ORIGINAL ARTICLE: GYNECOLOGY

The role of ethnicity in treating uterine fibroids with ulipristal acetate

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Objective: To study differences in treatment effect between black and white premenopausal women prescribed ulipristal acetate (UPA) for symptomatic uterine fibroids.
Design: Prospective observational cohort study.
Setting: Gynecology clinics.
Patient(s): Premenopausal women aged 18–55 years, at least one symptomatic uterine fibroid, UPA-naïve, and no contraindications for UPA treatment.
Intervention(s): One 3-month course of UPA at 5 mg daily.
Main Outcome Measure(s): Patients' ethnicity self-identification adapted from Statistics Canada National Household Survey. Change in fibroid symptoms according to Uterine Fibroid Symptoms Quality of Life Questionnaire symptom severity and health-related quality of life score. Bleeding symptoms and amenorrhea rates according to Aberdeen Bleeding Score.
Result(s): A total of 148 patients enrolled (45 black, 59 white, 44 other ethnicity). Black patients were younger (40.3 y vs. 44.5 y) with larger uteri (523 mL vs. 351 mL) than white counterparts. Baseline symptom severity was similar between groups. After 3 months of UPA treatment, both groups experienced similar improvements in symptom severity. White women had 52% greater improvement in bleeding score (−40.3 vs. −26.5) and were more likely to be amenorrheic at the end of treatment (66% vs. 41%). Both groups experienced adverse events at similar frequencies. Black women were more dissatisfied with UPA compared with white women (27.3% vs. 8%).
Conclusion(s): Black women had greater fibroid burden at baseline. Both ethnicities had similar improvement in fibroid symptomatology following UPA treatment, but white women experienced higher amenorrhea rates. Black women were more dissatisfied with UPA treatment, which may be related to the lower amenorrhea rates. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Uterine leiomyoma, medical therapy, ulipristal acetate, ethnicity

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Uterine leiomyomas, or fibroids, are the most common benign gynecologic tumor, affecting 20%–40% of reproductive-age women (1). Although fibroids can be asymptomatic (2, 3), many women will seek medical attention for their symptoms. The most common clinical presentation is heavy menstrual bleeding (2), although patients often report subfertility and bulk symptoms (4).

African ancestry is a well described risk factor for fibroids (5). The incidence of fibroids is two to three times greater among black women than among white women (5–7). Compared with white women, black women have an earlier age of onset (5), higher rates of fibroid-related hospitalizations (8), larger tumors, and heavier uterine weight (5, 7, 9). There are, however, few studies comparing these two racial groups regarding both imaging characteristics and fibroid symptomatology reported through validated questionnaires.

Most recently, selective progesterone receptor modulators have demonstrated efficacy for the medical management of fibroids (10–12). Pivotal randomized controlled trials have established safety of ulipristal acetate (UPA) and demonstrated reduction in fibroid size and improved menstrual bleeding (10–12). A major limitation of those trials is that participants were primarily women of white eastern European descent. Because black women made up less than 5% of the study populations, results may not be generalizable to that racial group.

Our primary objective in the present study was to determine if there

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was a difference in treatment effect between white and black premenopausal women prescribed a 3-month course of 5 mg ulipristal acetate daily for symptomatic uterine fibroids. Our secondary objectives were to evaluate differences in side effects profile and medication satisfaction between ethnicities.

MATERIALS AND METHODS

Setting

Mount Sinai Hospital is a university-affiliated tertiary care hospital in Toronto, Ontario, Canada.

Study Population

We included premenopausal women of ages 18–55 years who were prescribed a 3-month course of UPA for the treatment of symptomatic uterine fibroids. Participants were required to have at least one symptomatic fibroid of any size that was confirmed on imaging (ultrasound or magnetic resonance imaging [MRI]). The ability to complete questionnaires in English was a prerequisite.

We excluded patients with previous use of UPA (repeated courses), those who used GnRH agonist in the 3 months before enrollment, and women with an active gynecologic malignancy. Other exclusion criteria included pregnancy, breastfeeding, and sensitivity/allergy to UPA.

