Editorial

Long-term adherence to clinical therapy of overactive bladder

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Overactive bladder (OAB) is a highly prevalent symptom syndrome, with considerable personal and health economic impact. Conventional management requires conservative interventions, including adherence to fluid advice and bladder training (1). Medications can then be used, with antimuscarinics forming the mainstay of drug interventions for many years. The recent introduction of a beta-3 agonist established a new drug class for the indication, with a differing side effect profile from the antimuscarinics. Beta-3 agonists do not affect the cholinergic receptors responsible for salivation, so problems of dry mouth symptoms are unusual with the first-in-class agent, mirabegron.

Long-term persistence with antimuscarinics is reckoned to be weak, both as a consequence of perceived limited efficacy, and the intrusive nature of the side effects. This has long been a concern in the therapy of OAB. Due to the apparent better tolerability of the mirabegron, the potential to achieve improved adherence may be an advantage. The recently reported study in *European Urology*, with Christopher Chapple as the lead author, used a large United Kingdom prescribing database to evaluate long-term adherence to antimuscarinics and mirabegron (2). The principal outcome was persistence with medication, evaluated by the time to discontinuation. Mirabegron was evaluated, along with a wide range of antimuscarinic medications. One year prescriptions of nearly 22,000 people were evaluated. Persistence with mirabegron was greater than that with all the antimuscarinics. Failure to persist with the treatment appeared to be somewhat more likely in those who had not previously been treated for OAB; for some of the medications, failure to persist was more likely in women, in patients with comorbidities, patients receiving two or more other medications, and younger patients. For mirabegron, the median time to discontinuation was 169 days, which was significantly longer than for all the antimuscarinics (which fell in the range of 30 to 78 days). The 12 months persistence for mirabegron was 38%, which was clearly greater than for all the antimuscarinics (ranging between 8% and 25%).

The study provides an extremely clear signal of the difference in long term use of OAB medications. The long-term reliance on antimuscarinics as the mainstay of OAB therapy may well be significantly challenged as a result of the far better persistence rates seen with mirabegron. Accordingly, beta-3 agonist may become first-line drug therapy for OAB. Alternatively, a more tailored approach matching therapy to characteristics of the individual patients presenting may become the aspiration (3). Comparative studies of mirabegron against antimuscarinics are few, but the efficacy of the drug appears to match that of better antimuscarinics. This equal efficacy combined with a better tolerability places mirabegron in a strong position. Clearly, best use of the medication is made if the patient takes some sensible measures to reduce the impact of their condition on their day-to-day life. Mirabegron and other medications cannot be regarded as an antidote to behaviours that can worsen the condition, such as consumption of inappropriate fluids, notably caffeine. If patients do take the trouble to adhere to conservative measures and self-management, OAB therapy stands its

best chance of successfully ameliorating the problem.

An upcoming development may be the ability to combine the use of mirabegron with antimuscarinics. This was successfully demonstrated in a large population of patients remaining incontinent despite antimuscarinic monotherapy in the BESIDE study (4), and further combination therapies may become available in the future. This opens up the possibility to extend the management targeting to cover both storage and voiding LUTS, for example by combining beta-3 agonist with an alpha-1 adrenergic antagonist in male patients (5). Careful evaluation should enable the development of therapeutic protocols to optimise efficacy and minimise adverse effects. While this approach could carry additional cost implications, improved efficacy should yield an offset in economic benefits, alongside the quality of life improvement.

Professor Chapple's study concludes that patients prescribed mirabegron remained on treatment for longer and showed greater adherence than those prescribed traditional antimuscarinics. This is a very tangible observation to indicate the enhancement of the treatment armamentarium as a result of the introduction of the beta-3 agonist class.

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Footnote

Conflicts of Interest: Speaker/Advisory Boards/Research; Allergan, Astellas, Ferring, Pfizer.

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