

Patient perspectives in the management of overactive bladder, focus on transdermal oxybutynin

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Abstract: Overactive bladder syndrome (OAB) is a constellation of distressing symptoms that significantly impair quality of life, sexual function, and work productivity, and imposes a significant economic burden to society. Pharmacological treatment with antimuscarinic agents, behavioral modification, bladder retraining, and/or pelvic floor exercises are often used alone or in combination as the mainstay treatment in the management of OAB. Oxybutynin has been used in the treatment of OAB for over 20 years with proven efficacy and is often the comparator in drug treatment trials. Oral formulations of oxybutynin have proven efficacy, but not without significant antimuscarinic effects, which reduce patient persistence with medical treatment. Low levels of patient persistence with oral formulations of oxybutynin provided an impetus for the development of a transdermal oxybutynin delivery system. The oxybutynin transdermal formulation has been found to have side effects similar to that of a placebo in randomized controlled trials while providing excellent efficacy. Patient persistence with therapy, improved quality of life, sexual function and interpersonal relationships have been observed with use of the transdermal oxybutynin delivery system. Its twice weekly dosing, low side effect profile, and high efficacy have made it a good choice for initial treatment of overactive bladder syndrome.

Keywords: overactive bladder syndrome, oxybutynin, transdermal delivery

Introduction

Overactive bladder syndrome (OAB) is a highly prevalent condition in the USA affecting up to 17% or approximately 33 million adults with 12 million experiencing urge urinary incontinence (UUI) (Milsom et al 2000; Voytas 2002; Stewart et al 2003). UUI increases with age and affects 6.3 million community-dwelling senior citizens and 1.2 million nursing home inhabitants (Milsom et al 2000). In 2003, the National Overactive Bladder Evaluation program, which examined the prevalence of OAB and its impact in the US, demonstrated that 16% of men and 16.9% of women suffered from OAB. This is similar to the prevalence in Europe (Milsom et al 2001; Irwin et al 2006, 2008). This distressing condition is known to have an adverse effect on quality of life, sexual function, and work productivity (Wagner et al 2002; Lavelle et al 2006). Other health-related consequences include increased urinary tract infections, falls and fractures, and a reason for up to 50% of nursing home admissions (Voytas 2002; Wagner et al 2002; Hu and Wagner 2005). OAB can lead to depression, anxiety, social isolation and sleep deprivation (Wagner et al 2002; Stewart et al 2003; Sand et al 2007). Aside from health-related consequences, OAB poses a significant economic burden to society. Annual costs estimates are over US\$9 billion per year with US\$2.9, US\$1.5 and US\$3.9 billion for diagnosis and treatment, routine care and treatment for other health-related consequences, respectively (Hu and Wagner 2005). An over US\$800 million loss in work productivity has been reported because of fatigue and distraction resulting from symptoms of urgency, frequency, nocturia and sleep disturbances (Hu and Wagner 2005). The impact of this condition on society is profound.

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Urgency is the cardinal symptom of OAB, which is usually accompanied by frequency and nocturia with or without urge urinary incontinence (UUI). Detrusor overactivity or involuntary bladder contractions is the most common reason for UUI and OAB, and is the primary cause of urinary incontinence in older individuals (Gibbs et al 2007). Unstable detrusor contractions usually are symptomatic causing patients to complain of severe urgency, which is defined as a sudden, compelling desire to urinate that is difficult to defer, which is often accompanied by UUI where patients leak urine before reaching the toilet. Although neurogenic processes such as Parkinson's disease, cerebrovascular accidents, and multiple sclerosis are known etiologies, 90% of detrusor overactivity is idiopathic. The origin as well as pathophysiology of detrusor overactivity is multifactorial and often difficult to fully explain.

Pathophysiology

OAB is a very distressing condition and remains an enigma in regard to its pathophysiology. The etiology of OAB is likely to be multifactorial involving multiple interrelated processes. CNS and/or peripheral nervous system abnormalities, abnormalities of the bladder urothelium and/or the detrusor muscle have all been implicated (Goldberg and Sand 2002; Birder 2005; Fabiyi and Brading 2006; Brading 2007). Both afferent and efferent neural pathways are involved in the regulation of normal mictrurition, and these are controlled by a variety of central and peripheral neurotransmitters. Acetylcholine, which binds to muscarinic receptors in the detrusor muscle to effect bladder contractions, is one of the most common neurotransmitters. The M3 receptors in the detrusor muscle are primarily responsible for normal detrusor activity and M3 receptors in the urothelium may regulate afferent sensation (Scarpero and Dmochowski 2003). Afferent nerves are known to lie in proximity to the urothelium and are involved in sensory feedback to the brain (Andersson 2002; Ouslander 2004; Birder 2005; De Laet et al 2006). Derangements in the structure or function of the sensory afferent nerves to the urinary bladder or abnormalities in the sensory feed back mechanisms that regulate the normal mictrurition process may result in the symptoms of OAB.

