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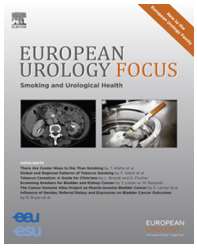

Review – Female Urology - Incontinence

Lower Urinary Tract Symptoms: What's New in Medical Treatment?

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Abstract

Context: Pharmacological treatment is a cornerstone in the management of patients with lower urinary tract symptoms (LUTS).
Objective: To review emerging evidence in the medical treatment of LUTS.
Evidence acquisition: An Embase/Pubmed-based literature search was conducted in December 2017, screening for randomized controlled trials (RCTs), prospective and retrospective series, animal model studies, and reviews on medical treatment of LUTS.
Evidence synthesis: The main medical innovation in recent years in overactive bladder (OAB) has been the approval of the first β_3-adrenoceptor agonists (mirabegron) and intradetrusor onabotulinum toxin A, while several other drugs such as antiepileptics, phosphodiesterase inhibitors, or other β_3-agonists have brought promising results in phase 3 trials. Intraprostatic injections of various drugs for LUTS/benign prostatic hyperplasia have been investigated, but results of phase 3 trials are still pending, while combination therapies of phosphodiesterase type 5 inhibitors + α-blockers or finasteride have been proved as superior to single therapies in RCTs conducted in these patients. Two new formulations of desmopressin have been approved for nocturia in the USA (desmopressin nasal spray) and Europe/Canada/Australia (desmopressin orally disintegrated tablet). Fedovapagon, a vasopressin V_2 receptor agonist, has recently completed a large phase 3 trial in male patients with nocturia. Other phase 3 trials are ongoing in bladder pain syndrome (AQX 11-25, a SHIP-1 activator) and in neurogenic detrusor overactivity (mirabegron and abobotulinum toxin A).
Conclusions: Medical treatment of LUTS is a very active research field with recently approved drugs for nocturia (desmopressin acetate nasal spray/orally disintegrated tablet) and numerous emerging drugs currently investigated in OAB, LUTS/benign prostatic hyperplasia, nocturia, bladder pain syndrome, and neurogenic detrusor overactivity.
Patient summary: Medical treatment of lower urinary tract symptoms is a very active research field with recently approved drugs for nocturia (desmopressin acetate nasal spray/orally disintegrated tablet) and numerous emerging drugs in overactive bladder, nocturia, neurogenic detrusor overactivity, bladder pain syndrome, or benign prostatic hyperplasia.

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1. Introduction

Numerous drugs have become available for the treatment of lower urinary tract symptoms (LUTS), including α-blockers, 5α-reductase inhibitors, antimuscarinics, phosphodiesterase type 5 inhibitors (PDE5Is), and intradetrusor injections of botulinum toxin. Many of these agents have become established as gold standard treatments of conditions such

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as overactive bladder (OAB), LUTS due to benign prostatic hyperplasia (BPH), or neurogenic detrusor overactivity (NDO) [1]. However, not all patients with LUTS can be managed satisfactorily with existing treatments. Therefore, experimental and clinical research continues. Moreover, new indications and/or additional data continue to emerge for existing drugs. This article aims to review recent developments in the medical treatment of LUTS.

2. Evidence acquisition

A literature search was conducted in February 2018 using the MedLine and Embase databases, screening for randomized controlled trials (RCTs), prospective and retrospective series, animal model studies, and reviews on medical treatment for LUTS. The search strategy included the following terms: "overactive bladder," "benign prostatic hyperplasia," "lower urinary tract symptoms," "voiding symptoms," "storage symptoms," "nocturia," "medication" or "pharmacotherapy" or "medical treatment" or "pharmaceutic" or "randomized" or "phase 2" or "bladder pain syndrome" or "interstitial cystitis" that were used alone or in combination. Only articles published in English between January 2016 and February 2018 and deemed to be relevant were included in this review. The websites of European Medicines Agency (EMA; http://www.ema.europa.eu/ema/) and US Food and Drug Administration (FDA; https://www.fda.gov) were also searched to look for recently approved drugs. Finally, clinicaltrials.gov was examined to retrieve ongoing or recently completed clinical trials of interest. Owing to the high number of drugs investigated currently and over the past few years, the current review focused mostly on those assessed through phase 2 and 3 trials. Any drug the phase 2/3 data of which were published/presented or which was approved before 2016 was not included in this review to address only the latest innovations in the field. The study selection process is presented in Fig. 1.

