>Brubaker 2009</td>
<td>Burch-Sling</td>
<td>655</td>
<td>PISQ-12</td>
<td>Same improvement</td>
</tr>
</tbody>
</table>

* Postoperatively significant increases the scores of the questionnaires (better sexual function) in all studies.

The effect of SUI surgery on the sexual function

Observation:

- The presence of a foreign body, such as polypropylene tape, provokes a reaction that compromises the anterior vaginal wall, which is a rich neurovascular area.
HYPOTHESIS:
The surgical techniques that perforate the paraurethral spaces to position a suburethral sling could diminish sexual functioning because of scarring and reduced elasticity of the vaginal wall, resulting in a reduced blood supply to the erectile tissues of the clitoris.

Clitoral Blood Flow Changes After Surgery for Stress Urinary Incontinence: Pilot Study on TVT Versus TOT Procedures
Savatore Canale, Salvatore Ruggia, Sebastiano Blandino, Daniela Mirabella, Antonio Casalino, and Antonio Cianci

In the TVT group, the mean pulsatility index and mean peak systolic velocity were significantly lower and the mean resistance index was significantly greater compared with the pretreatment values (\(P < 0.5\)).

In the TOT group, each color Doppler measurement was similar to that obtained at baseline (\(P\) NS).

Determining the Course of the Dorsal Nerve of the Clitoris

This somatic nerve lies along the lateral border of the mid-urethra up to the endopelvic fascia.

The effect of SUI surgery on the sexual function
HYPOTHESIS

- The pudendal nerve, which has its important sensitive termination in the area of pubocervical fascia surrounding the urethra, could undergo detrimental fibrosis after an anti-incontinence procedure.

The effect of POP surgery on the sexual function

- POP surgery has in general a positive impact on global sexual function.

- Satisfaction in most patients may be due to complete relief of feeling a vaginal bulge, improving self-image and absence of pain.
In a prospective study of subjects undergoing vaginal surgery for pelvic organ prolapse, Pauls et al (1), found no differences in FSFI domain or total scores between the pre- and postoperative period.


The deterioration in sexual function were likely to occur in women with better sexual function scores preoperatively.


In women with coital sexual activity and good sexual life before surgery, de novo dyspareunia is an important factor for postoperative deterioration in sexual function.

The effect of POP surgery on the sexual function

Effect of surgery for prolapse:

<table>
<thead>
<tr>
<th>Autor</th>
<th>Technique</th>
<th>Preop</th>
<th>Postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kahn 1997</td>
<td>Levator plication</td>
<td>18%</td>
<td>27%</td>
</tr>
<tr>
<td>Cundiff 1998</td>
<td>Site-specific fascia repair</td>
<td>29%</td>
<td>19%</td>
</tr>
<tr>
<td>Porter 1999</td>
<td>Site-specific fascia repair</td>
<td>67%</td>
<td>46%</td>
</tr>
<tr>
<td>Kenton 1999</td>
<td>Site-specific fascia repair</td>
<td>28%</td>
<td>8%</td>
</tr>
<tr>
<td>Glavind 2004</td>
<td>Site-specific fascia repair</td>
<td>12%</td>
<td>6%</td>
</tr>
</tbody>
</table>

M. Espuña Pons

Dispareunia de novo.

Anterior repair

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of surgery</th>
<th>Follow-up (months)</th>
<th>Symptoms (postop)</th>
<th>De novo dyspareunia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kahn 1997</td>
<td>Levator plication</td>
<td>18%</td>
<td>15%</td>
<td>0%</td>
</tr>
<tr>
<td>Cundiff 1998</td>
<td>Site-specific fascia repair</td>
<td>29%</td>
<td>9%</td>
<td>0%</td>
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<tr>
<td>Porter 1999</td>
<td>Site-specific fascia repair</td>
<td>67%</td>
<td>8%</td>
<td>0%</td>
</tr>
<tr>
<td>Kenton 1999</td>
<td>Site-specific fascia repair</td>
<td>28%</td>
<td>8%</td>
<td>0%</td>
</tr>
<tr>
<td>Glavind 2004</td>
<td>Site-specific fascia repair</td>
<td>12%</td>
<td>6%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Dispareunia de novo. Colpoacropexy

Espuña Pons M et al 2009

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of surgery</th>
<th>Follow-up (months)</th>
<th>Symptoms (postop)</th>
<th>De novo dyspareunia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North 2006</td>
<td>Laparoscopic sacrocolpopexy</td>
<td>26.5</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Cundiff 2008</td>
<td>Laparoscopic sacrocolpopexy</td>
<td>12.5</td>
<td>92%</td>
<td>0%</td>
</tr>
<tr>
<td>Summer 2008</td>
<td>Laparoscopic sacrocolpopexy</td>
<td>12</td>
<td>95%</td>
<td>9%</td>
</tr>
<tr>
<td>Port 2011</td>
<td>Laparoscopic sacrocolpopexy</td>
<td>20</td>
<td>95%</td>
<td>9%</td>
</tr>
<tr>
<td>Rizzo 2005</td>
<td>Laparoscopic sacrocolpopexy</td>
<td>20</td>
<td>95%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Conclusions

- Sexual dysfunction is prevalent in women with pelvic floor disorders
- Assessment and management of this problem is necessary when it causes distress

Surgical correction is generally beneficial but occasionally can result in negative alterations in sexual function.