Pharmacological treatment with antimuscarinic agents and behavioral modification are often used alone or in combination in the management of OAB (Burgio et al 2000). Drugs that have high affinity for M3 receptors may offer a therapeutic advantage in the treatment in OAB. Although M3 receptors are less numerous in the detrusor muscle than M2 receptors, M3 receptors are primarily responsible

for activating detrusor contractions and often interact with M2 receptors in pathologic states. However, drugs that act on muscarinic receptors may also affect receptors in other body organs such as the salivary glands, brain, eye, and gastrointestinal tract. These agents can cause significant side effects such as dry mouth, constipation, visual and CNS disturbances which can preclude patient compliance with their use. To contend with the adverse effects of antimuscarinic medications, various pharmacological agents with selective affinity to bladder M2 and M3 receptors and agents with different delivery systems have been developed.

The efficacy of these agents lies in their ability to inhibit involuntary detrusor contractions through blocking muscarinic receptors within the detrusor smooth muscle, urothelial presynaptic nerve terminals, and possibly at sensory afferent nerve terminals in or beneath the urothelium itself (Chapple 2000; Andersson and Yoshida 2003; Kumar et al 2005). Antimuscarinic agents mitigate the sensation of urgency by also acting on sensory afferents within the bladder urothelium and increase the storage phase of the bladder cycle. Specifically, the antimuscarinic oxybutynin decreases afferent nerve activity in C-fiber bladder bladder afferents (De Laet et al 2006). Although the 3rd International Consultation on Incontinence gave a grade A recommendation to six different pharmacologic agents for OAB, oxybutynin transdermal is the primary focus of this review (Andersson et al 1999).

Oxybutynin has been used in the treatment of OAB for over 30 years with proven efficacy and is often the drug against which new treatments are compared (Thuroff et al 1991; Anderson et al 1999). Oxybutynin hydrochloride is a tertiary amine that has been widely used in the treatment of overactive bladder syndrome. Antimuscarinic action on M2 and M3 receptors impart smooth muscle relaxant effects as well as anesthetic capabilities (Hegde 2006). It is commercially available as an immediate (IR) or extended release (ER) oral form and a transdermal patch. Intravesical instillations and rectal suppositories have also been investigated (Winkler and Sand 1998).

Review of pharmacology and pharmacokinetics

Oxybutynin undergoes extensive metabolism in the liver by the cytochrome P450 (CYP) enzyme system and principally CYP 3A4. It has a bioavailability of 6% and is metabolized in the gut and liver after oral dosing to its primary metabolite N-desethyloxybutynin (N-DEO). N-DEO is a pharmacologically active metabolite which produces a

wide range of systemic side effects which often reduce patient persistence on oral formulations of oxybutynin IR (Chancellor et al 2001; Appell et al 2003). In oxybutynin ER and oxybutynin IR, N-DEO circulates at concentration levels 4 and 10 times as high as the parent compound, respectively (Staskin 2003).

Untoward side effects are reduced with the oral extended-release formulation, which provides once daily dosing and improves patient persistence on therapy. The delivery system consists of an osmotic bilayer laser-drilled drug core with a delivery orifice which allows drug to be released at a controlled rate over 24 hours (Portera and Lipscomb 1998). The extended release formulation produces a more stable plasma level with absorption primarily in the colon diminishing first pass metabolism in the upper gastrointestinal tract. The plasma level of the metabolite N-DEO plasma levels are reduced by 69% when compared with immediate release formulations (Oki et al 2006). However, significant dry mouth remains due to N-DEO's purported higher affinity than oxybutynin, to the M3 receptors in the submaxillary gland (Oki et al 2006). Oral oxybutynin produces longer-lasting blockage of the muscarinic receptors abolishing the secretory response in the salivary glands which does not occur to the same degree with transdermal oxybutynin (Oki et al 2006).