3. Evidence synthesis

3.1. *Overactive bladder*

3.1.1. *New β_3-agonists*

While β_3-adrenoceptor agonists had been suggested as a promising treatment of OAB for over a decade, mirabegron was the first drug (and still the only to date) of this new therapeutic class to be approved by the FDA and EMA in 2012 after the publications of four large phase 3 RCTs (three

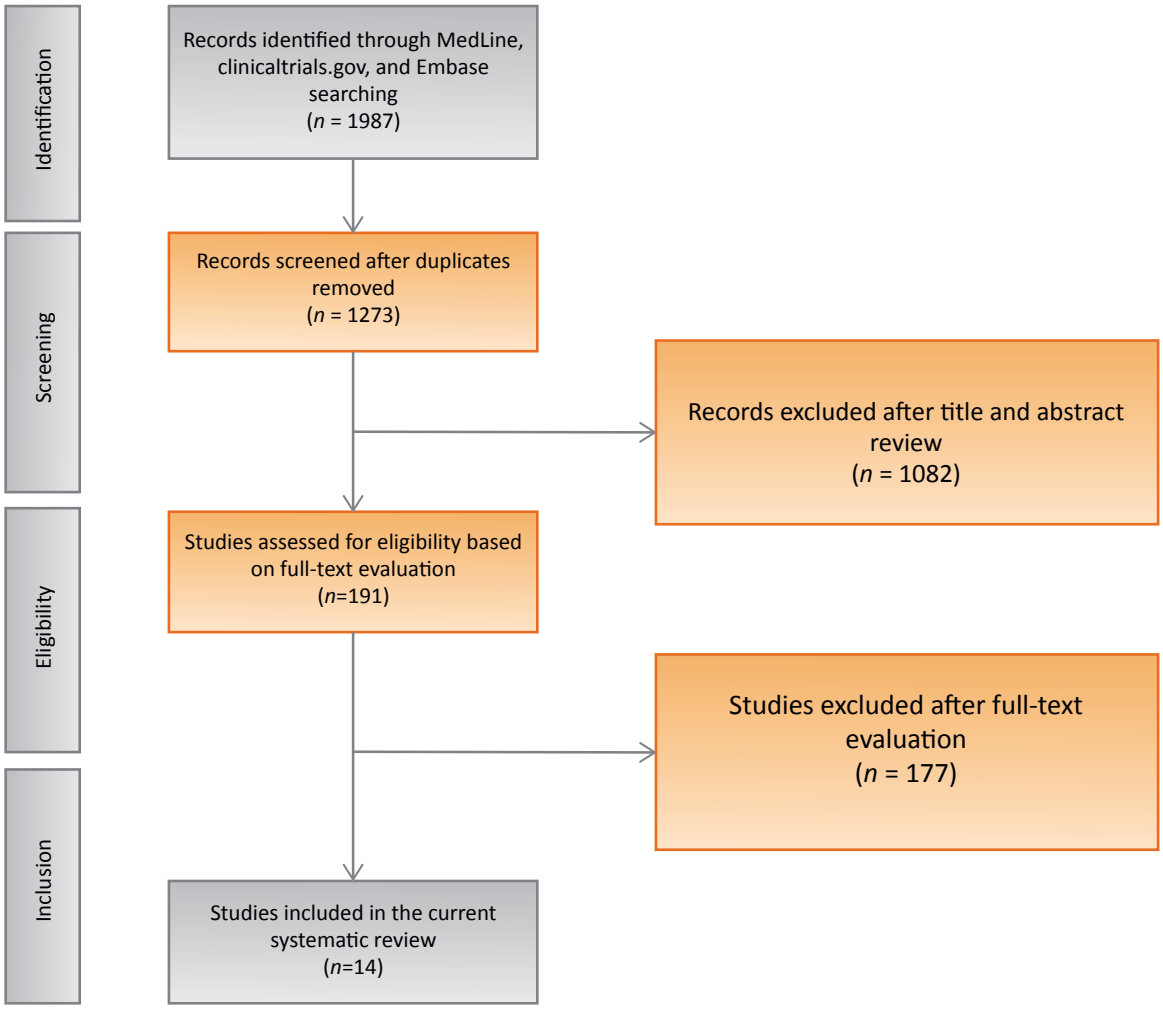

Fig. 1 – Flowchart showing the study selection process.