

Moderated Poster Session V: General Urology and Infertility

Friday, September 24, 3:00-4:30 p.m.

P62

Androgen Inducible Genes in Human Prostate Stromal Cells

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Purpose: The prostate gland is dependent on male steroids (androgens) for its development, adult maintenance and function. Androgen action in prostate cells requires the presence of the androgen receptor (AR) protein, a nuclear transcription factor that is conditionally active only when bound to an active androgen. Previously, others have shown that the AR expressed in prostate stromal cells is necessary for prostate development whereas AR expression in the epithelial cells of the tissue is not needed for prostate formation. Since AR is known to be involved in prostate cancer development and progression, all past work on defining AR regulated gene expression has focused on studies of prostate epithelial or cancer cells. Here, we attempted to define the gene products that are regulated by the AR in prostate stromal cells.

Materials and Methods: Using human WPMY-1 prostate derived stromal cells as a model, we first tested whether AR is expressed in these cells and whether it is able to activate androgen-inducible gene expression. Using Western blotting, we showed that parental WPMY-1 cells express 100-fold lower AR protein when compared to prostate cancer (LNCaP) cells. Additionally, WPMY cells do not activate reporter gene expression from androgen-inducible promoters unlike LNCaP cells. Therefore, we created a stable WPMY-1 variant (WPMY-AR) that overexpresses AR protein by transduction with an AR expressing lentivirus; this cell variant strikingly upregulates reporter gene expression from the androgen-sensitive probasin gene promoter. Then we undertook gene expression profiling using the Affymetrix ST 1.0 gene chips and compared gene expression in vehicle treated WPMY-AR vs androgen (dihydrotestosterone) treated WPMY-AR (72 hrs).

Results: One hundred and eighteen genes were found to be upregulated by androgen whereas 367 genes were downregulated by androgens in this paradigm.

Conclusion: The GO characterization of upregulated genes using the David Program showed a major class of genes in the "Developmental Signaling" category and some of the particular genes that were upregulated suggest that androgen stimulated WPMY-AR cells stimulate expression of genes involved in Wnt and BMP signaling suppression that might be consistent with a program of differentiation initiated by androgen signaling from prostate stromal cells.

P63

Role of Pelvic Floor Release (Osteopathic Technique) in the Management of Symptoms Associated with Chronic Non-bacterial Prostatitis (Type III) - A Pilot Study

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Background: Chronic non-bacterial prostatitis (NIH classification-type III) is a recurrent and bothersome condition with symptoms that may interfere with normal activities. It may be associated with pelvic floor muscle dysfunction that may be directly or indirectly contributing to some of these symptoms. Literature search failed to find any study indicating the use of pelvic floor release osteopathic technique to manage this condition. The purpose of this pilot study was to know if this treatment has any role in

the management of symptomatic and recurrent chronic non-bacterial prostatitis, in addition to medical and other conservative managements.

Methods: Institutional IRB approval was obtained prior to enrollment. All patients presenting to one of the author's Urology practice with the above condition were given the option of participating in this study and were enrolled after consent. All patients had more than 3 episodes of prostatitis and had received medications including antibiotics, anti-inflammatory drugs, and alpha-blockers and had cystoscopic evaluation with prostatic massage in the past. None of them had taken pentosan polysulfate ("Elmiron") or gabapentin ("Neurontin") or other related medications. Patient also had been instructed to avoid prostate irritants, regular sexual activity and to avoid strenuous exercise or work. At initial visit, in addition to pelvic and rectal examination, thorough osteopathic evaluation and urinalysis and culture were performed. All patients completed International Prostatic Symptom (IPS) and Pelvic pain and Urgency/Frequency Patient Symptom Scale (PUF) scores at initial visits and at subsequent follow-ups. The release treatments were performed weekly for 4 weeks and then on alternate weeks until patient was satisfactorily better or for a total of eight treatments. The technique involved application of direct passive force to levator ani and coccygeus muscles to allow relaxation and provide improvement of symptoms both directly and indirectly.

Results: A total of 6 eligible patients were enrolled. Two patients dropped out after one and 3 treatments and were lost for follow-up. Remaining 4 patients either reported 75 to 100% better with their bothersome symptoms and/or showed significant reduction in symptom scores, especially PUF score reduction of more than 50%. These patients had 4 to 8 treatments (mean of 5.4).

Conclusion: This pilot study has shown the possible role of osteopathic pelvic floor muscle release in selected patients with chronic non-bacterial prostatitis (type III) to improve their symptoms. However, a large scale study using control group may be needed before this treatment is being widely used.