The oxybutynin transdermal delivery system was developed to reduce first pass metabolism thereby minimizing side effects. Transdermal oxybutynin administration results in greater systemic availability of oxybutynin and minimizes first-pass metabolism to N-DEO compared with extended-release and immediate-release oral administration. The plasma metabolite N-DEO to oxybutynin ratio with the transdermal oxybutynin system is 1.2:1 compared to 4.1:1 in the oral formulation (Appell et al 2003). Lower N-DEO plasma concentration and greater salivary gland output during transdermal oxybutynin treatment provide a low incidence of dry mouth in patients with overactive bladder syndrome (Appell et al 2003). In a double-blind, randomized trial comparing placebo to transdermal oxybutynin in the treatment of patients with UI and OAB, there was no significant difference between the placebo and transdermal oxybutynin, in the incidence of constipation, dry mouth, CNS impairment, or visual changes (Dmochowski et al 2002).

Oxybutynin is an ideal compound for a transdermal formulation because it is a weak base ($pK_a = 8$) and the free base form exists at physiologic pH, allowing transdermal permeation (Staskin 2003). The oxybutynin transdermal system is 39 cm² with a three-layer matrix delivery system

containing oxybutynin and a skin permeation enhancer triacetin, which are dissolved in an acrylic block-copolymer adhesive that continuously delivers oxybutynin for 3 to 4 days (Zobrist et al 2003). Oxybutynin passively diffuses across the skin into the systemic circulation. Following the application of the first transdermal oxybutynin 3.9 mg/day system, oxybutynin plasma concentration increases for approximately 24 to 48 hours, reaching an average maximum concentration of 3 to 4 ng/mL. Steady concentrations are maintained for up to 96 hours until the second application when it is widely distributed throughout body tissues. Following the removal of the transdermal system, plasma levels of both oxybutynin and N-DEO fall rapidly. It has a 7- to 8-hour half-life. The transdermal oxybutynin delivery system offers the advantage of much lower active metabolite concentrations of N-DEO due to its unique mode of delivery (Oxytrol PI 2003).

There are fewer CYP3A4 isoenzymes in the skin than in the liver or intestine, markedly reducing N-DEO metabolite serum levels when using the transdermal delivery system. This difference in metabolism significantly increases the bioavailability of oxybutynin to 80%. This decrease in N-DEO levels reduces side effects and potentially improves patient persistence on therapy (Sahai et al 2008). The transdermal system contains 36 mg of oxybutynin and provides a consistent plasma drug level while delivering approximately 3.9 mg of oxybutynin/day. This leads to serum oxybutynin levels similar to those achieved with the 10 mg oral extended-release formulation (Appell et al 2003). The oxybutynin transdermal delivery system has equivalent bioavailability when applied to the hip, abdomen, or buttock. Its position should be alternated to avoid occluding the same area of skin repetitively over a short period of time. Potential therapeutic benefits of transdermal delivery of oxybutynin include greater saliva production, decreased peak and trough oxybutynin serum levels, decreased serum levels of the N-DEO metabolite, and greatly reduced first pass metabolism (Appell et al 2003; Zobrist et al 2003). Also transdermal systems deliver the drug at a predetermined rate consistent with zero order kinetics which produces stable drug plasma concentrations (Staskin 2003; Davila et al 2006). Transdermal delivery systems also offer the advantage of steady state serum levels avoiding drug peaks and troughs, which worsen adverse effects at the peak and loss of efficacy at the trough of serum oxybutynin levels. The bioavailability of oxybutynin in the serum is also increased which may reduce the dosage needed to treat OAB symptoms. Further, because there is a higher prevalence of OAB in the elderly who are on multiple oral medications, the transdermal

route may provide an attractive alternative for patients who do not want to take more oral medications.

