advantage exists with an increased number of nodes excised, including a group with high-risk cancer. Controversial data from European centers may be due to more advanced disease.

Dr. Andreas Bohle
Professor of Urology
HELIOS Agnes Karll Hospital
Bad Schwartau, Germany

FEMALE UROLOGY

Increased warning time with darifenacin: a new concept in the management of urinary urgency
Cardozo L, Dixon A
Urogynaecology Department, King’s College Hospital, London, United Kingdom
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Purpose: We assessed the effect of darifenacin, an M3 selective receptor antagonist, on the warning time associated with urinary urgency.

Materials and Methods: In this multicenter, double-blind study subjects with urinary urgency for 6 months or greater and episodes of urgency 4 times or greater daily were randomized to darifenacin controlled release tablets (30 mg once daily) or placebo. Warning time was defined as the time from the first sensation of urgency to voluntary micturition or incontinence. Data were collected using electronic event recorders during 6-hour clinic visits or 3 urge-void cycles, if shorter, at baseline and at treatment end.

Results: A total of 72 subjects entered the study and 67 were included in the primary efficacy analysis (darifenacin in 32 and placebo in 35). Darifenacin treatment resulted in a significant increase in mean warning time with a median increase of 4.3 minutes compared with placebo (p = 0.003). Overall 47% of darifenacin treated subjects compared with 20% receiving placebo achieved a 30% increase or greater in mean warning time (OR 5.6, p = 0.009). Median and minimum warning times were also significantly increased following darifenacin treatment vs. placebo (p = 0.004 and 0.017, respectively). The median difference in minimum warning time was 1.9 minutes in favor of darifenacin vs. placebo.

Conclusions: To our knowledge this is the first study to evaluate change in warning time, which is potentially important to individuals with symptoms associated with overactive bladder. Darifenacin increases mean, median and minimum warning time compared with placebo, allowing subjects more time to reach a toilet and potentially avoiding the embarrassing experience of incontinence.

Editorial Comment
The authors analyze the efficacy of darifenacin, a selective M3 receptor antagonist, with regard to the parameter of micturitional warning time. Warning time was defined as the point from first sensation of urinary urgency to the patient voluntarily voiding or experiencing episode of urinary urge incontinence. The authors found that darifenacin affected a significant increase in warning time over those patients treated with placebo.

This is an excellent paper from one of the world’s top urogynecologists. The analysis of warning time may produce a new benchmark of efficacy for OAB medications. This parameter, as it finds its way in use in more and more studies, will evolve. Currently, it is judged as the time between first sensation of urgency to the point of voluntary micturition or incontinence. Since voluntary micturition is a volitional act and urinary...
incontinence is not, this may be an area of further refinement. In reviewing the study groups, the differences in median baseline warning times between the darifenacin and placebo groups does present a potential “possible imbalance” as suggested by the authors.

In addition, darifenacin is a M3 selective receptor antagonist. The potential changes in M2 receptor density as opposed to M3 in the denervated bladder has been discussed previously in the literature (1). Consequently, some have postulated that M3 specific antagonists may be at a potential therapeutic disadvantage secondary to the M2 up regulation in the diseased bladder (2).

References

Dr. Steven P. Petrou
Associate Professor of Urology
Mayo Clinic College of Medicine
Jacksonville, Florida, USA

Incidence of urinary incontinence in postmenopausal women treated with raloxifene or estrogen
Goldstein SR, Johnson S, Watts NB, Ciaccia AV, Elmerick D, Muram D
From the Department of OB/GYN, New York University Medical Center, New York, NY; University of Iowa College of Medicine, Iowa City, IA; Department of Medicine, University of Cincinnati College of Medicine, Cincinnati, OH; and Women’s Health and Reproductive Medicine, Lilly Research Laboratories, Indianapolis, IN, USA


Objective: Determine the effect of raloxifene or estrogen, as compared with placebo, on the reporting of urinary incontinence in postmenopausal women participating in an osteoporosis prevention trial.