P64

Clavien Classification of Surgical Complications Applied to Urological Procedures and Evaluated According to Training Level

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Background: The Urological Surgery field has been growing vigorously throughout the past two decades. New procedures, mainly in the area of minimally invasive surgery were added to urologists' routine. However, it still lacks a reliable classification to report surgical complications. The Clavien Classification has shown to be accurate and trustworthy when applied to General Surgery operations. Briefly, instead of taking into account the complication per se, this classification gives scores (I to V) mainly considering the medications and procedures applied to fix such complications. The most important strength of this system is that it is standardized and has been well validated. We assessed the agreement rate among urologists applying this classification to actual scenarios. Considering that usually residents and fellows are in charge of reporting surgical complications, we have also compared Clavien scores given by fully trained urologists to scores given by residents or fellows.

Methods: During 12 months, consecutive surgical complications were prospectively recorded from four centers, composing the major areas of urological practice. Among these, twenty cases were selected to compile a survey. The cases were distributed in order to include a broad spec-

trum of frequent complications. After a briefing and explanation session concerning the classification, the survey was applied to 16 full trained urologists and 16 urology residents/fellows. During the presentation, each subject had the same amount of time to answer the questionnaire. Concordance rates were recorded for each scenario separately and as a pool of scores.

Results: Twenty scenarios and 32 subjects were included, totalizing 640 scores. Concordance rates for each scenario ranged from 45.2% to 100%. The mean concordance rate was 83.4%. Four out of 20 scenarios had concordance rates below 80%. In two scenarios, the scores given by residents/fellows were significantly lower when compared to scores given by fully trained urologists ($p < 0.05$). The same tendency was shown when all scenarios were collapsed and evaluated as a group.

Conclusion: The Clavien Classification has shown to be reliable when applied to urological procedures. In a small proportion of scenarios, the interpretation might diverge among urologists. In those cases, residents and fellows have the trend to underestimate the severity of the complication when compared to fully trained urologists.

P65

Photoselective Vaporization of the Prostate: Technical and Clinical Differences Between Potassium Titanyl Phosphate and Lithium Triborate Lasers in Prostates <80 Gm

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Background: To report early results of PVP using LBO laser aiming to identify any clinical difference to KTP laser in prostates <80 gm.

Methods: A total of 186 men with symptomatic benign prostatic hyperplasia with prostate size <80 gm underwent photoselective laser vaporization of the prostate using KTP ($n = 84$) between (October 2004-April 2007) or LBO ($n = 104$) between (July 2007 - January 2010). Functional follow up included measurement of maximum urinary flow rate (Qmax), post void residual urine (PVR), international prostate symptom score (IPSS), quality of life (QoL), and prostate specific antigen (PSA). Follow-up evaluations were done for the patients during their visits at 1, 3 and 6 and 12 months postoperatively.

Operative data, complications, catheter removal and hospital stay were also recorded.

Results: Base line characteristics of both groups were similar. Mean pre-operative prostate volume was 44.25 ± 13.3 and 45.5 ± 16.3 cc in KTP group and LBO group, respectively. KTP required more operating time than LBO (59.4 vs 50.6 minutes, $p = 0.02$).

All functional parameters improved significantly compared to base line values in both groups. There was no difference in IPSS, QoL, Qmax, PVR and percentage of PSA reduction between the two groups at 1, 3, 6 and 12 months postoperatively. At 12 months follow-up, the IPSS improved by 60.1%, QoL improved by 61.1%, Qmax increased by 141.2% and PVR decreased by 69.2% in KTP group. In LBO group, the IPSS improved by 69.6%, QoL improved by 65.7%, Qmax increased by 120.9% and PVR decreased by 72.7%. There were no significant differences regarding intra-operative and postoperative complications in both groups.

Conclusions: Despite some technical differences, KTP and LBO have comparable perioperative safety and produce similar early functional results for men with symptomatic benign prostatic hyperplasia in prostates <80 gm. However, KTP requires a longer operating times than LBO.

P66

New Sonographically Detected Voiding Urethral Regurgitation May be Initiating Factor in LUTS/CPPS

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Introduction and Objectives: LUTS was originally coined by Walsh referring to unexplained lower urinary tract symptoms on which 5 alpha reductase inhibitor was reported to have only a placebo effect. The term has eventually evolved to include a host of inflammatory conditions: male interstitial cystitis, Chronic Pelvic Pain Syndrome, etc. Previous investigators have tried to establish reflux as the initiating factor by

injecting radio-active carbon particles and scintiscanning the urethra while others have designed digital graphics but have not received adequate acceptance. Our team utilized real-time gray scale and spectral Doppler technology revealing voiding urethral regurgitation as an initiating factor in LUTS/male interstitial cystitis/CPPS, etc.