Efficacy and comparative studies

Davila et al (2001) showed that individuals who were randomized to oxybutynin transdermal versus oxybutynin immediate-release in a Phase 2 randomized trial demonstrated similar efficacy. Nearly equal reductions in the average number of incontinence episodes/day: 7.3 and 7.4 episodes decreased to 2.4 and 2.6 ($p < 0.0001$) in the oxybutynin transdermal versus oxybutynin immediate-release, respectively. Further analysis using visual analog scales revealed improved scores in both the transdermal and oral oxybutynin group and no difference in subjective continence scores. An increase in average bladder volume at first detrusor contraction and increase in maximum cystometric capacity was not significantly different between oral and transdermal oxybutynin. There was an increase in maximum cystometric capacity of 66 mL in the transdermal oxybutynin group ($p = 0.0055$) and 45 mL in the oral immediate-release ($p = 0.1428$) (Davila et al 2001). Mean maximum cystometric capacity was increased by 51 ± 138 mL ($p = 0.0538$) in the oral and 53 ± 88 mL ($p = 0.0011$) in the transdermal group. As anticipated, individuals given transdermal oxybutynin had significantly less dry mouth over immediate-release oral oxybutynin (38% versus 94% respectively, $p < 0.0001$). Further efficacy of transdermal oxybutynin was provided in a phase IIb trial using tolterodine extended-release 4 mg versus transdermal oxybutynin 3.9 mg/day. Both agents were found to decrease incontinence episodes, increase volume voided, and equally improve quality of life (Dmochowski et al 2003).

In a 12-week, double-blind randomized dose-ranging trial, 520 individuals were randomized to 3 doses of transdermal oxybutynin versus placebo; 447 (86%) completed the initial double-blind treatment period and 358 (87.1%) completing the open-label study. Those who received 3.9 mg/day transdermal oxybutynin had significant reductions in urinary frequency and incontinence episodes. Voided volume was also significantly increased in the transdermal oxybutynin group (Dmochowski et al 2002). Also, significant improvement in quality of life as measured by the Incontinence Impact Questionnaire and the Urinary Distress Index occurred in the transdermal oxybutynin group when compared to placebo. In patients who never received antimuscarinic treatment, transdermal oxybutynin reduced weekly incontinence episodes by 19, comparable to oral formulations without concomitant antimuscarinic side effects.

In phase III trials, a pooled analysis of the transdermal oxybutynin 3.9 mg/day reduced the median number of incontinence episodes by 75% versus a 50% reduction in the placebo group. There was also a decrease in urinary frequency of 18% with transdermal oxybutynin versus 8.7% with placebo ($p = 0.0023$). Also, urinary voided volume was increased by 15% with the active transdermal patch compared to 3.6% with placebo ($p < 0.00001$) (Dmochowski et al 2005). Similar findings were noted when transdermal oxybutynin was compared with oral tolterodine long-acting formulation and placebo where mean daily urge incontinence episodes and micturition frequency decreased (Dmochowski et al 2003). In this trial the most common adverse events with the oxybutynin transdermal delivery system included local skin irritation such as erythema (5.6%) and pruritis (16.8%) (Dmochowski et al 2005). This was most likely caused by adhesive removal of the stratum corneum or deeper layers, oxybutynin, the triacetin used as a permeation enhancer, occlusion of the skin or some combination of these factors (Staskin, 2003). Overall there was no significant difference in anticholinergic side effects in the transdermal oxybutynin versus placebo group with respect to: dry mouth (7% vs 5.3%, $p = 4303$); constipation (2.1% vs 2.0%, $p = 9843$); dizziness (0.8% vs 1.2%, $p = 6631$); abnormal vision 1.2% vs 0.8%, $p = 6431$); somnolence (0.8% vs 0.4%, $p = 5553$); and nausea (1.2% vs 0.8%, $p = 6631$) (Dmochowski et al 2005). The rates of discontinuation due to adverse events were 11.2% versus 1.2% in the oxybutynin transdermal group versus placebo group, respectively. Although dry mouth is a common cause of discontinuation of oral anticholinergics, no participant on transdermal oxybutynin withdrew from these two pooled studies because of dry mouth. The lack of persistence in the transdermal oxybutynin group was due primarily to skin reactions (Dmochowski et al 2005). Most antimuscarinics were associated with a significant incidence of dry mouth except oxybutynin transdermal, oxybutynin IR 5 to 7.5 mg/day, and propiverin IR 45 mg/day compared with placebo. However, the latter two formulations had a low number of subjects. Further, comparator trials revealed transdermal oxybutynin was associated with less constipation relative to oxybutynin IR (Chapple et al 2005). On the other hand, site reaction such as pruritis, vesicles, and rash were significant causes of lack of patient persistence on transdermal oxybutynin (Chapple et al 2005). These reactions may have been avoided with rotation of site application of the patch. Also, increased patient discontinuation (10.7%) relative to that of tolteradine (1.6%) could have been related to the uncharacteristic nature of the site reaction

versus predictable systemic effects associated with most antimuscarinics (Chapple et al 2005). Although transdermal appears to have less reported adverse reactions, most studies were not powered for adverse events or statistical testing was performed specifically for dry mouth.