Patient selection and methods used for surgical repair are important factors in determining anatomical and functional success.
El concepto de Vejiga Hiperactiva está definido por la ICS como la consulta por parte del paciente de una situación de urgencia con o sin incontinencia de urgencia, generalmente acompañada de aumento de la frecuencia miccional y de nicturia, en ausencia de cualquier condición metabólica o patológica subyacente. En más del 50% de estos pacientes aparece en el estudio Urodinámico un Detrusor Hiperactivo definido como la aparición de contracciones involuntarias del detrusor durante la fase de llenado de un Estudio Urodinámico.

El tratamiento de primera línea de esta disfunción es la adopción de medidas conductuales y la indicación de antimuscarínicos.

Existe un número despreciable de pacientes en los que los antimuscarínicos no son eficaces o bien se intoleran o bien no pueden ser usados por estar contraindicados.

El tratamiento de los pacientes con detrusor hiperactivo no tratable con anticolinérgicos es problemático, existiendo en la actualidad tres opciones:

- Inyección endoscópica de toxina botulínica en vejiga.
- Neuromodulación.
- Ampliación vesical (clamp) + autosondajes post SOS.

En el Protocolo diagnóstico y terapéutico de esta disfunción en nuestro hospital, aparece como siguiente opción a los antimuscarínicos, la inyección de toxina botulínica y la neuromodulación de raíces sacras, dejándose los criterios de elección entre ambas opciones a la decisión personalizada en cada caso y en cada paciente.

La opción de ampliación vesical queda muy limitada, pero es algo que se ofrece a los pacientes, los cuales suelen rechazar.

EXPERIENCIA EN NEUROMODULACION DE RAICES SACRAS.

Entre 2007 y 2010 se realizó la prueba de NRS (PNE y Tined Lead) por detrusor hiperactivo en 58 pacientes. Fueron implantados 20 IPGs. Tras un seguimiento medio de 112 meses (12,8 – 135) se analizaron los cambios antes y después del tratamiento en las variantes de: Diario miccional; Valoración subjetiva de mejora percibida (1-10); Se analizaron los datos según la prueba no paramétrica de Wilconson para datos apareados.

Resultados: Los cambios en el diario miccional pre/posttratamiento fueron estadísticamente significativos (p<0,01) en frecuencia diurna (9/5), frecuencia nocturna (3/2), volumen de micción (144/184). En 7 pacientes desapareció la incontinencia.
Doce pacientes refirieron mejoría percibida > 75 % y cuatro entre el 50 y 75 %.
Dos pacientes presentaron dolor y en uno se presentó un fallo técnico.

EXPERIENCIA EN TOXINA BOTULÍNICA

Se presenta una evaluación retrospectiva de los casos realizados entre Octubre y Noviembre 2010 de inyección de toxina botulínica intradetrusor en pacientes con detrusor hiperactivo no tratable con anticolinérgicos y demostrado urdinámicamente. 61 casos se consideraron como detrusor hiperactivo idiopático y 31 como neurógeno. Se incluyen 100 pacientes (68 mujeres, 32 varones) con edad media de 63 años, con síntomas de vejiga hiperactiva de más de 6 meses de evolución y detrusor hiperactivo con o sin incontinencia.

Evaluación preoperatoria consistió en historia clínica, exploración física, diario miccional, cuestionario de satisfacción (1-10) y estudio urodinámico completo.

Técnica: 1) Profilaxis antibiótica. 2) Anestesia local en mujeres y espinal en hombres. 3) 20 puntos de inyección de 0.5 ml, respetando el trígono vesical, de 100 u de Botox en idiopáticos y 300 u de botox en neurógenos.

Evaluación postoperatoria: A las 3 semanas, 2, 4, y 6 meses. Se realizaron: diario miccional, cuestionario de satisfacción y estudio Urodinámico (con valoración de: desaparición o persistencia de las contracciones no inhibidas del detrusor y en este último caso, volumen infundido en la primera contracción, contracción involuntaria máxima, capacidad cistométrica máxima).

Resultados: Tras un seguimiento de 2 semanas a 6 meses, se observó:
- Desaparición de la hiperactividad en 30 % de los casos.
- Incremento significativo de: capacidad cistométrica máxima.
- Disminución significativa de la contracción máxima del detrusor.
- Disminución significativa de la frecuencia miccional diurna y nocturna.

La variación observada en el volumen a la primera contracción involuntaria, Q.max. y residuo postmiccional no son significativas.

