34

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Title: TRANSDERMAL OXYBUTYNIN IS SAFE, EFFECTIVE, AND IMPROVES QUALITY OF LIFE IN PATIENTS WITH OVERACTIVE BLADDER

Aims of Study:

Transdermal (TD) oxybutynin avoids the pre-systemic metabolism that occurs with oral therapy, significantly reducing the formation of the active metabolite, N-desethyloxybutynin (DEO), that is associated with anticholinergic side-effects[1]. This randomized, placebo controlled, Phase III study evaluated TD safety and efficacy in a general population of patients with overactive bladder.

Methods:

Adult patients with overactive bladder symptoms enrolled at 40 US centers. The study was approved by central and local Institutional Review Boards and all patients provided written informed consent for participation. Randomized followed symptom stabilization or treatment withdrawal and a urinary diary showing ≥ 10 U-UI episodes/week, ≥ 8 normal voids/day, and average urinary volume of < 350ml. TD systems were applied twice weekly for 12 weeks, providing nominal doses of 0 (placebo), 1.3, 2.6 or 3.9 mg/day oxybutynin. Evaluations included patient urinary diaries, the Incontinence Impact Questionnaire, and general safety monitoring. End-of-treatment diary parameters were analyzed by ANCOVA adjusted for multiple group comparisons. Results are mean ± SD.

Results:

520 patients randomized and 447 completed the study. Patients were female (92%), Caucasian (91%), and 61.4 ± 13.3 years old. Response to placebo and the 2 lower TD doses were comparable (p=ns). The high dose TD group exhibited significant ($p<0.05$) changes vs placebo for median change in incontinence episodes (-19 vs -14.5 episodes/week), median change in micturition frequency (-2.0 vs. -1.0 voids/day), and median change in normal void volume (24 vs 6 mls). Quality of life (mean change in total score on the Incontinence Impact Questionnaire) improved significantly in the high-dose TD group compared to placebo (-56.0 ± 73.8 vs -44.3 ± 70.9). 73 patients withdrew from the study, 53 due to adverse events. Anticholinergic side-effects were comparable between active and placebo treatment groups. Dry mouth and constipation occurred in 8.8% and <1% of high dose TD patients vs. 8.3% and 3% of placebo patients. Application site pruritus was the most common adverse event (18% of high dose patients).

Conclusions:

Transdermal oybutynin treatment was well tolerated with minimal anticholinergic side effects. This improved tolerability profile combined with improvement in overactive bladder symptoms and quality of life demonstrates a significant potential improvement over current pharmacological treatments.

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[1] Davila GW, Daugherty CA, Sanders SW. A multicenter, randomized, double-blind, dose-titration study of the efficacy and anticholinergic side effects of transdermal compared to immediate-release oral oxybutynin treatment in patients with urge urinary incontinence. J. Urology (in press).