# Antimuscarinic Therapy- How Long Should We Treat Overactive Bladder?

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## INTRODUCTION

Overactive bladder (OAB) is a symptom complex characterized by urgency (the key symptom), with or without urgency incontinence, usually associated with frequency and nocturia, in the absence of metabolic factors or genitourinary pathologies which could elucidate the causes of these symptoms [1]. OAB is a highly prevalent condition with both men and women equally affected, and the incidence rate increases with age [2]. This condition imposes a serious impact on individuals as well as on society with enormous annual OAB-related costs [3]. Primary treatments for OAB include lifestyle modifications, behavioral therapy, bladder training, and pelvic floor muscle exercise. Antimuscarinic drugs are currently the first line pharmacologic therapy for OAB. Antimuscarinics have played an important role in treating the patient with OAB, and therefore it is imperative for physicians to have a clear perspective of currently-used antimuscarinic drugs, and know how long patients should be treated by antimuscarinics.

## CLINICAL EFFECTIVENESS OF ANTIMUSCARINICS

Seven antimuscarinic agents are now on the world market including tolterodine, fesoterodine, trospium, darifenacin, solifenacin, oxybutynin, and propiverine. They are all regarded as having level-1 evidence and a grade-1 recommendation. An update of the effects of antimuscarinic therapy in OAB was presented in a 2008 article using a systematic review and meta-analysis [4]. Chapple et al reviewed evidence on the efficacy, tolerability, safety, and health-related quality of life (HRQL) of 7 licensed antimuscarinics, all from randomized controlled trials (RCTs) with study lengths ranging from 2 to 52 weeks, most of which were 12 weeks. The results showed that antimuscarinics were more effective than placebos, and were well-tolerated. Few studies showed significantly higher withdrawal rates for antimuscarinics compared with placebos, and there were no serious statistically significant adverse effects for any drug in comparison with placebos. Xerostomia was the most commonly reported side effect (29.6% for antimuscarinics vs. 7.9% for placebos), followed by pruritus (15.4% vs. 5.2%). Improvements were seen in HRQL with antimuscarinic therapy. In conclusion, antimuscarinics are effective, safe, and well-tolerated in therapy for OAB.

Received: March 5, 2009 Accepted: March 5, 2009
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## DRUG PROFILES AND DOSAGES

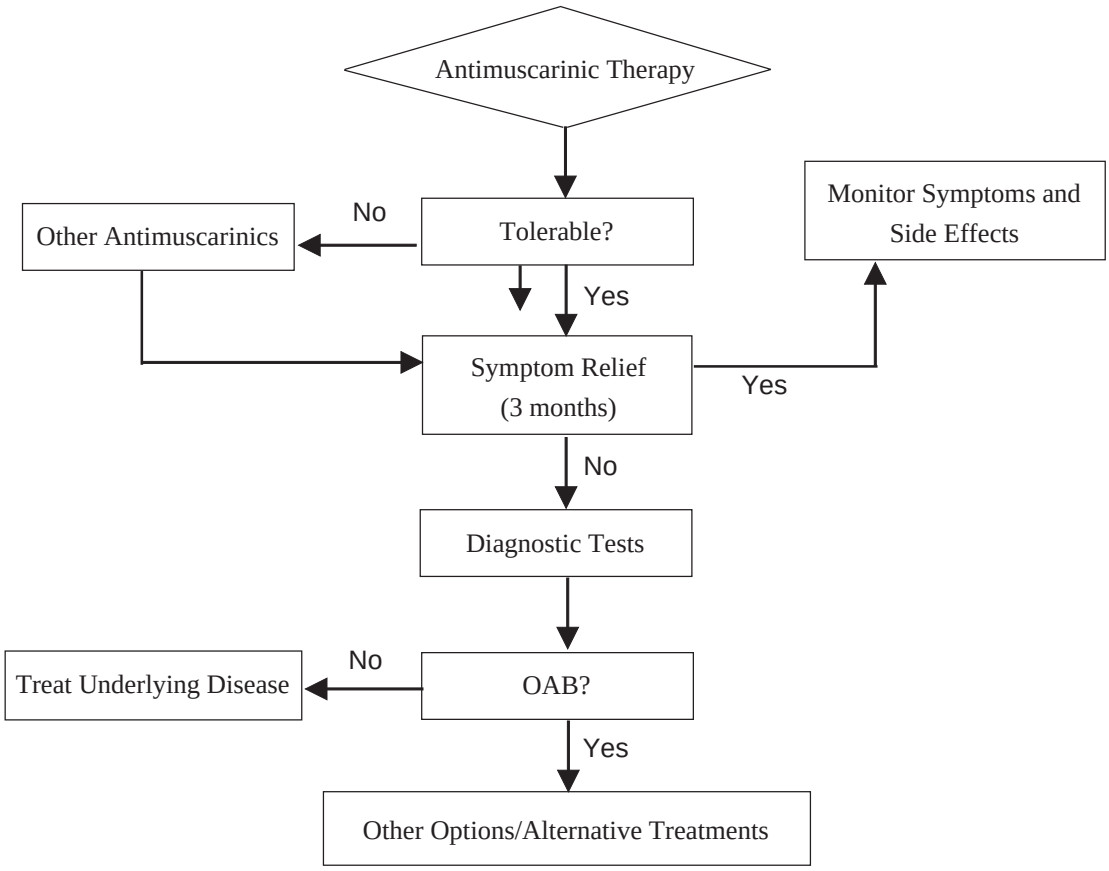
Different doses, formulations, and routes of administration are currently available for antimuscarinics, which usually makes treatment choices quite difficult. Novara et al reviewed 50 RCTs to evaluate the individualized efficacy and safety of these different aspects [5]. Dose escalation of immediate release (IR) formulations might result in some limited improvement in the efficacy but at the cost of a significant increase in the rate of adverse events. The extended-release (ER) formulations showed some advantages over IR. The transdermal route was not proved better than the oral one. Tolterodine IR exerted a more favorable profile of adverse events than oxybutynin IR. In summary, ER formulations are preferred to their IR counterparts. Dose escalation is not recommended for IR formulations. Based on current evidence, it is difficult to indicate which drug should be prescribed as the first choice in treatment.

## SIDE EFFECTS

Because of the altered pharmacokinetics of a given antimuscarinic, the risk of side effects may be increased in some patients, such as those with impaired renal or hepatic function, or those with co-medication causing drug-drug interactions. In addition, genetic differences in drug-metabolizing enzymes may result in altered drug exposure in some victims. For antimuscarinics, these enzymes include cytochrome P450, CYP2D6 and CYP3A4. To prescribe antimuscarinics efficaciously and safely for patients with OAB, the above-mentioned factors and individual product characteristics must be considered. Witte et al suggested checking the package insert [6]. Dose adjustments must be made in some specific conditions.

## DURATION OF TREATMENT

The purpose of treating patients with OAB is to eliminate symptoms without significant or untoward side effects. To meet this goal by optimizing the clinical effectiveness of antimuscarinic therapy, we need to understand the whole perspective of each antimuscarinic agent and the patients themselves. RCTs have shown that one type of antimuscarinic should be prescribed initially for 12 weeks, based on the patient's condition and individual drug profile. After three months of treatment, the outcome should be evaluated. The following treatment algorithm is suggested.




If antimuscarinic therapy fails, other options or alternative treatments should be chosen. OAB may be a lifelong problem and patients with OAB may need care until the problem is resolved, a new diagnosis is obtained, or the pathophysiology is completely elucidated.

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