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BLADDER

The influence of intermittent hypoxia, obesity and diabetes on male genitourinary anatomy and voiding physiology

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We used male BTBR mice carrying the Lepob mutation, which are subject to severe and progressive obesity and diabetes beginning at 6 weeks of age, to examine the influence of one specific manifestation of sleep apnea, intermittent hypoxia, on male urinary voiding physiology and genitourinary anatomy. A custom device was used to deliver continuous normoxia (NX, control) or intermittent hypoxia (IH) to wild type and Lepob/ob (mutant) mice for 2 weeks. Intermittent hypoxia was delivered during the 12-hour inactive (lighted) period in the form of 90 sec of 6% O2 followed by 90 sec of room air. Continuous room air was delivered during the 12-hour active (dark) period. We then evaluated genitourinary anatomy and physiology. As expected for the type 2 diabetes phenotype, mutant mice consume more food and water, weighed more, and voided more frequently and in larger urine volumes. They also have larger bladder volumes but smaller prostates, seminal vesicles, and urethras than wild type mice. IH decreases food consumption and increases bladder relative weight independent of genotype and increases urine glucose concentration in mutant mice. When evaluated based on genotype (NX+IH), the incidence of pathogenic bacteriuria is greater in mutant than wild type mice, and among mice exposed to IH, bacteriuria incidence is greater in mutant than wild type mice. We conclude that IH exposure and type 2 diabetes can act independently and together to modify male mouse urinary function.

Characterizing the Spectrum of Bladder Health and Lower Urinary Tract Symptoms (LUTS) among Women: Results from the CARDIA Study

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To operationalize a new definition for bladder health, we examined the distribution of lower urinary tract symptoms (LUTS) and impact, along with associated factors, among women in the Coronary Artery Risk Development in Young Adults (CARDIA) study. We performed cluster analyses using validated LUTS symptom burden and impact scales collected between 2005-06 and 2010-11. We performed multinomial logistic regression analyses to evaluate cardiovascular factors (metabolic syndrome, cardiovascular health behaviors, and inflammation) between clusters after adjusting for covariates (demographic, obstetric/gynecologic, co-morbidities). Among CARDIA women (median age 51, range 42-59) with complete LUTS data (n=1302), we identified and compared 4 cluster groups: women who reported no or very mild symptoms and no impact on well-being (bladder health, 44%, n=569), versus women with LUTS and negative impact on well-being ranging from mild (31%, n=407), moderate (20%, n=259), to severe (5%, n=67). With each 1-point lower BMI (kg/m2), odds of membership in mild (OR 0.97, CI 0.95-0.99), moderate (OR 0.95, CI 0.93-0.98), and severe (OR 0.90, CI 0.88-0.94) LUTS cluster groups versus the bladder health group were lower. Compared to women with metabolic syndrome, women without metabolic syndrome had lower odds of membership in mild (OR 0.67, CI 0.45-0.99), moderate (OR 0.51, CI 0.33-0.79), and severe (OR 0.48, CI 0.24- 0.94) LUTS cluster groups versus the bladder health group. Two out of 5 midlife women met our definition of bladder health. Bladder health and cardiovascular health among women may share common factors, including lower BMI and the absence of metabolic syndrome.

Gene Therapy for Overactive Bladder: A Review of BK-Channel α-Subunit Gene Transfer

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A need exists for local (ie, bladder-specific) interventions to treat overactive bladder (OAB) with low risk of unwanted postprocedural outcomes. Gene therapy targeted to leverage endogenous physiology in bladder cells may assist in restoring normal cell and organ function. Herein, we review the potential promise of gene therapy for treating OAB, focusing on gene transfer of URO-902, a non-viral naked plasmid DNA expressing the big potassium (BK) channel. We searched PubMed for articles concerning functional aspects of the BK channel and its potential use for gene transfer as local OAB treatment. Results from preclinical, phase 1, and phase 2 studies of URO-902 for erectile dysfunction and phase 1 studies of URO-902 for OAB are included. The BK channel has been extensively studied; however, URO-902 is the first gene therapy used in clinical trials directed toward treating OAB via the BK channel. In both URO-902 studies, there were no serious adverse events considered treatment related and no adverse events leading to early withdrawal. Both studies included secondary efficacy endpoints with promising results suggesting improvement in OAB symptoms, and quality of life, with use of URO-902 versus placebo. Gene therapy involving the BK channel, such as gene transfer with URO-902, has demonstrated promising safety and efficacy results in women with OAB. Findings warrant further investigation of the use of URO-902 for OAB treatment.

- Jennifer Allmaras, MPH, 6/16/2021

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