Patient-focused perspectives and quality of life

Health-related quality of life and degree of functional impairment and bother are significant issues in the management of overactive bladder syndrome. Patient perceptions of OAB impact health seeking behaviors and may have a great deal to do with age, gender, caregiver/family, or physician perceptions (Marschall-Kehrel et al 2006). However, quality-of-life questionnaires are valuable instruments for determining the impact of OAB on patients' quality of life before and after treatment. When administered after treatment these instruments may more accurately demonstrate the effect of successful treatment than other methods such as voiding diaries and records of urinary frequency. The positive effects of antimuscarinic agents on health related quality of life (HRQOL) in patients with OAB has recently been reported in a meta-analysis of placebo-controlled trials using the Kings Health Questionnaire (KHQ) which showed that clinically meaningful changes were associated with a ≥ 5 point change from baseline in the individual domain scores which were associated with significant changes in the effect size. However, this was done only for tolterodine IR and tolterodine ER (Chapple et al 2005). This is a meta-analysis of 57 trials, 25 of which demonstrated the true treatment benefit and improved quality of life with antimuscarinic treatment. Collective data of 4 antimuscarinics that included transdermal oxybutynin demonstrated significant mean score changes favoring antimuscarinics in 73% of HRQOL domains. Improvement in sleep and energy, physical activities, emotions, and relationships HRQOL domains were significantly improved over placebo (Khullar et al 2006).

The MATRIX (Muticenter Assessment of TRansdermal therapy In overactive bladder with transdermal oxybutynin (Sand et al 2007) was an open-label, randomized, community-based, prospective study in which all subjects received 3.9 mg/day of transdermal oxybutynin applied twice weekly for up to 6 months. Quality of life and depression were assessed in 2878 patients during clinic visits at baseline, after 3 months and after 6 months of treatment using the KHQ and the Beck Depression Inventory II (BDI-II). Subjects were significantly affected by their OAB

symptoms according to a 6-point Likert global subjective response scale. Seventy-eight percent of subjects rated their OAB syndrome as a moderate to severe problem at baseline. Responses to the KHQ revealed that 57.4% of patients said their social life was affected and 41.4% reported that OAB interfered with their social activities. However, after treatment with transdermal oxybutynin quality of life was significantly improved as measured by the KHQ. Nine of the 10 domains of the KHQ showed statistically significant improvement at 6 months compared to baseline. In men specifically, HRQOL significantly improved in 8 or 10 domains by 6 months. These results were clinically relevant as demonstrated by mean score changes exceeding the 3- to 5-point minimally important difference threshold (Kelleher 2004). Domains that were most significantly improved included Incontinence Impact, Symptom Severity, Role and Physical Limitations, as well as Sleep/Energy. Improvement was reported for all individual response items within each domain as well. These results demonstrate the multidimensional impact of OAB on quality of life measures and its responsiveness to treatment with transdermal oxybutynin. The KHQ will be included as a component of the new International Consultation on Incontinence modular questionnaires because of it is fast and simple enough for routine clinical use. The Beck Depression Inventory was used to assess depression. Beck Depression Inventory (BDI-II) scores were significantly improved from baseline in men within this trial (Staskin 2008). Baseline BDI-II summary scores >12 (which are associated with clinical depression) decreased from 23.9% to 17.9% ($p = 0.0055$).

In a randomized, double-blind, placebo-controlled, multicenter trial transdermal oxybutynin dose-finding study of 637 Japanese subjects with OAB, it was determined that a 30% reduction in incontinence frequency constituted a minimally important clinical difference after treatment. Specifically, a change in incontinence episodes of more than 3 times per week was also demonstrated to be the minimal clinically meaningful difference needed to produce improvements in health-related quality of life (Homma and Kawabe 2006; Homma and Koyama 2006). The average number of urge urinary incontinence episodes with 3.9 mg/m² transdermal decreased from 20.8 at baseline to 6.3 after treatment ($p = 0.014$) (Homma and Koyama 2006). Clinically significant changes for all KHQ domain scores were noted for the transdermal oxybutynin group when compared to the placebo group in this study.

Sexual function, as a quality of life measure and the effects of OAB on sexual function has been poorly studied.

