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CASE REPORT

Experience with ospemifene in a patient with vulvovaginal atrophy and dyslipidemia: a case study

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Abstract

The changes that occur in sex hormone levels, body composition, and lipid/lipoprotein levels during the menopause transition, together with vascular remodeling, increase the risk of cardiovascular disease (CVD) in postmenopausal women. Any treatments prescribed for concomitant conditions during menopause should not exacerbate CVD risk factors. Ospemifene is the first non-hormonal, non-estrogenic drug approved to treat moderate-to-severe vulvovaginal atrophy (VVA), a component of genitourinary syndrome of menopause, in women unsuited to receive vaginal estrogen therapy. This case study reports the experience of a postmenopausal woman with VVA who required escalation from local therapy and presented CVD risk factors (family history and hypertension). During the first 6 months of ospemifene treatment, and before initiating concomitant simvastatin for persistently elevated total cholesterol concentrations, improvements were observed in several lipid parameters (decreases of 11% in total cholesterol, 16% in low density lipoprotein cholesterol, and 15% in triglycerides) which may have been attributable at least in part to ospemifene. Improvements in lipid parameters during ospemifene treatment for VVA may contribute toward reducing long-term CVD risk.

Keywords: dyslipidemia, ospemifene, vulvar and vaginal atrophy.

Citation

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Introduction

The changes that occur in sex hormone levels, body composition (e.g. fat deposition), and lipid/lipoprotein levels during the menopause transition, in conjunction with vascular remodeling, are associated with an increased risk of cardiovascular disease (CVD) in postmenopausal women.[1] However, because biological aging is difficult to separate from reproductive aging, the mechanisms for this association are unclear.[2] The prospective Study of Women's Health Across the Nation found that total cholesterol, low density lipoprotein cholesterol (LDL-C), and apolipoprotein-B were markedly increased within the 1-year timeframe before and after the final menopausal period, consistent with menopause-induced changes.[3] A follow-up study showed that, within 1 year of the final menopausal period, smaller increases in high density lipoprotein cholesterol (HDL-C) and apolipoprotein A-1 were related to greater interadventitial diameter, while greater increases in LDL-C were related to increased plaque scores.[4] The findings suggest that, during perimenopause, increased surveillance and treatment of elevated LDL-C and other factors that may influence a woman's health (e.g. sex hormone levels, vasomotor symptoms) are indicated.[5]

Irrespective of causality, any treatments prescribed for concomitant conditions during menopause should not exacerbate CVD risk factors. Numerous potential pathophysiological aberrations can contribute to increased risk. This article reviews lipid changes in a patient during treatment with ospemifene for vulvovaginal atrophy (VVA), a component of genitourinary syndrome of menopause, to ascertain their likely impact on cardiovascular risk. As patient-specific information was deidentified to ensure anonymity, patient consent was not required.

Case 1

The case describes a 57-year-old woman (weight: 68 kg; height: 1.6 m) who experienced menarche at age 11 years, menopause at 50 years, and was nulliparous. Relevant personal history included a total hysterectomy 2 years previously (55 years) with removal of the uterus and cervix due to atypical

endometrial hyperplasia, and hypertension treated with enalapril 10 mg/day. Relevant family history included a sister with breast cancer and a father with myocardial infarction at age 74 years.

At age 51 years, the patient presented with dyspareunia. Her Vaginal Health Index score[6] was 9/25. A diagnosis of VVA was confirmed by physical examination (Figure 1) and Pap smear. Consistent with the usual consequences of VVA, the patient complained of low sexual desire and arousal problems (Figure 2).

In the years since her diagnosis, the patient had been managing her symptoms using lubricants/moisturizers with or without phytotherapeutic agents (isoflavones), but further-line therapy was currently indicated. Local menopausal hormone therapy was suggested but she refused due to breast cancer concerns. In January 2018, treatment was initiated with ospemifene 60 mg/day. Six months later, her Vaginal Health Index score had improved from 9/25 to 16/25 and a Pap smear confirmed normal vaginal trophism.

Figure 1. Vulvovaginal atrophy.

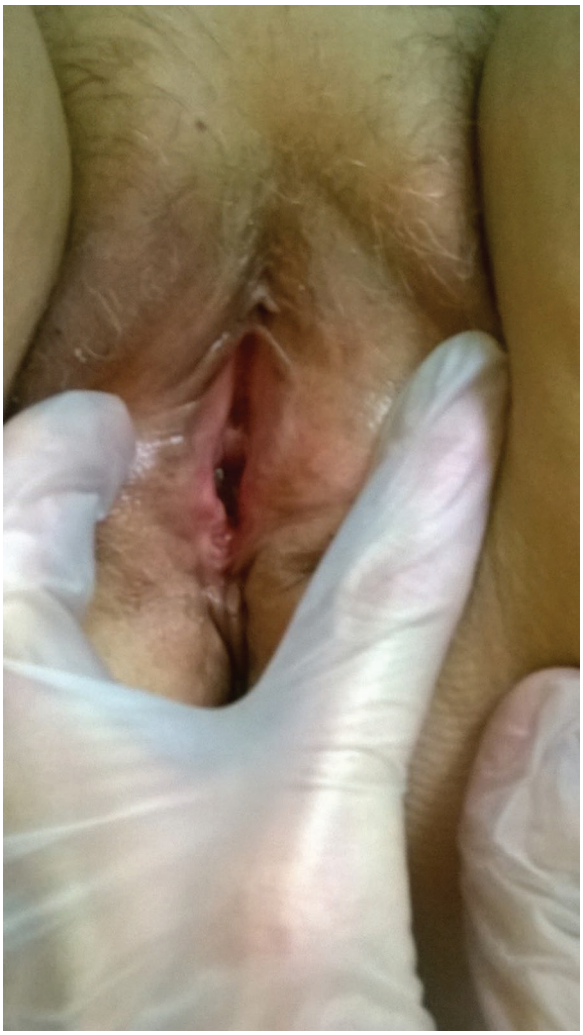
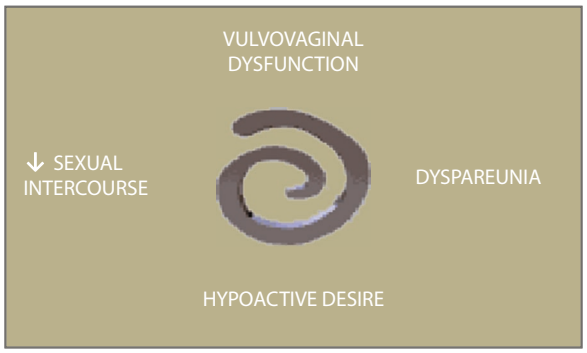