Complicaciones:
5 episodios de hematuria macroscópica autolimitada
3 retenciones agudas de orina tras un intervalo medio de 2 semanas.
ICS- SINUG
Salvador Bustamante Alarma
University Hospital Puerta de Hierro Majadahonda
(Madrid-Spain)

Refractory Overactive Bladder
(anticholinergic treatment)

How I treat it


- Part of the contraction is atropine-resistant. Bayles et al. J Urol 162:1833-1839. 1999

- In terms of hyperactivity the atropine-resistant component is significantly increased. Anderson KE, Armit A. Physiol Rev 84: 935-986. 2004

Smooth muscle involvement

Noradrenaline (NA)


- In most species $\alpha$ agonists contract the detrusor that is increased in the overactive bladder, which also knows a predominance of $\beta$ receptors. Perlberg S et Caine M. Urology 20: 524-527. 1982

- Presence of receptors $\beta_1 \beta_2$ and $\beta_3$ predominantly where $\beta_3$ is responsible for muscle relaxation. Perlberg S et Caine M. Urology 20: 524-527. 1982

- In the bladder neck NO act during bladder parasymptomatic activation resulting in relaxation of the bladder base. Hernández, M et al. Neurourol Urodynam 26: 626-630. 2007

Adenosine triphosphate (ATP)


- The initial contractile component is due to release of ATP, whereas the sustained phase is due to the release of Ach

- ATP contraction of the bladder is produced by activation of P2X receptors. O'Reilly et al. BJU Int 87: 617-622. 2001


Nitric oxide (NO)


- No evidence of NOSn produced in the detrusor. There has not been consistently demonstrated nerve relaxation produced by NO release. Elliot VA and Castelein CM. Br J Clin Pharmacol 36: 479. 1993

- In the bladder neck NO act during bladder parasymptomatic activation resulting in relaxation of the bladder base. Hernández, M et al. Neurourol Urodynam 26: 626-630. 2007
Endothelins

- In the outlet obstruction increases the expression of ETa indicating possible involvement of endothelin receptors in BPH and detrusor hypertrophy associated with this clinical picture. Khan MA et al. Urol Res 27: 445-493, 1999

Prostanoids

- The way of Cyclooxygenase (COX) responsible for the synthesis of prostanoids (PG and thromboxanes). There are 2 isoforms, COX-1 and COX-2, the latter is increased during inflammation. Tramontana M et al. Neurourol Urodynamics 31: 452-459, 2000
- In PGs are known 4 receptors named EP1 to EP4 that have been located in mucosa, muscle and intramural bladder lymph nodes, where EP1 is responsible for modulating bladder. McCaffery GP et al. Am J Physiol Renal 295: F507, 2008

Hygienic measures

- Physiotherapy
- Oral care
- Relaxation
- Heat
- Acupuncture

Avoid
- Citrus
- NSAIDs
- Caffeine
- Antibiotics
- Decongestants
- Alcohol
- Ibuprofen
- Peppers, tomatoes

Treatment of refractory overactive bladder (OAB) to antimuscarinics

Botulimum toxin A (Allergan) 300 IU

- yes
- No

Repeat same dose over time

Stimulation Test S2-S3 sacral roots

- neurogenic -300 UI
- non neurogenic -200 UI

OAB- therapeutic targets

- Opening of K+ channels
- P2X3 receptors blockade
- TVP receptors
- ETA endpoints
- NK1 receptors
**Targeted Therapy**

- **Acetylcholine**
  - Antimuscarinic
  - Antagonists TRPV1 ?
- **Prostaglandins E2**
  - Antagonists EP1 ?

**Muscles**

- **β3 ARS**
  - Agonists β3 ARS
- **PDE**
  - PDE-5 Inhibitors
  - Rho Inhibitors ?

**Central**

- **GABA ?**
- **Opioid ?**
- **Antagonists NK, ?**

---


- The GW427353 is a β3 antagonist receptor that induces relaxation of the spontaneous activity in the human detrusor. Biers SM et al. BJU Int 98(6) 1310-1314. 2006


- In rats treated with blocking vitamin D3, there is an improvement in bladder pressure. Schroder A et al. BJU Int 98(3): 637-642. 2006

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- Urothelial cells may secrete neurotrophins, peptides, ATP, ACh, prostaglandins, NO and cytokines that can influence the excitability of sensory neurons.
STATEMENT OF RELATIONSHIP WITH THE PHARMACEUTICAL INDUSTRY AND MEDICAL DEVICES

I have no conflict of interest with the business of these devices.

ADJUSTABLE MESH FOR THE TREATMENT OF URINARY INCONTINENCE

Dr. Luis Prieto Chaparro
Hospital General Universitario de Elche, Alicante.

Stigma
involvement variable
Suffering in secret
disease quality of life
whenever we are required more
provide more and better results

First, prevention

Urgency
Obstruction lower urinary tract
Complications
Conflicting expectations
Inefficiency
technical failure
**Urgency Prevention**
- Study prior to surgery
- Avoid excess tension
- Associated prolapse
- Study after surgery

**Obstruction lower urinary tract**
- Post void residual volume
- Low flow
- Associated prolapse
- Underactive detrusor
- Mesh misplaced
- Mesh migration
- Technical defect
- Comorbidities

**Complications Prevention**
- Learning curve
- Always the same mesh in series with significance
- Test results: clinical exploration QoL
- Inform patients that there are failures

**Inefficiency Prevention**
- Technical failure
- No fewer than 20 procedures / year
- Test of cough in operating room
- TOT-TVT: TVT Much better hypermobility
- Adjustable

---

**Reunión Nacional del Grupo de Urodinámica**
**La Coruña Marzo de 2001**

**SITUACIÓN ACTUAL DE LA CIRUGÍA DE LA INCONTINENCIA URINARIA FEMENINA**

Dr. L. Prieto Chaparro

**10 YEARS AGO**
Complications

- Excess sling tension of 4 cases (6.6%)
- Section - restructuring by default tension (sling ineffective) 3 cases (5%)
- Adjusting sling tension or new Bladder perforation 2 cases (3.3%)
- Infection-abcess in 1 case mesh anchor
- Suprapubic pain, rectal itch and 6 cases (10%)
- Wound infection in 1 case

