

528 Abstracts

log transformation. Baseline readings and correlations between observations on the same patient were allowed for within the model and F-statistics were used to test for differences between sodium bicarbonate and placebo.

Results:

35 women completed the study. The mean age of the women was 49 years (range 23 to 71 years). The mean daily pH was 6.1 for the baseline week, 6.1 for the placebo week and 6.9 for the week when sodium bicarbonate was taken. Table 1 shows the mean number of daily episodes of urgency and wetting, frequency and 24 hour pad weights. The difference in 24 hour pad weights was the only statistically significant result with increased leakage occurring in the week that sodium bicarbonate was ingested.

There was no difference in the quality of life impact of urinary symptoms for either group with the mean impact of their urinary symptoms on their daily life reported as "somewhat" for the period of the study.

Table 1: comparing the mean number of daily episodes of urgency and wetting, frequency and pad weights. The means reported are geometric rather than arithmetic means in view of the log transformation of the data.

| | sodium bicarbonate week (95% CI) | placebo week (95% CI) | p value |
|--------------------------------------|----------------------------------|-----------------------|---------|
| mean no. urge episodes per 24 hrs | 7.5 (6.9-8.0) | 7.1 (6.6-7.6) | 0.07 |
| mean no. wetting episodes per 24 hrs | 2.2 (1.9-2.4) | 2.2 (2.0-2.5) | 0.64 |
| mean 24 hr frequency | 8.8 (8.4-9.3) | 8.6 (8.2-9.1) | 0.43 |
| increase in 24 hr pad weight (gms) | 10.8 (8.1-14.3) | 8.5 (6.4-11.2) | 0.01 |

Conclusions:

It is a common belief that urinary pH may affect detrusor instability, and the variation between the pH of infused fluids and urine has been proposed as the reason for the presence of increased detrusor contractility during ambulatory monitoring when compared with routine cystometry. However, our study has not confirmed this belief, as increasing urinary pH had no effect on the symptoms associated with detrusor instability, apart from the 24 hour pad weight. The number of wetting episodes did not change with treatment and therefore the clinical significance of this result is unclear. Urinary pH alone does not therefore appear to be related to the symptoms of detrusor instability. We feel that this is important clinical information as it negates the advice often given to patients with urinary frequency.

References:

- 1 Br J Urol 1987 60: 516-518
- 2 Neurourol 1990 9: 331-332

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

ONE-YEAR, PROSPECTIVE, OPEN-LABEL TRIAL OF CONTROLLED-RELEASE OXYBUTYNIN FOR OVERACTIVE BLADDER IN A COMMUNITY-BASED POPULATION

Aims of Study: Conventional oxybutynin is safe and effective for the treatment of overactive bladder (OB), but discontinuation of treatment due to dry mouth often precludes long-term treatment. Controlled-release oxybutynin has been shown to be comparably effective with less dry mouth than conventional oxybutynin in short-term studies. In a long-term, open-label study, we assessed improvement in the bothersomeness of the condition, patient satisfaction with treatment, and discontinuation of treatment due to dry mouth in over 1000 community-based patients using controlled-release oxybutynin for 12 months.

Methods: This was an open-label, non-randomized study enrolling adults with OB. Patients received their individual optimum dose of controlled-release oxybutynin ranging from 5-30 mg/day. Adverse effects and reasons for discontinuation of treatment were recorded. At baseline and after 3, 6, or 12 months of treatment with controlled-release oxybutynin, patients completed four instruments to assess different aspects of quality of life: General Health and Bothersome Scale, Sleep Impact Questionnaire, Individual Incontinence Impact Questionnaire, and Patient Satisfaction Scale.

