ESSENTIAL AND RELEVANT INFORMATION

ProductBrief

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Oxytrol Patch - a new look at oxybutynin for overactive bladder

Introduction

Overactive bladder syndrome (OAB) is a set of symptoms, outlined in **Table 1**, which is characterised primarily by urinary urgency.[1,2] It is usually accompanied by nocturia and frequency, with or without urge-incontinence, and occurs in the absence of urinary tract infection or other obvious pathology.[2]

Table 1: Definitions of overactive bladder syndrome.[1]

Detrusor overactivity	A urodynamic observation characterised by involuntary spontaneous or provoked detrusor contractions during the filling phase
Nocturnal polyuria	An excess (>20-30%) proportion of urine excretion at night
Polyuria	>40 mL urine/kg body weight during 24 hours
Postvoid residual volume	The volume of fluid remaining in the bladder at the completion of micturition
Urgency	A sudden compelling desire to void that is difficult to defer
Urinary frequency	>8 micturitions/24 hours
Urgency urinary incontinence	Involuntary loss of urine associated with urgency

Adapted from: Arnold J, McLeod N, Thani-Gasalam R, Rashid P. Overactive bladder syndrome - management and treatment options. Aust Fam Physician. 2012;41(11):878-83.

The worldwide prevalence of OAB is 12.8% for women and 10.8% for men and increases with age.[1]

It adversely affects quality of life, being associated with embarrassment, low self-esteem and a reduction in economic productivity.[3] Patients with OAB also report less sexual satisfaction, poorer quality of sleep and significantly poorer mental health.[1] In the older population it is also associated with falls, fractures, dermatitis, urinary tract infections and institutionalisation.[3]

Difficulties with treatment

First-line treatment for OAB consists of a combination of lifestyle interventions, bladder training and behavioural modifications.[1] If these measures fail to control symptoms, antimuscarinic medicines are recommended.[1]

Persistence with antimuscarinic drug treatments such as oral oxybutynin in OAB has been shown to be poor.[3] Patient-initiated discontinuation of the drug often occurs due to the significant incidence of anti-cholinergic side effects, which include dry mouth, constipation and cognitive impairment.[4,5] Blurred vision and somnolence have also been associated with antimuscarinic drugs, including oral oxybutynin. These anti-cholinergic side effects can contribute to poor adherence to oral oxybutynin treatment.[2,6]

In older populations, antimuscarinics such as oral oxybutynin may have different pharmacokinetic properties due to age-related reduction in first-pass metabolism, and more serious adverse events can occur in this population.[4] These include cognitive dysfunction, including memory loss and attention deficits, cardiac effects and confusion.[1,2] In addition, elderly patients also frequently take many concomitant medicines that have antimuscarinic properties, including antiparkinsonian agents, antihistamines, antiemetics and antipsychotics.[4]

Practice points

- Consider the use of antimuscarinic medicines in those patients with OAB for whom first-line non-pharmacologic treatment has failed to control symptoms.[1]
- Transdermal administration of oxybutynin is as effective as oral formulations and has a relatively reduced anticholinergic adverse effect profile.[5]
- The twice-weekly dosing of transdermal oxybutynin and its ease of use may also improve adherence to treatment among patients with OAB.[7]
- Local reactions to transdermal application of oxybutynin can be managed by the use of moisturisers and, if necessary, topical corticosteroids.[4]

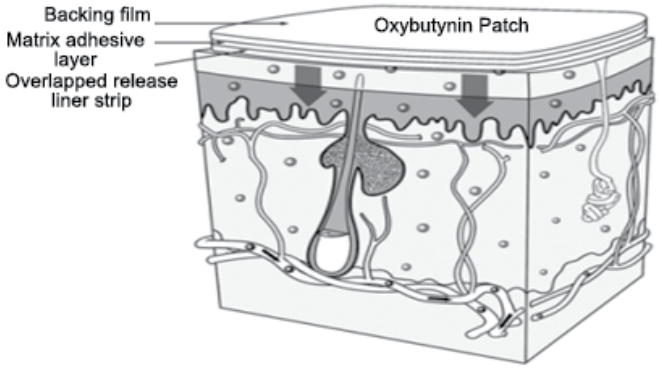
Overcoming difficulties in treatment

Transdermal delivery systems have been available since the 1980s and are known for increasing the bio-availability of drugs that are subjective to extensive first-pass metabolism.[7,8] Transdermal delivery systems are popular among patients due to their ease of use and a lower total dosage is required, leading to lower incidence of dose-dependent side effects.[7,8] Furthermore, transdermal administration of a medicine facilitates stable plasma levels, reducing the exacerbation of side effects associated with peaks, and ineffectiveness associated with troughs.[8] Oxybutynin, an antimuscarinic used in the treatment of OAB, is well suited for transdermal delivery.[8]

Oxytrol Patch

Oxytrol Patch uses a transdermal drug delivery system, as shown in **Figure 1**, which is indicated for the treatment of OAB.[9] Each 39cm^2 patch contains 36mg of oxybutynin and is designed to deliver 3.9mg of oxybutynin per day over a 3 to 4 day interval.[9]

Figure 1: Transdermal oxybutynin system.[5]

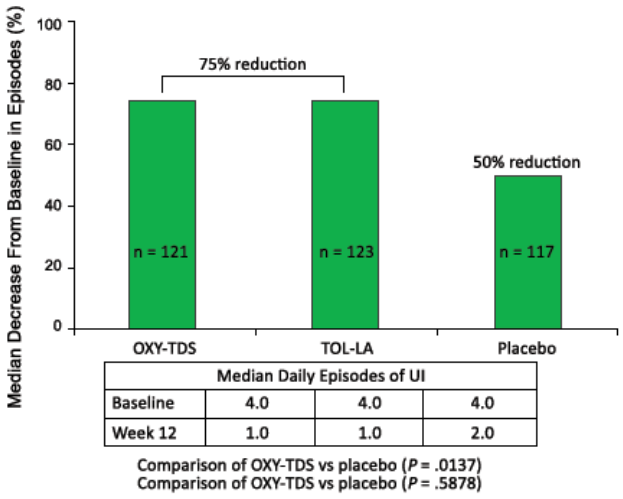


Adapted from: Arnold J, McLeod N, Thani-Gasalam R, Rashid P. Overactive bladder syndrome - management and treatment options. Aust Fam Physician. 2012;41(11):878-83.