Results

urgency in 19 of 102
11 cases after
4 de novo continence 91%
(operating failures)

Clinical History
250 ml into bladder
Flowmetry
Residue
Urodynamics
SUIQ Questionnaire
I-QoL questionnaire
ICIQ-SF
PG-I-S questionnaire
PG-I-H questionnaire

Ajuste: 16 y 120 horas
Llenamos vejiga con 250 c.c.
Tos en decúbito y bipedestación

No fugas

Fugas

Flujometría

Tensamos hasta continencia

> 10 ml/sg. RESIDUO 0

> 10 ml/sg RES. 100

< 10 ml/sg

Retirada talla y puntos
Alta.

Destensar y nuevo proceso
### Hypothesis / aims of study

**Study design, materials and methods**

Within-subject study initiated in January 2005. TOA (AM) is a macroporous polypropylene monofilament non-elastic tape with two groups of polypropylene threads permitting postoperative readjustment of tension that are removed when continence without obstruction is achieved. Seventy-seven incontinent women (29.3% stress incontinence, 70.1% mixed incontinence) received TOA tape. The local ethics committee approved the study.

**Results**

Fifty-one (66%) were continent in the immediate postsurgical evaluation. Twenty-six (34%) were incontinent. Eight of the 51 continent patients were obstructed (Qmax inferior to 10 ml/s and/or more than 50 ml residue). After adjustment, all patients rendered continent, none had PVR and mean Qmax was 16.7±5.7 ml/s. Mean follow-up was 14.8±6.5 months. Objective cure rate was 69.6%, with 7.3% greatly improved. Subjective cure rate; 54.7% of patients never leak urine. The subjective failure depended on the existence of urgency incontinence 25 patients (32%), mixed incontinence 4 patients (5%) and pure stress incontinence 6 patients (8%). Qmax was 21.3±7.2 ml/s. The QoL questionnaire improved from 31.4±20.3 to 85±17.2 points and the PGI showed 91% of patients to be better or very much better than before. There were no cases of bowel, nerve or major vessel injury. No infection or urethral erosions were identified. Two small vaginal erosions were detected.

### Interpretation of results

This is the first time that an adjustable transobturator regular mesh has been described that allows post-operative adjustment of the tension applied during surgery. This has allowed that all our patients have been discharged without any incontinence or any PVR.

Our data suggests that with TOA tape better results can be obtained than with the traditional non-adjustable mesh, furthermore without increasing surgical complications.

**Concluding message**

TOA adjustable tape procedure allows adjustment of tension for a number of days after surgical intervention, thus permitting correction of postoperative incontinence or obstruction.

**References**


### Conclusion

- 1. Not all meshes are well established on the day of surgery, can improve outcomes.
- 2. We do not think that is a short-stay surgery and outpatient, to know what the situation is the patient is essential and can be changed if you can avoid a new surgical procedure

3. Add a few threads setting lets you modify a trouble to the patient and the urologist

4. In complex or multi-operator sick is a good alternative
• 5. What makes the result in terms of quality of life and from the functional point of view rather than a failure of a surgical procedure for incontinence is:
  - Urgency “de novo” OR PERSISTENT
  • OBSTRUCTION
  • COMPLICATIONS

Never forget to follow the patients, not just the result, but because there are complications.
Occult SUI and POP

Occult SUI is defined as urinary leakage which is prevented by POP and only becomes symptomatic after surgical correction of the pelvic anatomy.

The International Continence Society has been reported that after reduction of the prolapsed organs 30-86% of continent woman with severe POP are at risk of symptomatic SUI.
Occult SUI and POP

OUR EXPERIENCE:
- 40% SUI
- 9% URGE INCONTINENCE
- 8% STRESS AND URGE INCONTINENCE
- 43% NON URINARY INCONTINENCE:
  - 76% NON OSUI DURING URODYNAMIC STUDY
  - 24% OSUI DURING URODYNAMIC STUDY

How I do it?

Thank you!
Occult incontinence
How I manage?

Omar Grossi
Federación Argentina de Urología

I. O. U. G. A.

Occup incontinence

How I manage?

Omar Grossi
Federación Argentina de Urología

I. O. U. G. A.

Does OSUI observed on urodynamic accurately predict the need for anti-incontinence surgery?

Does the absence of OSUI on urodynamic safety predict that prolapse repair alone is adequate?

Predicting the need for anti-incontinence surgery in continent women undergoing repair of severe ureteral prolapse.


Preoperative urodynamics evaluation is essential, decision to perform concomitant surgery "tailored" to individual urodynamics findings.

The Correlation Between Clinical and Urodynamic Diagnosis in Classifying The Type of Urinary Incontinence in Women: A Systematic Review of the Literature

Sanne van Leijsen et al. The Netherlands Neurol. and Urodynamics 30:495-502; 2011

Review 23 articles 6282 women wht UI .

Concluding: The level of agreement between classification based on Clinical Evaluation and Urodynamics investigation is poor. Urodynamic observations are regarded as gold standard, but based on the poor correlation, this assumption should be questioned.