Methods

This was a prospective observational cohort study. We enrolled premenopausal women with symptomatic fibroids who began a 3-month course of 5 mg UPA daily from May 2014 to August 2015. The study was approved by the Mount Sinai Hospital Research Ethics Board (approval no. 14-0085-E).

After providing informed written consents, participants completed a baseline questionnaire before starting UPA therapy. Information collected included demographics, fibroid symptomatology, and uterine bleeding characteristics. Patients' self-identification of ethnicity was adapted from the Statistics Canada National Household Survey (13). Participants were asked to declare "ethnic or cultural origin" and were prompted to check all applicable categories. Only women self-identifying as "white" or "black" were included in the analysis.

A second questionnaire was administered to participants after 3 months of UPA treatment. This questionnaire asked about UPA tolerability, side effects, and patient satisfaction. It also assessed fibroid symptomatology and uterine bleeding.

Baseline imaging information (from ultrasound or MRI) was abstracted from the patient charts. Uterine size, dimensions of the largest fibroid, and presence of suspected adenomyosis were recorded.

Outcome Measures

Assessment of fibroid symptomatology. Fibroid symptomatology was assessed with the use of the Uterine Fibroid Symptoms Quality of Life Questionnaire (UFS-QoL) (14, 15). The UFS-QoL is a validated, disease-specific, 37-question tool consisting of two parts: a symptom severity score, and a health-related quality of life (HRQL) total score. The symptom severity score (range 0–100) assesses bleeding, abdominal pressure, urinary frequency, and fatigue. A high symptom severity score means more severe fibroid symptoms. The HRQL total score (range 0–100) is composed of six domains: concern, activities, energy/mood, control, self-consciousness, and sexual function. A higher HRQL score signifies better quality of life. In the development of the UFS-QoL, women without fibroids (healthy control subjects) had a mean symptom severity score of 22.5 and HRQL score of 86.4. Therefore, for our study, the "healthy state" was defined as symptom severity ≤ 23 or HRQL ≥ 86.

Assessment of uterine bleeding. Bleeding symptoms and rates of amenorrhea were measured with the use of the Aberdeen Bleeding Score, a validated method for assessing abnormal uterine bleeding (16). Scores range from 0 (amenorrhea) to 100, with higher numbers indicating more severe bleeding.

Satisfaction. The follow-up questionnaire used a 5-point Likert scale to assess satisfaction. Patients were asked about their overall satisfaction/dissatisfaction with UPA and specifically about the side effects they experienced.

Statistics. The minimal clinically important difference for the UFS-QoL has not been established. Based on validation studies, a 20-point difference in symptom severity following treatment is clinically meaningful (15). Sample-size calculations were based on the mean percentage change in UFS-QoL scores after a 3-month course of UPA reported in previous studies (12). Based on the PEARL III (PGL4001 Efficacy Assessment in Reduction of Symptoms Due to Uterine Leiomyomata) data (12), a 20-point difference would translate to a 50% difference in symptom severity score change between groups at follow-up. Therefore, we estimated that 35 subjects per group would achieve 80% power to detect $\geq 40\%$ difference in symptom severity UFS-QoL score change between black and white women, assuming a type 1 error of 5%.

The study population was summarized descriptively. Patient characteristics at baseline were compared between the two ethnic groups with the use of the chi-square test for categoric variables and Student *t* test for continuous variables. Highly skewed data were first normalized with the use of log-transformation if applicable. To examine the difference in treatment effect between the two groups, changes in continuous outcomes from baseline to follow-up were compared between groups with the use of the Student *t* test, and the change in binary outcomes were compared with the use of a linear probability model with generalized estimating equation (GEE) approach to account for repeated measures. Side effects and medication satisfaction assessed at follow-up were compared between the two groups with the use of the chi-square or Fisher exact test as appropriate. Logistic regression was used to adjust for differences in baseline characteristics. Data management and all statistical analyses were performed with the use of SAS 9.3 (SAS Institute) and R 2.15 (www.r-project.org). A two-sided significance level of