ORIGINAL RESEARCH—EJACULATORY DISORDERS

Impact of Medical Treatments for Male Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia on Ejaculatory Function: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction. Several drugs, currently used to treat lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH), can be associated with bothersome sexual side effects, including ejaculatory dysfunction (EjD).
Aim. To provide a systematic review and meta-analysis of the available randomized clinical trials (RCTs) reporting the impact of medical treatments for LUTS due to BPH on ejaculatory function.
Main Outcome Measure. EjD related to medical treatments for LUTS.
Methods. A systematic literature search was performed using PubMed, Scopus and Cochrane databases. EjD was identified using both free text ("ejaculat*," "retrograde ejaculation," "anejaculation," "ejaculatory dysfunction") and Mesh ("Ejaculation") searches.
Results. Of 101 retrieved articles, 23 were included in the present meta-analysis. EjD was significantly more common with alpha-blockers (ABs) than with placebo (OR:5.88; $P < 0.0001$), in particular, considering Tamsulosin (OR:8.58; $P = 0.006$) or Silodosin (OR:32.5; $P < 0.0001$), with Tamsulosin associated with significantly lower risk of EjD than Silodosin (OR:0.09; $P < 0.00001$). Conversely, Doxazosin and Terazosin were associated with a risk similar to placebo. Meta-regression showed that EjD was associated with IPSS and with Qmax both before and after treatment with ABs, while multivariate analysis demonstrated that EjD was independently associated with the improvement of IPSS (adj.r:0.2012; $P < 0.0001$) and Qmax (adj.r:0.522; $P < 0.0001$).

EjD was significantly more common with 5ARIs as compared with placebo (OR:2.73; $P < 0.0001$). Both Finasteride (OR 2.70; $P < 0.0001$) and Dutasteride (OR 2.81; $P = 0.0002$) were associated with significantly higher risk of EjD than placebo. EjD was significantly more common with combination therapy as compared with ABs alone (OR:3.75; $P < 0.0001$),or with 5ARIs alone (OR:2.76; $P = 0.02$).
Conclusions. ABs and 5ARI were both associated with significantly higher risk of EjD than placebo. More the AB is effective over time, greater is the incidence of EjD. Finasteride has the same risk of Dutasteride to cause EjD. Combination therapy with ABs and 5ARIs resulted in a 3-fold increased risk of EjD as compared with ABs or 5ARIs alone. These data can be relevant both for drug selection and patients counseling. **Gacci M, Ficarra V, Sebastianelli A, Corona G, Serni S, Shariat SF, Maggi M, Zattoni F, Carini M, and Novara G. Impact of medical treatments for male lower urinary tract symptoms due to benign prostatic hyperplasia on ejaculatory function: A systematic review and meta-analysis. J Sex Med 2014;11:1554–1566.**

Key Words. Lower Urinary Tract Symptoms; LUTS; Benign Prostatic Hyperplasia; BPH; Medical Treatments for LUTS; Ejaculatory Function; Ejaculatory Dysfunction; EjD; Alpha Blockers; 5 Alpha Reductase Inhibitors; PDE5-I

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Introduction

Benign prostatic hyperplasia (BPH) is a common condition [1] and a frequent cause of lower urinary tract symptoms (LUTS) in adult men [2].

Sexual dysfunctions (SD), including decreased libido, erectile dysfunction, ejaculatory dysfunction (EjD) and overall dissatisfaction, are also highly prevalent and potentially bothersome for the elderly men [3]. With the term EjD are usually described several disturbance of ejaculation, including premature or delayed ejaculation, retrograde ejaculation or anejaculation, and painful ejaculation [4]. Several drugs, such as antihypertensive, frequently assumed by elderly patients, can also negatively affect ejaculation [5]. Preclinical trials and population based epidemiological studies underline the associations between LUTS and SD, based on common pathogenetic mechanisms, and coexistence of additional contributing factors, such as chronic inflammation and sex steroid ratio imbalance [6]. Moreover, the multinational survey of the aging male (MSAM-7) study demonstrated that EjD, increased significantly with LUTS severity, regardless of age and comorbidities [7].

The main goals of medical treatments for LUTS/BPH are the relief of bothering symptoms, improve quality of life and prevent disease progression [8,9]. Alpha-blockers [AB],5-alpha reductase inhibitors [5ARI], anticholinergic and their combinations thereof are commonly used in the treatment of male LUTS [8,9]. Moreover, a phospodiesterase-5 inhibitor [PDE5-I], Tadalafil 5 mg once daily, has been recently approved for the same indication [9]. Several drugs used for LUTS/BPH may strongly affect sexual function and bother, with different impact across drug classes and even within the same class. Many RCTs have widely analyzed the overall impact of medical treatments for BPH on erectile function, but only a few have extensively and systematically investigated the treatment related EjD.

Aim

The aim of the present study is to provide a systematic review and meta-analysis of the available randomized clinical trials reporting the impact of medical treatments for LUTS due to BPH on ejaculatory function.

Methods

Systematic Literature Search

A literature search was performed in January 2013 using the Pubmed, and Scopus databases. The Pubmed search included both "free text" and "MeSH" protocols. Free text searches included the following terms to identify medical therapies for LUTS: "prostatic hyperplasia," "lower urinary tract symptoms," "alfusosin," "doxazosin," "tamsulosin," "terazosin," "silodosin," "fiansteride," "dutasteride," "sildenafil," "tadalafil," "vardenafil," "oxybutynin," "tolterodine," "trospium chloride," "darifenacin," "solifenacin," "fesoterodine," "mirabegron," and "serenoa." Similarly, the following MeSH terms were used to identify medical therapy for LUTS: "Prostatic Hyperplasia," "Adrenergic alpha-Antagonists," "5-alpha reductase inhibitors," "phosphodiesterase 5 inhibitors," "cholinergic antagonists," "doxazosin," "terazosin," "alfuzosin," "tamsulosin," "finasteride," "dutasteride," "sildenafil," "vardenafil," "tadalafil," "oxybutynin," "tolterodine," "trospium chloride," "darifenacin," "solifenacin," "fesoterodine," "2-(2-aminothiazol-4-yl)-4′-(2-((2-hydroxy-2-phenylethyl)amino)ethyl)acetanilide" (the MeSH term related to Mirabegron), "serenoa." Free text and MeSH searches were pooled using the "OR" bolean operator to identify papers concerning medical therapy of LUTS. EjD was identified using both free text ("ejaculat*," "retrograde ejaculation," "anejaculation," "ejaculatory dysfunction") and Mesh ("Ejaculation") searches. Free text and MeSH searches were pooled using the "OR" bolean operator to identify papers concerning EjD. Finally, the two resulting searched were pooled using the "AND" bolean operator to identify papers concerning medical therapy for LUTS and EjD. No limitations were applied. The searches of Scopus database used the same free-text protocol and the same key words, applying no limit.

Two authors separately reviewed the records to select the studies reporting ejaculatory dysfunction during medical therapies for male LUTS. In addition, Cochrane database of systematic review was searched for systematic reviews evaluating medical therapies for male LUTS. Finally, other relevant studies cited in the reference lists of the selected papers were evaluated, as well as further studies published after the systematic search whom the authors were aware.

Study Selection

Trials included in the present systematic review were selected using the following inclusion criteria: (i) they were randomized controlled trials, with at least 12 weeks duration (ii) the subject of the

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