ORIGINAL RESEARCH—FSD PHARMACOTHERAPY

The Efficacy and Safety of Ospemifene in Treating Dyspareunia Associated with Postmenopausal Vulvar and Vaginal Atrophy: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction. Ospemifene, a novel selective estrogen receptor modulator, has been developed for the treatment of vulvovaginal atrophy and dyspareunia in postmenopausal women.

Aim. We carried out a systematic review and meta-analysis to assess the efficacy and safety of the drug for treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy.

Methods. A literature review was performed to identify all published randomized double-blind, placebo-controlled trials of ospemifene for the treatment of vulvovaginal atrophy and dyspareunia. The search included the following databases: MEDLINE, EMBASE, and the Cochrane Controlled Trials Register. The reference lists of the retrieved studies were also investigated. A systematic review and meta-analysis was conducted.

Main Outcome Measures. Six publications involving a total of 1,772 patients were used in the analysis, including three randomized controlled trials (RCTs) that were short-term (12 weeks) comparisons of ospemifene with placebo and three RCTs that were long-term (1 year) comparisons of ospemifene with placebo.

Results. For the comparison of short-term ospemifene with placebo, parabasal cells (the standardized mean difference [SMD] = –37.5, 95% confidence interval [CI] = –41.83 to –33.17, $P < 0.00001$), superficial cells (SMD = 9.24, 95% CI = 7.70 to 10.79, $P < 0.00001$), vaginal PH (SMD = –0.89, 95% CI = –0.98 to –0.80, $P = 0.00001$), and dyspareunia (SMD = –0.37, 95% CI = –0.43 to –0.30, $P = 0.00001$) indicated that ospemifene was more effective than the placebo. For the comparison of long-term ospemifene with placebo, endometrial thickness (SMD = 0.90, 95% CI = 0.58 to 1.23, $P = 0.00001$), treatment emergent adverse event, discontinuations due to adverse event, and serious adverse event indicated that ospemifene was generally safe.

Conclusions. This meta-analysis indicates that ospemifene to be an effective and safe treatment for dyspareunia associated with postmenopausal vulvar and vaginal atrophy. **Cui Y, Zong HT, Yan HL, Li N, and Zhang Y. Treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy: A systematic review and meta-analysis. J Sex Med 2014;11:487–497.**

Key Words. Ospemifene; Dyspareunia; Sexual Pain; Vulvovaginal Atrophy; Meta-Analysis; Randomized Controlled Trial

Introduction

Vulvar and vaginal atrophy (VVA), a chronic postmenopausal health condition that occurs because of a hypoestrogenic state [1,2], is common yet often underreported [3]. In untreated postmenopausal women, the incidence of VVA symptoms, such as vaginal dryness, itching, burning, and dyspareunia, is estimated to be approximately 60% [4]. Unlike some symptoms of menopause, such as hot flushes that lessen or disappear with time, symptoms like dyspareunia related to VVA usually persist and can even worsen without treatment [5]. Moreover, the condition has the potential to negatively affect the life of a woman and her sexual partner [6,7].

Current treatment options for VVA consist of systemic hormone therapy, vaginal estrogen

products, and over-the-counter nonhormonal lubricants and moisturizers [8–11]. Their use is limited, and they are administered at low doses because of the potential for associated systemic estrogenic effects, especially with long-term use [12]. Ospemifene is a novel oral selective estrogen receptor modulator (SERM), with a unique set of tissue-specific estrogenic agonist/antagonist effects [13], which has been shown to be well tolerated and to have a favorable pharmacological profile, including a significant antitumor effect in experimental breast cancer models [14,15] and positive effects on vaginal epithelium and bone turnover in postmenopausal women [16–19].

The goal of the present study was to perform a meta-analysis to evaluate the safety and efficacy of ospemifene in treating dyspareunia associated with postmenopausal VVA, which may resolve some of the current controversies over use of this drug.

Materials and Methods

Search Strategy

MEDLINE (1966 to July 2013), EMBASE (1974 to July 2013), and Cochrane Controlled Trials Register databases were searched to identify randomized controlled trials (RCTs) that referred to the impact of ospemifene in treating VVA; we also searched the reference lists of the retrieved studies. The following search terms were used: *ospemifene*, *vulvovaginal atrophy*, *dyspareunia*, *randomized controlled trial*.

Inclusion Criteria and Trial Selection

RCTs that met the following criteria were included: (i) the study design included treatment with ospemifene; (ii) the study provided accurate data that could be analyzed, including the total number of subjects and the values of each index; and (iii) the full text of the study could be accessed. When the same study was published in various journals or in different years, the most recent publication was used for the meta-analysis. If the same group of researchers studied a group of subjects with multiple experiments, then each study was included. A flow diagram of the study selection process is presented in Figure 1.

Quality Assessment

The quality of the retrieved RCTs was assessed using the Jadad scale [20]. All the identified RCTs

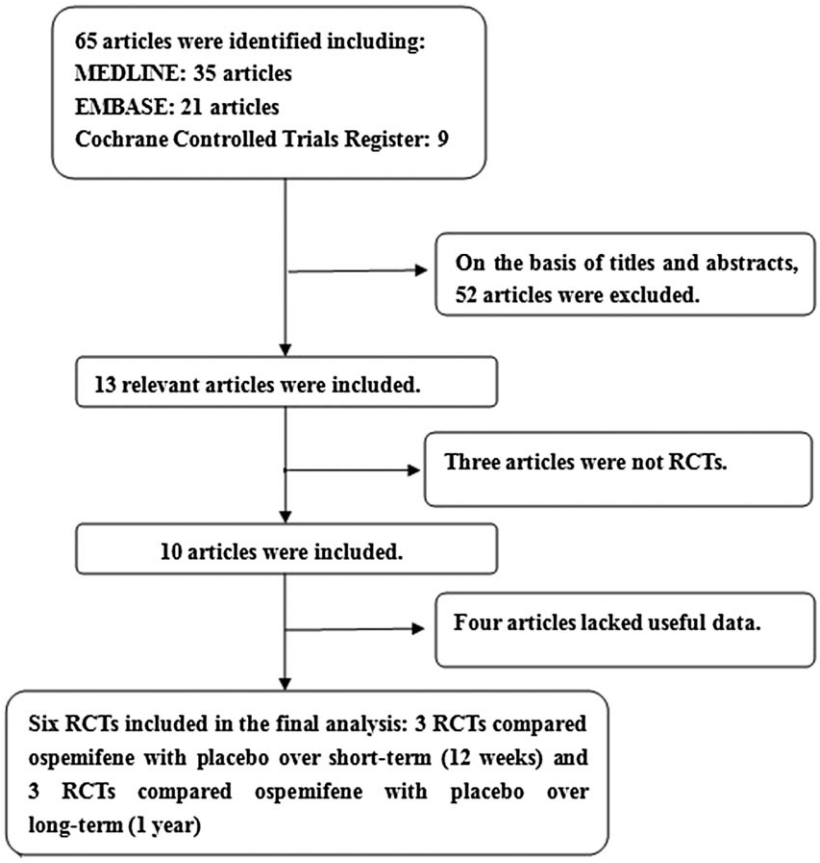

Figure 1 A flow diagram of the study selection process. RCT = randomized controlled trial.