become commercially available. The aim of the study was to confirm or to reject the current knowledge on the topography of the vanilloid receptor in the normal human bladder.

Methods: Bladder tissue was taken from cystectomy specimens or transurethrally.

In all cases a biopsy of the bladder neck or trigone was taken as well as a biopsy of the fundus of the bladder, including the muscularis.

Immunohistochemstry was performed on frozen bladder specimens with a polyclonal anti-capsaicin-antibody (Chemicon Int.®), using a three-step unlabeled peroxidase-anti-peroxidase (PAP) method, as described previously (2). Colocalisation studies were performed for CGRP and Substance P using laser confocal microscopy.

Results:

1) The presence of the vanilloid receptor on unmyelinated nerves is confirmed.

2) Immunoreactivity was also noted on the Schwann cells (perineurium) of myelinated nerves.

3) Strong immunoreactivity was noted on the smooth muscle cells of the muscularis layer and of the lamina propria. The heterogeneity of the immunoreactivity in the muscular layer pleads against eventual background colouring.

4) The reported higher concentration at the level of the bladder neck is caused by the presence of more muscle fibers in the region and by the compactness and orientation of these fibers and not by a higher individual immunoreactivity.

Discussion: The presence of the receptor on the unmyelinated afferent nerves is confirmed. The presence on the perineurium and the abundant immunoreactivity of the smooth muscle is more puzzling. Possibly vanilloidreceptor blockade by intravesical capsaicin or resiniferatoxin not only results in an indirect smooth muscle relaxation by desensitisation of the afferent branch of a spinal C-fiber mediated reflex arc, but also in a direct relaxation by interaction with the smooth muscle itself.

References:

1) Naunyn-Schmiedeberg's Arch Pharmacol 347:624-629,1993.

2) Histopathology 23:519-525,1993.

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Title (type in CAPITAL LETTERS, leave one blank line before the text):
EXTRAMURAL AMBULATORY CYSTOMETRY AS A RESEARCH TOOL TO QUANTIFY BLADDER OVERACTIVITY IN RANDOMIZED CLINICAL TRIALS

Introduction

Bladder overactivity is poorly defined by the ICS. Descriptive terms like 'a disorder of the filling/storage phase', 'involuntary bladder contractions, while the patient is attempting to inhibit', 'detrusor hyperreflexia' or 'detrusor instability' are today's confusing clinical practice. In this study *"Bladder overactivity is a dysfunction of the bladder, in which a subject has no or decreased control over sudden occurring contractions of the musculus detrusor, in such a way that this leads to premature passing of urine".*

Aims of study

In this study we investigated the applicability of Ambulatory CystoMetry (ACM) to assess efficacy of therapeutic modalities in patients suffering from bladder overactivity.

Methods

ACM is performed according to ICS standards [1] with event markers at the actual start and end of it, at initiation and cessation of voiding (entering, leaving toilet). Episodes of urgency, time and volume of fluid intake (at least 200 ml/h), voiding as well as time and leakage volume of pad and pad change are registered in a diary. Duration of an average ACM is approximately 6 hours, taking place between 9:00 a.m. and 4:00 p.m. Gaeltec equipment and microtip catheters are applied. There are no special provocative tests defined. After installation and instruction patients may go home. At the end of the 6-hour period they return to the urodynamic labobatory to finish the investigation.

Results of the ACM are: total monitoring time, number of contractions during the filling phases and (mean) duration and amplitude of these contractions. The diary provides number of micturitions, the mean volume voided, the total volume drunk. Data of results are then used to calculate the Detrusor Activity Index (DAI, [2]); the theoretical range of the outcome of this quantitative model is lying between zero (non-overactive) and 1 (severe overactive bladder). Construct validity of the DAI has been investigated by the sensitivity /specificity with respect to correctly classified detrusor overactivity, the ICC_R (test-retest reliability) and the ICC_A (inter assessor agreement). The padtest (urineloss per hour during the A0CM) was also evaluated by the ICC_R. Finally, we compared the DAI (loss/hour, mean volume) as efficacy outcome in clinical trials of treatment modalities for overactive bladders with conventionally applied outcome variables like incontinence episodes/week, frequency/24-hours, mean volume/micturition and number of pads/24-hours. For this purpose we used the data from a recent trial (n=1022) investigating the efficacy of tolterodine [3] and from a recently finished own trial (n=28) investigating the efficacy of functional electrostimulation (FES).

