Antimuscarinics for overactive bladder – how do adverse effects compare?

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A meta-analysis comparing antimuscarinic agents for the treatment of overactive bladder found similar overall adverse event profiles for usually prescribed starting doses, although oral oxybutynin was found to be associated with a less favourable adverse event profile compared with some agents. However, the analysis has several important limitations and clinicians should continue to follow NICE guidance in this area.

Overview and current advice

Overactive bladder syndrome (OAB) is characterised by urgency that occurs with or without urge urinary incontinence and usually with frequency and nocturia. It can seriously influence a person’s physical, psychological and social wellbeing and can cause significant lifestyle restrictions. Treatment of OAB may include lifestyle interventions (e.g. fluid modification), physical therapies (e.g. pelvic floor muscle training), bladder training and drug therapies (e.g. antimuscarinic drugs).

NICE guidance on the management of urinary incontinence in women recommends offering immediate release generic oxybutynin as first-line drug treatment if bladder training has been ineffective. This recommendation was based on cost effectiveness as there was no evidence of a clinically important difference in efficacy between antimuscarinic drugs. If oxybutynin is not well tolerated, darifenacin, solifenacin, tolterodine, trospium, or an extended release or transdermal formulation of oxybutynin should be considered. Other drugs may be an option in specific circumstances.

An update to the NICE clinical guideline on urinary incontinence is currently underway and is due to be published in July 2013.

See the NHS Evidence topic page on urinary incontinence for a general overview of the condition.
New evidence

This meta-analysis (Kessler T.M et al, 2012) aimed to quantify and compare the adverse events profiles of antimuscarinic drugs used to treat OAB. It included 69 randomised controlled trials (RCTs) with 26,229 participants, with a mean duration of treatment of 8 weeks (range 1 to 52 weeks). A similar overall adverse event profiles were found for solifenacin, trospium chloride, tolterodine and fesoterodine. Oral oxybutynin was associated with a statistically significantly higher adverse event score than these agents. Darifenacin, transdermal oxybutynin and propiverine, although the point estimate for the adverse events was similar to the other drugs, the the 95% confidence intervals (CIs) were wide and overlapped with those for oxybutynin 10mg/day. Darifenacin, fesoterodine, orally administered oxybutynin, propiverine, and solifenacin showed a positive and significant dose-adverse event relationship.

Several limitations may affect the clinical significance of the findings of this meta-analysis. Almost all of the studies included were fixed dose trials and studies that did not clearly specify the dose regarding adverse events were excluded. This is an important limitation since in clinical practice the dose is often titrated to response and flexible dose studies tend to report fewer adverse events. The validity of the method for assessing the impact of adverse events was unclear. The authors graded each adverse event using a visual analogue scale (0 = minimum severity, 10 = maximum severity) based on the consensus of 10 independent experts. However, the views of patients was not taken into account. While this attempted to grade the adverse effects for severity, the number of people withdrawing from treatment due to adverse effects was not measured. This is often a more useful indicator of tolerability.

Commentary

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The clinical usefulness of these drugs represents a balance between efficacy and adverse effect profiles. Current NICE guidance on the use of antimuscarinics in urinary incontinence in women considers them to have similar efficacy and places oxybutynin as the recommended first-line therapy on cost-effectiveness grounds. From the, albeit limited, meta-analysis discussed here, oxybutynin appears to be associated with a higher prevalence of adverse effects than many of the other antimuscarinics.

An update to the NICE clinical guideline on urinary incontinence is currently underway and is due to be published in July 2013. It remains to be seen whether oxybutynin is still recommended as the sole first-line antimuscarinic. However, the methodological weaknesses of this meta-analysis, limits its contribution to this debate.

Another factor is that tolterodine – which was associated with a lesser adverse effect profile than oxybutynin in this meta-analysis and in other studies – is, in the near future, coming off patent. Any reduction in its price may have an impact on the heath economic assessment of these agents.

References


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