Methods: Medical records of patients with urethral, perineal, testicular, bladder and pelvic pains with dysuria, obstructive symptoms, e.g. hesitancy, dribbling, slow stream, incomplete emptying and irrigative, e.g. frequency, urgency were reviewed. Initially, 30 patients were worked-up routinely with negative yields. Our team then tested voiding urethral Doppler using external 7 Mhz transducer which showed regurgitation on spectral Doppler due to a distal urethral web shown on real-time gray scale ultrasound and direct visualization. Resection of the web was undertaken after initial satisfactory outcome with the first group.

Results: 403 patients with LUTS and sonographically detected voiding urethral regurgitation (Fig.1) from a gray scale ultrasound and direct vision visualized distal urethral web (Fig. 2) underwent resection of the web supplemented by antibiotics per microbiology and alpha blockers/5ARI per urodynamics/lower urinary ultrasound/cystoscopy. 386 reported satisfactory results while 16 were unsatisfactory. 5 were female with irreversible interstitial cystitis from a distal urethral ring of Lyon (Fig.3) reported in *J Urol* (Vol 63, 1965). 16 were younger females in whom development of IC was avoided by early intervention with age-specific urethrotomy.

Conclusions: This is a clinical report and not a randomized placebo-controlled study on 403 patients with new sonographically detected voiding urethral regurgitation from a distal urethral web, resection of this was followed by satisfactory outcome. In the female, early transurethral incision by age-specific urethrotomy of the distal ring of Lyon prevented development of IC.

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P67

Combined Anticholinergic Therapy with Long Term Followup in Refractory Overactive Bladder

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Background: To evaluate the efficacy and tolerability of combined multiple anticholinergic therapy in the treatment of refractory overactive bladder (OAB).

Methods: Twenty-three patients (14 female, 9 male) followed at a referral neurourology clinic were identified in retrospective chart review. Charts of patients with diagnoses of overactive bladder, urgency, frequency, urge incontinence, or mixed incontinence, with office visits within the last 2 years were reviewed. Inclusion criteria were patients on multi-drug therapy after failing dose-escalated monotherapy. All patients had overactive bladder with urge incontinence ($n = 13$) or without incontinence ($n = 10$), and had undergone urodynamic studies ($n = 21$). Patients were all treated with combined double, triple, or quadruple anticholinergic therapy (tolterodine 4 to 8 mg, oxybutynin 10 to 20 mg, oxytrol patch 3.9 mg, solifenacin 5 to 10 mg, darifenacin 7.5 to 15 mg, trospium 20 to 60 mg, imipramine 75 mg, and/or flavoxate 300 mg) after failing monotherapy. Mean age was 64 years (range 33-86). Mean age at start of therapy was 60 years (range 22-85). Combined drug therapy was given and patients were followed for mean of 5 years (range 1-15).

Results: Continence improved in all 23 patients. 19 patients (83%) had significant improvement in their symptoms, including 3 patients (13%) with resolution of symptoms. Four patients (17%) had mild improvement. 18 patients (78%) received double drug therapy. 4 patients (17%) received triple therapy. 1 patient (4%) was maintained on quadruple therapy. Mean post-void residual (PVR) was 31.5 mL, with 9 patients (39%) with PVR of 0. Incontinence events decreased to 23.8% of base-line incontinence on monotherapy. 3 patients (13%) could not tolerate the addition of a second anticholinergic (dry mouth, nausea, headache) and stopped treatment despite symptom relief. 4 patients (17%) were tried on 2 or more different combinations of double therapy before being maintained on the most efficacious therapy.

Conclusions: Eighty-three percent of OAB patients refractory to single drug therapy responded successfully to combination anticholinergic therapy. These included the newer generation selective receptor drugs. Long term followup in our study showed durable effect, improved quality of life, satisfaction, and tolerability. Side effects were comparable to single drug therapy. Combination anticholinergic therapy may be an efficacious, non-invasive treatment option for refractory OAB.

P68
Relationship Between Prostate Volume and Silodosin-Mediated Improvement of Symptoms Associated with Benign Prostatic Hyperplasia

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Background: Combined data of 2 placebo-controlled phase 3 studies showed that silodosin significantly improved International Prostate Symptom Score (IPSS) and peak urinary flow rate (Qmax) in patients with symptoms of benign prostatic hyperplasia (BPH). In this post hoc analysis, we evaluated the relationship between estimated prostate volume (PV) and symptom improvement.