Figure 2. Consequences of vulvovaginal atrophy: vulvovaginal dysfunction can lead to a loss of sexual desire.



The patient's lipid profiles immediately before starting treatment with ospemifene (baseline) and 6 months later are shown in Table 1. A total cholesterol concentration of 241 mg/dL at baseline (January 2018) indicated increased cardiovascular risk. Two months later (data not shown), total cholesterol and LDL-C were reduced, and HDL-C was similar, relative to baseline. By July 2018, further improvements in lipid parameters were observed. Compared with baseline, there were decreases of 11% in total cholesterol, 16% in LDL-C, and 15% in triglycerides. HDL-C was unchanged. As total cholesterol (214 mg/dL) was above the threshold (200 mg/dL), the patient's primary care physician initiated treatment with simvastatin 10 mg. At follow-up in February 2019, after approximately 13 months' treatment with ospemifene and 7 months' treatment with simvastatin, there were further improvements in her lipid profile.

Coagulation indices were all within reference ranges at baseline and were not remeasured at 6 months. Homocysteine decreased by 23% from 20.4 µmol/L at baseline (reference range: 3.7–13.9 µmol/L) to 15.7 µmol/L after 6 months' treatment with ospemifene, although remained above the reference range.

Clinical overview

The case describes a postmenopausal woman with persistent symptoms of VVA despite treatment with lubricants/moisturizers ± phytotherapeutic agents. Treatment with a local estrogen was refused. Ospemifene was selected based on the results of meta-analyses confirming its efficacy and safety in severe symptomatic VVA.[7,8] Ospemifene's estrogen agonist activity in the vaginal epithelium[9] led to its approval as the first non-hormonal, non-estrogenic drug for treatment of moderate-to-severe VVA in women unsuited to receive vaginal estrogen therapy.[10] By regenerating vaginal cells and improving lubrication, ospemifene treats the underlying cause of vaginal dryness and dyspareunia.[11] Most women notice symptom improvement within the first 4 weeks of treatment.[11]

In our patient with dyslipidemia, ospemifene 60 mg/day for 13 months had no negative impact on lipid parameters or

Table 1. Lipid and homocysteine levels at baseline (before treatment) and after 6 months' treatment with ospemifene.

Parameter	Visit 1 (Month 0)	Visit 2 (Month 6)	Reference range
Total cholesterol (mg/dL)	241	214	100–200
LDL-C (mg/dL)	154	129	Higher risk: >160
HDL-C (mg/dL)	67	68	Higher risk: <35
Ratio TC: HDL-C	3.6	3.1	<4.5
VLDL-C (mg/dL)	20	17	<40
Triglycerides (mg/dL)	101	86	35–200
Homocysteine (µmol/L)	20.4	15.7	3.7–13.9

HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; VLDL-C, very low density lipoprotein cholesterol.

coagulation factors. Improvements in lipid parameters in the 6-month period before the start of simvastatin were likely attributable to ospemifene, and possibly also to dietary changes. A post hoc analysis of pooled data from 2166 postmenopausal women found no detrimental effects on serum lipid and coagulation parameters during treatment with ospemifene 60 mg/day for up to 12 months.[12] In this analysis, mean increases from baseline in HDL-C were significantly greater with ospemifene than placebo at 3 months (4.4 *versus* 0.2%; $p<0.0001$), 6 months (5.1 *versus* 1.5%; $p=0.0359$), and 12 months (2.3 *versus* -1.9%; $p=0.0086$). Likewise, changes from baseline in LDL-C significantly favored ospemifene over placebo at 3 months (-5.2 *versus* 2.4%; $p<0.0001$), 6 months (-6.7 *versus* 2.4%; $p=0.0002$), and 12 months (-7.0 *versus* -2.1%; $p=0.0293$). A significant reduction from baseline in total cholesterol was observed with ospemifene at 6 months compared with placebo (-1.8 *versus* 1.6%; $p=0.0345$). Increases in triglycerides at 3, 6, and 12 months did not differ between ospemifene and placebo. In our patient, the improvements observed in total cholesterol (-11%), LDL-C (-16%), and triglycerides (-15%) during ospemifene treatment could potentially contribute to a reduction in long-term CVD risk.

Conclusion

Ospemifene is a suitable choice to treat VVA in postmenopausal women with dyslipidemia who are not candidates for local estrogen therapy. Ospemifene-associated improvements in lipid parameters, as observed in the patient featured in this case study, may contribute toward reducing long-term CVD risk.

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