Surgery for Stress Urinary Incontinence

Transient Incontinence

Permanent

Grade 1 Clinic Type I
VLPP "+90

VLPP

VLPP

VLPP

VLPP

Mini-slings

T.O.T Slings

Pubo-vaginal Slings

Burch

Grade 2 Clinic Type II
VLPP 60-90

VLPP

VLPP

VLPP

Grade 3 Clinic Type III
VLPP 30-60

VLPP

VLPP

VLPP

Grade 4 Clinic Type IV
VLPP

VLPP

VLPP

Cross-over Sling

Urethral reconstruction and support or Artificial Sphincter

CONCLUSIONS

There is Level 2/3 evidence that when prolapse repair surgery is performed at the same time as a TVT to treat stress incontinence, the cure rate for the stress incontinence is not adversely affected.

• GRADE B usually depends on consistent level 2
A single RCT provides level 1 evidence that concomitant Burch colposuspension is recommended in women without symptoms of stress incontinence at the time of open sacrocolpopexy.

Level 1 evidence exists from the CARE study which randomized 322 stress-continent women with Stage II-IV POP to a Burch colposuspension or no concomitant procedure at the time of concomitant open abdominal sacrocolpopexy [11]. The trial demonstrated the significant reduction of de novo SUI three months after surgery in women who were assigned to the Burch colposuspension compared to the group without a concomitant procedure.

In women without stress incontinence who are undergoing abdominal sacrocolpopexy for prolapse, Burch colposuspension significantly reduced postoperative symptoms of stress incontinence without increasing other lower urinary tract symptoms.

Level 1 evidence exists from the CARE study which randomized 322 stress-continent women with Stage II-IV POP to a Burch colposuspension or no concomitant procedure at the time of concomitant open abdominal sacrocolpopexy [11]. The trial demonstrated the significant reduction of de novo SUI three months after surgery in women who were assigned to the Burch colposuspension compared to the group without a concomitant procedure.


Colposuspension performed during sacroeyJse as prophylaxis for postoperative incontinence seems to emerge as over-treatment. These preliminary data cast doubts on whether Burch colposuspension should be performed during sacrocolpopexy. As our approach partially corrects urethral hypermobility, Burch colposuspension is not always required.

A PROSPECTIVE RANDOMISED CONTROLLED TRIAL COMPARING VAGINAL PROLAPSE REPAIR WITH AND WITHOUT TVT IN WOMEN WITH SEVERE GENITAL PROLAPSE AND OCCULT SUI: LONG TERM FOLLOW UP

Schieritz, L. Dwyer P et al. Australia
Neuro. and Urodynamics 806-7. 2010
ICS-IUGA Meeting Toronto

80 pts. Stage + 2 POP + OSUI Follow up 2 years.

Concluding message: The results indicate that the routine insertion of a mid-urethral slinging, TVT, in women with OSUI + POP cannot be recommended.
**Management SUI and POP**

Anterior Compartment
- **ABDOMINAL**
  - Burch
  - Colpotomy
  - Anterior Tape

- **VAGINAL**
  - Sling + Mesh
  - Sling + Lattis
  - Sling + Tape + Ant Post

Medium Compartment
- **ABDOMINAL**
  - Burch + Ant

- **VAGINAL**
  - Sling + Pelvic Fixation
  - Sling + Vaginal Fixation

Posterior Compartment
- **ABDOMINAL**
  - Site Specific + Pelvic Fixation

- **VAGINAL**
  - Promontopexy + Tape
  - Promontopexy + Lefort

**Multi-Compartmental**
- Burch + Ant (or not) + Promontopexy + Tape
- Burch + Great Hammock + Promontopexy
- Combined Abdominal + Vaginal
- One or two times
- Sling + Vaginal Fix (or not) + Tape (or not) + perineorraphy
- Sling + Vaginal Fix + Total Colpectomy + perineorraphy

**Video**

Stage IV POP and Ocular SUI

80 years old

TOT + Vaginal Hysterectomy + Total Colpectomy

**Literature Conclusions**

**Preoperative evaluations: No concluding**

Occult incontinence does not seem to predict the need of anti-incontinence procedure

There are some data providing doubt on whether or not an anti-incontinence procedure should be performed during sacrocolpopexy or prolapse repair in both continent and incontinent women

We have to balance the risk of SUI vs overtreatment and anti-incontinence surgery related complications

**Our Conclusions**

Vaginal and abdominal routes

One or two times

High grade POP + OSUI in women with coital activity
1st. Abdominal without TVT and 2nd Vaginal + TVT if necessary

High grade POP + OSUI in women coital activity negative
Vaginal route + TVT or TOT

"Common sense" is probably more important than "Evidence"
Occult SUI and POP: how I do it?