Methods: PV was estimated from prostate-specific antigen (PSA) levels as described (Roehrborn et al. *J Urol.* 1999;53:581-589). Changes from baseline to week 12 (with last observation carried forward) were compared between patients with estimated PV <30 mL and those with estimated PV ≥30 mL, using ANCOVA with baseline as the covariate.

Results: Of 466 patients who received silodosin (mean age, 65 years), 450 provided PSA data at baseline (range of estimated PV, 18.4 to 76.8 mL); of those, 100 patients had an estimated PV <30 mL. The 2 subgroups had similar baseline values for IPSS and Qmax (Table 1). Silodosin-mediated reduction in IPSS from baseline to week 12 tended to be slightly greater in patients with larger estimated PV, but the mean difference between the 2 PV subgroups was not statistically significant (Table). Mean changes in Qmax from baseline to week 12 were ≥2.3 mL/sec in both subgroups, indicating that silodosin provided clinically important improvement in Qmax, regardless of estimated prostate volume.

Conclusions: Silodosin provided improvements in IPSS and Qmax in patients with estimated PV <30 mL and in those with estimated PV ≥30 mL.

Funding: Watson Pharma, Inc. provided funding for this research.

| | | <30 mL (N=100) | ≥30 mL (N=350) |
|--------------|-------------------------------|-------------------|-------------------|
| IPSS | Baseline, mean ± SD | 21.0 ± 5.2 | 21.4 ± 5.1 |
| | CFB to wk 12, mean ± SD | -5.4 ± 6.4 | -6.7 ± 6.7 |
| | Adj. mean difference (95% CI) | -1.2 (-2.6, 0.2) | |
| Qmax, mL/sec | Baseline, mean ± SD | 8.9 ± 2.4 | 8.7 ± 2.6 |
| | CFB to wk 12, mean ± SD | 3.3 ± 5.4 | 2.3 ± 4.1 |
| | Adj. mean difference (95% CI) | -1.1 (-2.0, -0.1) | |

P69
Detection of Vitamin D Deficiency in a General Urology Practice
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 Vitamin D deficiency has been reported to be prevalent in the general population in the United States. Vitamin D has been associated with numerous health benefits ranging from bone health to cancer prevention. An emerging group of individual urologists consider themselves, and are perceived as “Men’s Health” experts. Since Vitamin D deficiency is a significant men’s health concern, a prospective analysis (Vitamin D 3 levels checked by blood samples) of 100 consecutive male patients was performed in a general urology practice. Vitamin D deficiency was detected in 74% of the patients tested. Urologists, particularly those interested in providing more comprehensive men’s health care to patients, should consider testing for Vitamin D levels as part of their evaluation of new and established male patients. Treatment is simple, inexpensive, and effective. This simple modification in urology practice can augment the urologist’s role in providing more comprehensive care as a “Men’s Health” specialist.

P70
 WITHDRAWN

P72
Do Urologic Procedures Such As Prostate Needle Biopsy and Vasectomy Cause Erectile Dysfunction?

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Background: Patients undergoing active surveillance for prostate cancer may be subject to multiple prostate biopsies. Prior studies suggest that prostate needle biopsy (PNB) and vasectomy may cause erectile dysfunction (ED). We explored the relationship between a prior PNB or vasectomy and rates of ED.

Methods: We reviewed a prospectively organized database of 890 patients who underwent transrectal ultrasound (TRUS)-guided PNB. ED was modeled as a categorical variable as either any, moderate-severe, or severe based on International Index of Erectile Function (IIEF) scores. Binary logistic regression was used to analyze the predictive ability of PNB and vasectomy. They were adjusted for age in multivariate analysis. Results: Median age and IIEF score were 63 years and 19 points, respectively. According to IIEF scores, 22%, 11%, 15%, 34% had severe, moderate, mild-moderate, and mild ED, respectively. 18% had no ED. Vasectomy status was available in 391 patients, of whom 41% had prior vasectomy. On univariate analysis, age (OR=1.1, *p* < 0.001), prior PNB (OR=1.83, *p* < 0.002) and prior vasectomy (OR=0.41, *p* < 0.001) were all associated with moderate-severe ED. Only age (OR=1.1, *p* < 0.001) and vasectomy (OR=0.39, *p* < 0.002) were predictive for severe ED. On multivariate analysis, age was predictive for moderate-severe (OR=1.08, *p* < 0.001) and severe (OR=1.09, *p* < 0.001) ED, while vasectomy was protective against moderate-severe (OR=0.41, *p* < 0.001) and severe (OR=0.41, *p* < 0.003) ED. PNB status was no longer significant (*p* > 0.05) after adjustment for other covariates.