Design: The current analysis is based on adverse event data that were collected as part of a double-blind, randomized, placebo-controlled trial designed to assess the efficacy and safety of raloxifene for osteoporosis prevention in postmenopausal women. Women were 40 to 60 years of age at study entry and had a prior hysterectomy. A total of 619 women were randomized to placebo, raloxifene 60 or 150 mg/d, or conjugated equine estrogen 0.625 mg/d and followed for up to 3 years. Urinary incontinence was self-reported and rated by participants as “mild”, “moderate” or “severe”.

Results: The prevalence of urinary incontinence as reported by patients at baseline was similar across treatment groups (3% to 6%, P = 0.46). During 3 years of follow-up, new or worsening urinary incontinence was reported with the following frequency: placebo (1.3%), raloxifene 60 mg/d (0.7%), raloxifene 150 mg/d (0.6%), and conjugated equine estrogen (7.0%). The percentage of estrogen subjects reporting urinary incontinence was significantly greater than that for placebo and both doses of raloxifene (P ≤ 0.02).

Conclusions: During 3 years of follow-up, conjugated equine estrogen was associated with an increased incidence of reports of urinary incontinence in women with a prior hysterectomy and this was significantly greater than both placebo and raloxifene.
Editorial Comment

The authors analyze the effect of raloxifene, estrogen and placebo on the incidence of urinary incontinence in postmenopausal women that were participating in an osteoporosis prevention trial. Urinary incontinence was self reported and self rated by the patients during the study as mild, moderate or severe. There was no clear differentiation between symptoms of urinary urge incontinence, stress urinary incontinence, or mixed urinary incontinence. After three years of follow-up, the authors noted that estrogen was found to be associated with a statistically greater increase of urinary incontinence in women with prior hysterectomy than that found with either placebo or raloxifene.

This paper raises interesting issues regarding the potential use of medical therapy as a prophylaxis against urinary incontinence. In addition, an interesting sidebar is made in the article about the potential effects of raloxifene on the incidence of female pelvic prolapse. The biological actions of raloxifene are mainly through the binding of estrogen receptors with secondary effect on estrogenic pathways. This result will potentially decrease the resorption of bone to that noted in the premenopausal state. The use of raloxifene has been noted to increase the risk of venous thromboembolism and thus the medication should be discontinued at least 3 days prior to any potential surgery, which would result in prolonged patient immobilization.

Of specific note is that the incidence of incontinence in this patient population through self reporting was vastly lower than that previously reported in the United States (1). In addition, potential points of contention in this paper are self noted by the authors and do include that the screening for incontinence was not completed through a validated questionnaire and there was no differentiation between urge or stress incontinence. This article does bring up some fascinating points in the discussion section about the use of estrogen therapy and its effect on collagen content and architecture in the paraurethral tissues and vaginal epithelium.

Reference

Dr. Steven P. Petrou
Associate Professor of Urology
Mayo Clinic College of Medicine
Jacksonville, Florida, USA

PEDIATRIC UROLOGY

Subureteral injection of Deflux for correction of reflux: analysis of factors predicting success
Lavelle MT, Conlin MJ, Skoog SJ
Oregon Health Sciences University, Portland, Oregon 97239-3098, USA
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Objective: To review, prospectively, our experience with endoscopic Deflux injection and evaluate the volume injected, grade, endoscopic appearance after injection, and presence or absence of voiding dysfunction as predictors of success. Subureteral injection of dextranomer/hyaluronic acid copolymer (Deflux) has become an effective treatment of vesicoureteral reflux.

Methods: A total of 52 patients (50 females and 2 males; 80 ureters) were treated with a single subureteral injection of Deflux. The mean patient age was 7.6 years (range 14 months to 22 years). The presence or absence of voiding dysfunction was evaluated with a preoperative questionnaire and patient history. The volume of