Prof Paulo Palma
Titular Urologia UNICAMP
Diretor Escola Brasileira de Urologia

Bases Anatómicas: Ligamento pubouretral
Zaccharin, Pereira

Bases Anatómicas
Palma, Grossi

Reposo

Esfuerzo

Micción
1 = ligamento pubouretral
2 = Inserción uretral del PUL

1 = Ligamento pubouretral
2 = Inserción del PUL

1 = lig. pubouretral externo
2 = Inserción uretral del PUL

1 = lig. pubouretral externo
2 = Inserción uretral LPU
3 = “Hammock”
4 = Base Vesical
1 = Lig. pubouretral externo
2 = Inserción uretral de LPU
3 = “Hammock”
4 = Base vesical
5 = Arco Tendíneo

Teoría Integral

1 = Ligamento pubouretral
2 = Inserción uretral LPU
3 = “Hammock”
4 = Base vesical
5 = Arco tendíneo

Teoría Integral

Cirugías Virtuales

Cirugía virtual: IUE Tipo III

Petros, Macmillan, 2007

Cirugía Virtual & Prolapsos

Calistar A: monoprotección para IUE, defecto apical y anterior
EGGS: goal-based approach

- Expectations
- Goal setting
- Goal achievement
- Satisfaction

How I do it? Occult SUI and POP

Paulo Palma,

Prof. Titular de Urologia, UNICAMP, SP, Brazil

Director Brazilian School of Urology (SBU)
CAU General Secretary

Occult SUI is associated with posite anterior vaginal wall prolapses and with utrine descensus in 60% of the case.

Virtual surgery, as proposed by Peter Petros, may help to disclose occult SUI.

When positive, surgical correction of SUI is indicated at the same time.

Although the concept of prophylactic sling is advocated by some researchers (Shlomo Raz), for “de novo” SUI may occur in 30% of patients after mesh repair, The potential risks of complication is the major drawback for this approach.

To overcome this situation, a new mesh (Calistar A – Promedon, Argentina) was developed to treat concomitantly anterior and apical prolapses even when associated to stress urinary incontinence (SUI). It is made of type I macroporous polypropylene with 6 millimeter diameter orifices in the body to improve tissue in growth and to provide flexibility. The suburethral portion of the mesh is attached to two self-anchoring polypropylene arms with a multi point fixation design, especially developed to be anchored at the internal obturator muscle bilaterally, in order to provide a strong suburethral primary fixation. Each arm is attached to a polypropylene stitch, to move it backwards during the procedure, if necessary, for a fine suburethral adjustment. A new tissue anchoring system was also developed, to fix the mesh’s arms to the sacrospinous ligament bilaterally, which represent the other anatomical landmark of the procedure. The set also includes a disposable retractable insertion trocar (Fig. 1).

In this study, it is evaluated the safety, feasibility and the results of this technique in a cohort of patients with stage 3 anterior / apical prolapses.

(A) (B) (C)

Figure 1. (A) Polypropylene mesh and multipoint fixation arms (B) Tissue anchoring system and trocar. (C) Surgical set.

Study design, materials and methods
From January 2010 to March 2011, 31 patients were enrolled in the study. Only patients with Pelvic Organ Prolapse Quantification System (POP-Q) stage 3 anterior vaginal wall prolapse were included. Concomitant SUI were diagnosed in 19 (61%) patients. The work-up included history, physical examination, stress test, standardized 1-h pad test, POP-Q staging, and
validated questionnaires (International Consultation on Incontinence Questionnaire Short Form – ICIQ-SF; International Consultation on Incontinence Questionnaire Vaginal Symptoms – ICIQ-VS). Sexual function was assessed with the Female Sexual Function Index (FSFI). Follow-up was performed at 1, 3, 6 and 12 months post implant.

The procedure was carried on with the patient in lithotomy position. The anterior vaginal wall was incised from midurethra towards the uterine cervix and the pubocervical fascia is carefully dissected. Blunt dissection was performed until identification of the ischial spines and the sacrospinous ligaments. Then, the retractable insertion guide was primed with the tissue anchoring system and was introduced into the sacrospinous ligament 1.5 cm medial from the ischial spine bilaterally. The same retractable guide was connected to the multipoint fixation arm for fixation of the suburethral part of the mesh bilaterally to the internal obturator muscle, one centimeter above the vaginal fornix. Then the polypropylene stitches were attached to the arms of the implant bilaterally. Stitches were placed at the posterior body of the implant and fixed at the remanents of cardinal ligaments or pericervical ring in order to avoid high cystocele recurence. Finally, the vaginal incision is closed in the usual manner. Cystoscopy was not mandatory (Fig. 2).

![Figure 2. Surgical procedure. (A) Suburethral insertion. (B) Anchoring of mesh to the stitches placed at sacrospinous ligaments. (C) Mesh at correct place before vaginal wall suture.](image)

**Results**

The mean age of patients is 59 ± 8.5 years old. Other demographic data are summarized in Table 1. All surgeries were performed under spinal anesthesia. Severe bleeding and technical or mechanical problems of the device were not observed. Until march 2011, seven patients (22%) completed 12 months follow up but as soon as 11 patients (35%) who completed 6 months follow up showed successful POP-Q staging improvement, as showed in Table 2. Also, all of the patients with concomitant SUI presented negative stress test and improvement of the ICIQ-SF score (Table 2). One patient (3%) presented mesh exposure, diagnosed in the second post-operative day, and were treated with excision and vaginal suture / topical estrogen replacement and antibiotics. This patient presented mesh infection (3%). Urinary retention were observed in one patient (3%), and solved spontaneously at the third day post-operative. One subject who maintained urgency in the post-operative was treated successfully with anticholinergics. The Female Sexual Function Index (FSFI) was 26 ± 1.4 before surgery, 48± 21.5 in six months and 49 ± 12.7 in one year follow up.
Table 1. Demographics