The effect measured by the different outcome variables was translated into a so-called 'standardized effect' (St.Eff.) in order to enable a proper comparison. If the St.Eff. for two groups is lying at 0.20 it can be defined as a 'small effect size', if it is at 0.50, it can be defined as a 'medium size', and at 0.80 it can be defined as a 'large effect' [4].

Results

The DAI-score has a sensitivity and specificity of 86%, if 0.41 would be considered as the discriminating cutoff point between overactive and normal bladder activity during the filling phase. In a group of 21 female patients with LUTS (mean age 51.6; sd 11.4) the test-retest of the DAI (appr. 2 months) showed an ICC_R = 0.85. The ICC_A for 1 observer obtained in data from 2 blinded observers analyzing 111 ACMs was 0.96. The volume of urineloss/hour of padtest obtained in the previous patient group (n=21) showed an ICC_R = 0,87. Table 1 shows the standardized effects of each outcome variable in both studies. It is striking that loss/hour and incontinence episodes/week, respectively, frequency/6 and /24-hours show almost the same St.Eff. for two different treatment modalities representing a minimal effect, while the DAI shows a large effect for FES.

TABLE 1

Study	Efficacy variable	Standardized effect
FES	DAI	0.78
	Frequency/6-hours	0.09
	Loss/hour	0.21
	Mean volume/micturition	0.49
Tolterodine	Incontinence episodes/week	0.23
	Frequency/24-hours	0.16
	Mean volume/micturition	0.34
	Number of pads/24-hours	0.19

Conclusions

This study can be seen as a contribution to the construct validity of ambulatory urodynamics and the Detrusor Activity Index for research purposes. The results also indicate that for overactive bladder assessment, the DAI is a relatively strong instrument for efficacy measurements compared to conventionally applied outcome variables.

References:

1. Neurourol Urodyn, vol. 19, 2000: p. 113-125
2. BJU, vol. 83, Suppl. 2, 1999: p. 16-21
3. Clin-Drug-Invest, vol. 19, 2000: p. 83-91
4. Foundations of clinical research,Appleton & Lange, Norwich, Connecticut 1993: p. 653

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

CAN ULTRASOUND REPLACE AMBULATORY URODYNAMICS WHEN INVESTIGATING DETRUSOR INSTABILITY?

Aims of Study. Urodynamics remain the standard diagnostic technique when assessing women with lower urinary tract symptoms. Laboratory urodynamics has been shown to be less sensitive than ambulatory studies[1] at detecting detrusor instability. However since ambulatory studies are labour intensive and time consuming they remain a second line investigation for those women with symptoms that are not explained by laboratory urodynamics. The use of ultrasound assessment of bladder wall thickness has previously been described as a sensitive screening method for diagnosing detrusor instability in symptomatic women without outflow obstruction[2]. It has been postulated that women with detrusor instability develop detrusor hypertrophy secondary to repeated isometric contractions against a closed bladder neck. We have investigated the possibility that ultrasound assessment of bladder wall thickness in women with equivocal laboratory urodynamics would replace the need to perform an ambulatory study.

Methods.A prospective study was performed of women with equivocal laboratory urodynamic findings who were booked to undergo an ambulatory study. In all women ultrasound assessment of bladder wall thickness was undertaken prior to ambulatory urodynamics to avoid bias. A transvaginal ultrasound scan was performed using a 7.5 mHz probe in the supine position with an empty bladder. The bladder wall thickness was measured in three places; in a plane perpendicular to the luminal surface of the bladder at the thickest part of the trigone, at the dome of the bladder, and at the anterior wall. All measurements were made at maximal magnification. Ambulatory urodynamics were then performed using a single, solid state 7F Gaeltec microtransducer with two pressure transducers in the bladder and a separate solid state transducer in the rectum. The test lasted four hours and the women were asked to drink 200 mls of fluid every 30 minutes and to keep a diary of events and symptoms. The results were analysed using a personal computer and detrusor instability was only diagnosed if a detrusor pressure rise was recorded in association with urgency or urge incontinence. Mean bladder wall thickness and 95% confidence intervals were analysed.

Results.121 women were recruited to the study. Ambulatory diagnosis and mean bladder wall thickness are shown below with the 95% confidence intervals. **(Table 1).** Only one subject was found to have voiding difficulties and was therefore excluded from further analysis. Examination of the 95% confidence limits reveals no overlap in the groups