Yip et al (2003) found that women with detrusor overactivity had significant deterioration of their marital relationships which was inversely associated with sexual satisfaction compared to those given placebo. Detrusor overactivity was more negatively associated with sexual function compared to stress urinary incontinence (Gordon et al 1999). Other studies have shown that incontinent women, especially women with mixed urinary incontinence, have worse sexual function and quality of life (Temml et al 2000; Yip et al 2003). The impact of OAB on sexual function was examined in the MATRIX trial both before and after treatment with transdermal oxybutynin (Sand et al 2006a). In this trial, 569 (22.8%) participants admitted to leakage of urine during intercourse at baseline; whereas 438 (19.3%) leaked with intercourse after treatment. A 12.6% improvement in leakage during intercourse occurred while worsening of leakage during coitus occurred in 7.5% of subjects ($p < 0.0001$). The MATRIX study also demonstrated that 52.1% of women with OAB had decreased interest in sex, with 17.2% reporting a complete loss of interest. This complete loss of interest in sex was associated with older age, female gender, prolonged OAB symptoms, history of prior OAB therapy, and menopausal status in the female respondents ($p = 0.0312$). For male participants predictors of loss of interest in sex included age ($p = 0.0283$) and duration of OAB symptoms ($p = 0.0312$) on multivariate analysis. However, twice as many participants showed improvement in their interest in sex compared to those that worsened after 6 months of treatment with transdermal oxybutynin (23.4% versus 12.2%, $p < 0.0001$) (Sand et al 2006a). Relationships with their partners were improved in 444/2269 (19.6%) versus 271 of subjects (11.9%) who had worsening of their relationships ($p < 0.0001$).

Further analysis of the MATRIX study demonstrated improvements in work productivity as measured by the Work Productivity Questionnaire (WPQ) (Sand et al 2006b) was presented at the 31st Annual Meeting of the International Urogynecological Association in Athens, Greece in September 2006. WPQ index data were available for 697/2878 participants at the end of the study and was found to be significantly improved from baseline (8.2 to 5.5, $p < 0.0001$). Further, this study also revealed that treatment with transdermal oxybutynin improved nocturia and related symptoms. Baseline KHQ scores revealed that 97.6% of patients were affected by nocturia and 32.9% by nocturnal enuresis. Working individuals were significantly impacted; worsening nocturia was associated with significant impairment on WPQ scales. Nocturia improved in 41% of

subjects and worsened in 10.1% and nocturnal enuresis improved in 17.3 and worsened in 10.2% ($p < 0.0001$). At the end of the study, all mean WPQ scale scores were also significantly improved from baseline.

Conclusion

OAB is a symptom complex including urgency with or without urge urinary incontinence and commonly associated with frequency and nocturia. OAB is more prevalent in the elderly but has been found to permeate all age groups with consequent deleterious effects on quality of life. Sexual dysfunction, decreased work productivity, sleep disturbances, and social isolation are a few consequences of this disturbing syndrome. Fear of embarrassment leads to social isolation and adaptive behaviors such as avoiding travel or social activities. The association of OAB with other co-morbidities such as diabetes, hypertension, depression, and fractures often exacerbates the impact of OAB on daily functioning. Further, economic burden and other health related consequences confirm that treatment is imperative.

Although treatment with behavioral therapy is adequate for many, greater success is obtained if behavioral therapy is combined with pharmacotherapy. Antimuscarinic medications have been widely used to treat these symptoms for over four decades. Oxybutynin has been the most widely used of the antimuscarinic agents and is available in several formulations. Untoward side effects of oral formulations provided an impetus for the development of a transdermal oxybutynin, which reduces side effects and has equal efficacy and tolerability. With transdermal oxybutynin there is limited impact on salivary production which minimizes dry mouth. Skin reactions are commonly cited as reasons for lack of patient persistence on transdermal oxybutynin which can often be avoided by alternating the application site. HRQOL is an important measure of treatment success. Transdermal oxybutynin has been shown to significantly improve HRQOL, sexual function, marital relationships, as well as to enhance work productivity in a multicenter study of 2878 men and women of all ages. Transdermal oxybutynin is an appropriate first line treatment of OAB, particularly in patients who are on multiple medications and have significant side effects on other antimuscarinic agents.

Disclosures

PS discloses the following conflicts of interest: Watson Pharma, advisor, lecturer; Ortho, advisor, lecturer; Allergan,

advisor, lecturer, investigator; Astellas/GSK, advisor, lecturer; Pfizer, advisor, lecturer; Sanofi-Aventis, advisor.

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