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Previous gestation (mean ± SD)</td>
<td>3.0 ± 2.6</td>
</tr>
<tr>
<td>Stress urinary incontinence - Stamey (%)</td>
<td>54.1%</td>
</tr>
<tr>
<td>Previous anti-incontinence surgery (%)</td>
<td>29.1%</td>
</tr>
<tr>
<td>Body Mass Index (mean ± SD)</td>
<td>27.7 ± 4.6</td>
</tr>
</tbody>
</table>

Table 2. Follow up

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>31</td>
<td>6</td>
<td>7</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Aa POP-Q point</td>
<td>+2 ± 1.5</td>
<td>-2 ± 0.9</td>
<td>-2 ± 0.7</td>
<td>-2 ± 0.8</td>
<td>-2 ± 0.9</td>
</tr>
<tr>
<td>Ba POP-Q point</td>
<td>+4 ± 1.7</td>
<td>-2 ± 1.1</td>
<td>-3 ± 0.6</td>
<td>-3 ± 0.7</td>
<td>-3 ± 0.9</td>
</tr>
<tr>
<td>C POP-Q point</td>
<td>+1 ± 3.4</td>
<td>-7 ± 3.1</td>
<td>-7 ± 1.5</td>
<td>-7 ± 1.7</td>
<td>-7 ± 2.1</td>
</tr>
<tr>
<td>Positive stress test</td>
<td>37.5%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>9%</td>
<td>0.0%</td>
</tr>
<tr>
<td>ICIQ-SF score (0-21)</td>
<td>31</td>
<td>6</td>
<td>7</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>FSFI</td>
<td>26 ± 1.4</td>
<td>--</td>
<td>--</td>
<td>48 ± 21.5</td>
<td>49 ± 12.7</td>
</tr>
</tbody>
</table>

Interpretation of results

In opposite to the transobturator approach, anchoring the mesh to sacrospinous ligaments allows for a D’Lancey level one correction as showed by the optimal POP-Q point C results in the follow-up. Also, the multipoint fixation arms provided primary and stable suburethral support, keeping the mesh in the proper place and allowing for an effective treatment of SUI, if present.

Conclusion

Initial results demonstrate that this technique represents an effective option for the treatment of prolapse and SUI. It introduces the advantages of simultaneous treatment of anterior and apical vaginal prolapses and SUI by a single vaginal incision, building safety and a fully level I correction.
**Future targets for Pharmacological therapy of Urinary incontinence**

Francisco Cruz  
Department of Urology  
Hospital S. João & Faculty of Medicine  
Porto, Portugal

**Drugs with antimuscarinics effects**

Non-subtype selective  
- Atropine, hyoscyamine  
- Propantheline  
- Trosplum  
- Tolterodine  
- Fesoterodine  
- Solifenacin

Mixed actions  
- Antimuscarinic + other actions

Oral route

- **Non-subtype selective**
  - Atropine, hyoscyamine
  - Propantheline
  - Trospium
  - Tolterodine
  - Fesoterodine
  - Solifenacin

Subtype selective (M₃)  
- Darifenacin

**Non-oral routes for oxybutynin**

Intravesical oxybutynin  
Transdermal oxybutynin

<table>
<thead>
<tr>
<th>Treatment duration</th>
<th>Mean change of urgency</th>
<th>Placebo</th>
<th>1.3 mg</th>
<th>2.6 mg</th>
<th>3.9 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>-10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>-7</td>
<td>-7</td>
<td>-7</td>
<td>-7</td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>-6</td>
<td>-6</td>
<td>-6</td>
<td>-6</td>
<td></td>
</tr>
<tr>
<td>3 weeks</td>
<td>-5</td>
<td>-5</td>
<td>-5</td>
<td>-5</td>
<td></td>
</tr>
<tr>
<td>6 weeks</td>
<td>-4</td>
<td>-4</td>
<td>-4</td>
<td>-4</td>
<td></td>
</tr>
<tr>
<td>9 weeks</td>
<td>-3</td>
<td>-3</td>
<td>-3</td>
<td>-3</td>
<td></td>
</tr>
<tr>
<td>12 weeks</td>
<td>-2</td>
<td>-2</td>
<td>-2</td>
<td>-2</td>
<td></td>
</tr>
</tbody>
</table>

**β₃ Adrenoceptor agonist YM178**

**BLOSSOM trial**

**Urgency**

**Frequency**

**Aprepitant, a new NK-1 receptor antagonist**

Effect on the number of events/day

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo</th>
<th>Aprepitant</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>-0.5</td>
<td>-0.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>-1</td>
<td>-1</td>
<td>-1.5</td>
</tr>
<tr>
<td>-1.5</td>
<td>-1.5</td>
<td>-2</td>
</tr>
<tr>
<td>-2</td>
<td>-2</td>
<td>-2.5</td>
</tr>
<tr>
<td>-2.5</td>
<td>-2.5</td>
<td>-3</td>
</tr>
</tbody>
</table>

**PDE-5 inhibitors**

12 weeks of silodenal (50-100 mg/day) vs placebo in BPH patients

<table>
<thead>
<tr>
<th>ISR total score</th>
<th>Placebo</th>
<th>Silodenal</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>10</td>
<td>15</td>
</tr>
</tbody>
</table>