Conclusions: Age is a strong predictor of ED. Prior vasectomy is associated with a reduced risk of ED. Prior PNB, after adjustment for other variables, does not increase the risk of ED. Patients should be re-assured that PNB does not cause ED. Furthermore, ED was common in this cohort, and thus patients undergoing definitive therapy for prostate cancer should expect ED post treatment due to prior dysfunction.

P73
 WITHDRAWN

P74
 WITHDRAWN

P75

Penile Injury is Apparently Not the Underlying Etiology for Peyronie's Disease in 450 Consecutive Canadian Men: A Single Center Results

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Background: The most widely-accepted explanation for the development of abnormal collagen deposits in the tunica albuginea covering of the penis, known as Peyronie's disease (PD) is that it follows aberrant wound healing after penile injury. It is suggested that following trauma to the erect penis, probably during sexual intercourse, microscopic tears develop in the tunica albuginea. Contemporary data suggests incidence in 5-9% of men, as "tunica scarring" results in development of penile plaques and subsequent penile curvature or other deformity during erection and in some, erectile dysfunction. On the other hand, data to support the involvement of penile trauma in precipitating PD are inconclusive. Interestingly, while the testes have a similar tunica albuginea covering to that of the penis, testicular injury (direct trauma) does not seem to result in tunical scarring. The aim of this study was to clarify the prevalence of penile injury in a large contemporary cohort of patients diagnosed with PD.

Methods: Patients were evaluated between January 2008 and February 2010 and diagnosed with PD based on history, genitourinary examination and high resolution penile ultrasound (US). Penile US was used to confirm the penile plaques sites, size, and presence/absence of calcification. If erectile function was compromised, color penile US was done. Patients were questioned for injury events (self and/or partner stimulation) to the erect penis prior to the development of penile deformity. Institutional approval was obtained.

Results: The 450 consecutive patients included in this study had a mean age of 52y and duration of disease prior to presentation of 1.1 y. Plaque distribution was primarily dorsal or dorso-lateral. Calcification of the penile plaques was present in 18% (n = 81) of patients, while only 15% (n = 67) of patients reported history of penile injury. There were no significant differences between the patients with and without history of penile injury regarding age, penile plaque size, site and presence of calcification.

Conclusions: This large prospective series confirms recent evolving data that penile injury does not appear to be the primary cause of PD; potential causes may include immunological or inflammatory disorders, or as yet unidentified causes.

P76

Sex, Sexuality and Procreation in Complex Uro-Genital Anomalies

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Background: Surgeons endeavour to reconstruct lower genitourinary anomalies early in childhood. Considerable success is achieved in restoring functionality but these individuals must make various lifestyle adjustments to cope with numerous challenges. Such patients managed in a Community Urology practice over the past 20 years were studied to identify these challenges and the strategies used in their management. Results of treatment as they affect sex, sexuality and procreation were examined in 4 cases.

Methods: Records from hospitals and Physicians' offices were reviewed for demographic data, surgical procedures and diagnostic imaging studies performed and follow up patterns. Parents when available were interviewed. For this report, complex anomalies were those who had more than 2 attempts at corrective surgery.

Results: The 4 cases identified out of 15 and lessons learned are presented (1) Baby born with cloacal anomaly, imperforate hymen and solitary left kidney. After numerous surgeries she got married, conceived twice, 2 living sons delivered by caesarean section. Tubal ligation achieved birth control. At 40, she is happily married and grateful for mother's and family support. (2) Baby boy born with complex hypospadias had numerous surgeries in early life. In his late teens, required further surgeries to correct multiple urethral diverticulae, strictures and stones. Graduated from University and got married. Currently challenged by oligospermia and fertility issues at 26. (3) Baby born with urethral duplication and genital anomaly. With parental consent, baby was raised as a girl. At age 14, she requested for a gender re assignment. With the support of the parents, the urologist and the legal system her request was granted. (4) Baby born with Bladder Exstrophy. Multiple reconstructive surgeries achieved good cosmesis and functionality. At 25, she is in a sexual relationship, carrying out self catheterization with occasional UTIs.

Conclusions: Complex lower urogenital anomalies can present challenges and long term lifestyle adjustments. Parental support, excellent reconstructive surgeries, ongoing urological/medical care in adulthood can produce good results. Patient's cooperation and resilience are paramount.