Results: Overall 1069 patients enrolled in the study, and 558 had 12-month data available as of September 30, 1999. At baseline the mean level of bothersomeness of the condition was 70.8 on a scale from 0 (not bothersome at all) to 100 (as bothersome as I can imagine). Patients reported a 41.5% improvement over baseline in the bothersomeness of the condition after 3 months, a 45.2% improvement after 9 months, and a 49.7% improvement after 12 mos of treatment ($p < 0.0001$ for each comparison with baseline). At baseline 69.6% of patients reported that nighttime awakenings due to UI interfered with daily activities some, most or all the time compared with 31.3% of patients after 3 months of treatment. At baseline 39.5% of patients indicated that at least 5 of 9 daily activities (household chores, relationships, exercise, work, etc.) were impacted by urine loss frequently or all the time; after 3 months of treatment, the percentage decreased to only 13.4% of patients. Adverse effects were the most common cause for discontinuation during the first 3 months and included dry mouth and other anticholinergic effects. Adverse effects were less frequently the cause for discontinuation after 9 months. The total rate of discontinuation over the 12 months due to adverse effects was 22.9%, including 8.1% for dry mouth and 6.3% for other anticholinergic effects.

| Reasons for discontinuation: | Prior to 3 mos. | 9-12 mos. |
|------------------------------|-----------------|-----------|
| Adverse effects (total) | 14.2% | 1.6% |
| Dry mouth | 4.5% | 0.7% |
| Other anticholinergic | 5.0% | 0.2% |
| Lack of efficacy | 3.8% | 0% |

Discontinuation of treatment due to lack of efficacy was low (3.8%) prior to 3 months and did not occur after 9 months. After 3 and 6 months of treatment, 74.7% and 80.3% of patients, respectively, reported the drug worked well, very well or excellent, and 79.2% and 86.8%, respectively, were pleased, very pleased or extremely pleased with treatment.

Conclusions: In this long-term, community-based study, discontinuation of controlled-release oxybutynin treatment due to dry mouth was much lower than that reported in the literature for conventional oxybutynin and occurred mostly in the first 3 months. Treatment of overactive bladder with controlled-release oxybutynin substantially improved the quality of life of patients as assessed by four different instruments.

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DETRUSOR INSTABILITY - ARE GAP JUNCTIONS RESPONSIBLE FOR INCREASED MEMBRANE EXCITABILITY?

Aims of Study: Gap junctions are specialized cell membrane structures, which allow for rapid communication between adjacent cells. They permit the rapid propagation of action potentials between cells. Membrane channels (connexons) of one cell form gap junctions, which are aligned with apposing channels from another cell to form patent water filled passages across two membranes. These connexons are composed of the structural protein connexin. Recent work has identified connexin 43 in the human laboring uterus (1).

Brading and Elbadawi have advanced a myogenic basis for detrusor instability. Smooth muscle cells from the detrusor of patients with detrusor instability are more easily excited by direct electrical stimulation when compared with controls. Elbadawi et al (2) identified the presence of 'alien' junctions in elderly patients with detrusor overactivity. They concluded that these junctions were de-differentiated gap junctions capable of mediating electrical coupling between detrusor smooth muscle cells and formed the basis of detrusor instability. They based their conclusions on electron microscopy findings alone. Cell junctions in more rudimentary forms may be difficult to characterize, increasing the likelihood of misclassification and misinterpretation of function. This problem can be overcome by the additional use of immunohistochemistry to identify the junction types.

The aim of this study was to test the hypothesis that detrusor instability was associated with the presence of gap junctions using an immunoperoxidase technique for the identification of connexin 43. Electron microscopy and vinculin immunohistochemistry were used to assist in the identification of detrusor smooth muscle junctions and other membrane structures.

Methods: Seven women 32 to 68 years old median 55 years with severe detrusor instability and no stress incontinence and 5 controls aged 41 to 64 (median 50) with genuine stress incontinence and stable bladders and no symptoms of sensory/urgency or urge incontinence were studied. Three bladder biopsies, approximately 2-4cm above the trigone and near the midline were taken from each patient. Specimens were processed for electron microscopy by standard methods. Two investigators blinded to the urodynamic diagnosis analyzed the electron micrographs. Specimens were also processed for immunohistochemistry using an immunoperoxidase technique for