Change from baseline of patients with IPPS total score > 20
TRPV1 receptor

• Intravesical: Vanilloids (RTX), BONT/A
• Intrathecal: Vanilloids (RTX)
• Oral: TRPV1 small molecule antagonists

Intravesical RTX desensitizes TRPV1

RTX instillations in patients with refractory IDO

- Placebo, 28 patients
- RTX, 26 patients

At 6 month treatment remained effective in 50% of patients

- RTX with different origins/preparations
- RTX solutions still very unstable

BoNT-A decreases TRPV1 (but not PGP 9.5) immunoreactivity in the suburothelium of NDO patients

BoNT-A prevents SNARE-dependent TRPV1 trafficking in neurones

Intrathecal RTX decreases the expression of TRPV1 but not IB4 fibers at L6 spinal cord

TRPV1 antagonists

GluacoSmithKline: SB-705498
Abbott: A-425619
Amgen: AMG-8810
Neurogen: BCTC, Nrgn-3
Glenmark: GRC 6127
Johnson & Johnson: JNJ 17203212
Bayer: WO 040023440, 04052845, 04072020, 05044786
Takeda: WO 04074695
Novartis: WO 04033434, 020779476
Merck, Sharp & Dohme: WO 04074290, 05049601, 05049613

GRC 6211

Piperazine
Pyrolidine
Aryl-urea
Anilamide
Quinazoline
Benzozipran
Aminoazoles
Oral GRC 6211: Effect on rat intact bladders

| Vehicle: 0.5% methylcellulose | Charns et al., J Urology, in press |

<table>
<thead>
<tr>
<th>Contractions / minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01 mg/kg</td>
</tr>
</tbody>
</table>

Oral GRC 6211: Effect on CMG with 0.5% acetic acid

| Vehicle: 0.5% methylcellulose | Charns et al., J Urology, in press |

<table>
<thead>
<tr>
<th>Contractions / minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01 mg/kg</td>
</tr>
</tbody>
</table>

Oral GRC 6211: Effect on bladder reflex contractions in SCI-rats

<table>
<thead>
<tr>
<th>Conractuals/20 minutes CMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01 mg/kg</td>
</tr>
</tbody>
</table>

NGF bladder content in BOO and PBS/IC

<table>
<thead>
<tr>
<th>NGF protein in normal and hypertrophied (BOO) human bladders</th>
</tr>
</thead>
<tbody>
<tr>
<td>NGF protein in the bladder of patients with IC</td>
</tr>
</tbody>
</table>

NGF and IDO-NDO

<table>
<thead>
<tr>
<th>Urinary NGF and PIG in controls and female patients with GBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donal Root Ganglia</td>
</tr>
</tbody>
</table>

Effect of NGF neutralization on CMG of SCI rats

<table>
<thead>
<tr>
<th>Effect of NGF neutralization on CMG of SCI rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, SCI vehicle-treated</td>
</tr>
<tr>
<td>B, SCI/NGF-Ab treated</td>
</tr>
<tr>
<td>C, SCI/NGF-Ab treated</td>
</tr>
</tbody>
</table>
Sequestration of BDNF by Intravenous recombinant protein TrkB-Ig2 decreases bladder reflex contractions in rats with cystitis

Cys+saline
Cys+TrkB-Ig2 (200 µg)

** **

0, 5, 1, 5

Naive
Saline 100 µg 200 µg

Inhibition of spinal ERK phosphorylation (i.t. PD98059) and reflex bladder contractions in cystitis

Rat with intact bladder
Rat with inflamed bladder

Inhibition of spinal ERK phosphorylation and reflex bladder contractions in SCI rats

0, 5, 1, 5

0, 5, 1, 5

Inhibition of spinal ERK phosphorylation and reflex bladder contractions in SCI rats

Activation of Smooth Muscle by Noradrenaline

RhoA
PKC
PLC
MLC
MLC
Relaxation

Noradrenaline

K-E Anderson, 2005
Conclusions

• Oral route is probably the ideal one to deliver compounds for OAB/DO
• B3 adrenoreceptor agonists, NK1 antagonists and PDE-5 inhibitors are already in clinical trials
• Oral TRPV1 antagonist GRC 6211 is promising
• Neurotrophins and intracellular pathways are emerging as new potential targets

Trends in antimuscarinic therapy

• Oral route
• Long half-life/slow releasing formulations
• Good intestinal absorption
• High muscarinic receptor subtype selectivity
• Organ selectivity
• Dosage flexibility
Pelvic Floor dysfunctions in women represent an important health problem. The major risk factor for developing these conditions is vaginal birth.

Biomechanics is considered one of the main topics of current pelvic floor research recommendations. It is only recently that researchers have begun biomechanical analysis to evaluate the mechanism of pelvic floor normal support and its failures as well as sequelae of vaginal birth.

Bioengineering is the science that deals with structure-function relationships. The translation of biomechanics research to clinical settings may contribute to understand the etiology of these complex conditions and improve assessment and treatment of pelvic floor dysfunctions.

The combined technology will allow us to identify mechanisms of pelvic floor disorders, assume preventive strategies and optimize surgical procedures.