Efficacy

Transdermal oxybutynin has been shown to be effective in reducing median episodes of daily incontinence (-3.0 vs -2.0, p = 0.0004), daily urinary frequency (-2.0 vs -1.0, p = 0.0023) and increasing voided volume 25 vs 5.5 mL, p < 0.00001) in a 12-week placebo-controlled randomised trial.[8] Another multi-centre double-blind study also showed a significant improvement in the number of incontinence episodes, mean daily urinary frequency, average voided volume and quality of life.[5] Results regarding urinary incontinence are summarised in **Figure 2**.

Figure 2: Reduction in daily incontinence episodes; oxybutynin transdermal delivery system (OXY-TDS) and extended release tolterodine (TOL-LA) vs. placebo. UI = urinary incontinence.[10]



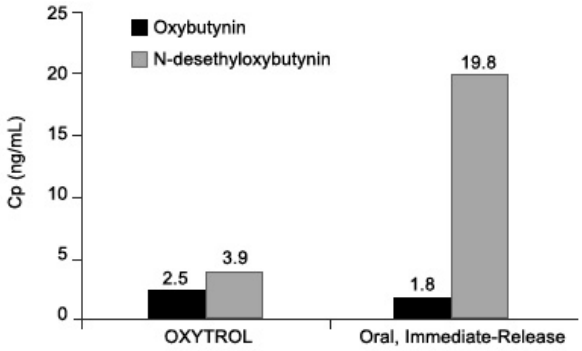
Dr Heyworth's take-home message

Overactive bladder is common in our community and often underrecognised and undertreated. The effects of an overactive bladder can severely impact a patient's quality of life. Although exercises and education are first line, the patch, if suitable, provides an easy application, and a reduced side effect delivery system for our patients.

Adverse events

The anti-cholinergic side effects of oral oxybutynin are thought to be largely related to the metabolite of oxybutynin called N-desethyloxybutynin (N-DEO) that is formed during first pass metabolism in the liver.[11] Transdermal administration of oxybutynin has been shown to reduce the levels of the N-DEO metabolite by approximately 80% compared with oral oxybutynin, as demonstrated in **Figure 3**.[9]

Figure 3: Average plasma concentrations (Cp) of oxybutynin.[9]



Adapted from Actavis Pty Ltd. Oxytrol transdermal drug delivery system (Oxybutynin). 2013.

Lower levels of N-DEO were shown to correspond to lower incidence of dry mouth, the most common anticholinergic side effect associated with therapy for OAB.[11, 12] No major differences between placebo and transdermal oxybutynin were observed in relation to the most common anticholinergic adverse events, including dry mouth, abnormal vision, dizziness, somnolence and constipation in a clinical study involving 520 OAB patients.[13, 14]

Similarly, an observational study demonstrated no cognitive impairment in elderly patients with OAB treated with transdermal oxybutynin.[15]

Mild adverse events related to transdermal delivery have been reported, most commonly including erythema (5.6%) and pruritus (16.8%) at the patch application site.[5] Allergic contact dermatitis, irritant dermatitis and skin pigmentation have also been reported.[10] Erythema usually resolves spontaneously without a requirement for treatment, while itchiness can often be relieved with the use of skin moisturisers and rotating the site where the patch is placed.[10] Application-site reactions can also be minimised by the application of local topical corticosteroids or antihistamines.[4]

Adherence to treatment

Long-term treatment in many chronic diseases is often associated with poor adherence, but this is especially the case with antimuscarinic drugs such as oral oxybutynin in OAB.[3] Patient adherence to prescribed treatment is affected by a number of factors, including pill burden, complexity of dosing schedule and adverse events.[10] Adherence has been shown to be improved by less-frequent dosing intervals and so the twice-weekly application of transdermal oxybutynin can be helpful, especially in an older patient with polypharmacy.[10] The combination of reduced side effects and ease of administration can further improve patient adherence to therapy.[7]

PBS reimbursement

Oxybutynin 3.9mg/24 hour patch (Oxytrol) is available in packets of eight and approved for detrusor overactivity on the Pharmaceutical Benefits Scheme (PBS).[16] It is, however, a restricted benefit for those patients who are either unable to tolerate oral oxybutynin or unable to swallow oral oxybutynin.[16] The poor tolerance profile of oral oxybutynin contributes to the widespread applicability of the patch formulation.[10]

Place in therapy

In the primary care setting, patients with OAB whose condition has been refractory to non-pharmacologic treatment can be treated empirically with an antimuscarinic agent.[1, 8] Adverse effects of this class of medicines, however, are largely responsible for high discontinuation rates.[8] Transdermal oxybutynin offers an alternative option for the treatment of OAB with an improve side effect profile and the potential to thereby increase treatment adherence.[8]

Course resource centre

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