# SYSTEMATIC REVIEW AND META-ANALYSIS EXAMINING THE CURE RATES OF ANTIMUSCARINIC DRUGS USED TO TREAT URGENCY URINARY INCONTINENCE

### Hypothesis / aims of study

To perform a systematic review and meta-analysis of randomised controlled trials which examined the cure rate for antimuscarinic medication used to treat urgency urinary incontinence.

## Study design, materials and methods

A thorough literature search of randomised controlled trials was undertaken for the use of antimuscarinic drugs in the treatment of overactive bladder and urgency urinary incontinence. The literature cut off date was December 2010, papers available online ahead of print were accepted as well. All papers were appraised using a structured methodology and examined for the outcome of interest. Cure was defined as having no episodes of urgency urinary incontinence after treatment on a minimum 3 day bladder diary after treatment in patients who had at least one episode on bladder diary at baseline. Meta-analysis was performed using the Review Manager software from Cochrane.

#### Results

A total of 16 published studies used cure as an outcome out of 134 randomised controlled trials of antimuscarinic drugs. 10 of these studies were placebo controlled. A meta-analysis of these trials (Figure 1) favours the use of antimuscarinics over placebo (Odds Ratio 1.82, 95% confidence interval of 1.62 - 2.03). There is a high cure rate with placebo of 33.4% based on pooled numbers from all the studies. However there is a moderate degree of heterogeneity associated with the meta-analysis which is still present when the studies are sub-grouped by type of antimuscarinic drug. It would appear that the Kaplan 2010 study is contributing to this. Anderson 1999 and Birns 2000 compared the cure rates of Oxybutynin extended release with immediate release. There was no difference in cure rate on meta-analysis with a wide confidence interval crossing the midline (OR 0.92, 95% CI 0.54 - 1.56). Choo 2008, Herschorn 2010, Kaplan 2011 and Halaska 2003 compared newer drugs: Solifenacin, Fesoterodine and Trospium to either Tolterodine or Oxybutynin. The meta-analysis favoured the newer drug (OR 1.28, 95% CI 1.12 - 1.47).

#### Interpretation of results

In the meta-analysis of drug vs placebo (Figure 1) the Kaplan study is the cause of the heterogeneity. This was a large, well conducted trial which used similar outcome measures to the others and no reason could be found to account for the difference. However due to the relatively small number of trials reporting cure rates in the literature, there is likely to b a significant publication bias associated with this outcome measure.

#### Concluding message

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Whether antimuscarinic drugs can be used to cure urgency urinary incontinence would appear to be a sensible question to ask, however it is not widely reported in the literature. This would seem to indicate a high degree of selective outcome reporting in trials mostly sponsored by industry. More work should be done to persuade trial sponsors to examine outcomes which are of interest to clinicians and patients.

	Antimuscarinic		Placebo		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Chu 2009	119	225	80	237	8.2%	2.20 [1.51, 3.21]	<b>_</b> _
Dmochowski 2003	47	123	26	117	3.7%	2.16 [1.23, 3.82]	
Dmochowski 2008	95	267	58	276	8.2%	2.08 [1.42, 3.04]	_ <b>_</b>
Herschorn 2010	754	1245	138	307	19.5%	1.88 [1.46, 2.42]	
Hill 2006	55	189	17	101	3.5%	2.03 [1.10, 3.73]	
Kaplan 2011	1109	1834	242	448	34.3%	1.30 [1.06, 1.60]	
Millard 1999	13	116	6	61	1.6%	1.16 [0.42, 3.21]	
Staskin 2007	54	263	31	273	5.4%	2.02 [1.25, 3.26]	
Yamaguchi 2007	480	839	105	283	15.0%	2.27 [1.72, 2.99]	
Zatura 2010	18	26	18	54	0.8%	4.50 [1.64, 12.32]	│ ———→
Total (95% CI)		5127		2157	100.0%	1.82 [1.62, 2.03]	•
Total events	2744		721				
Heterogeneity: Chi <sup>2</sup> = 18.38, df = 9 (P = 0.03); l <sup>2</sup> = 51%							
Test for overall effect: $Z = 10.38$ (P < 0.00001)							Favours Placebo Favours Antimuscarini

Figure 1. Meta analysis of Antimuscarinic drugs vs Placebo

#### References

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