Hot Flashes in a Young Girl: A Wake-up Call Concerning Serenoa repens Use in Children

abstract

Extracts of the plant Serenoa repens are widely used in male adults for the treatment of benign prostatic hyperplasia. Recently, therapy with S repens has been proposed as a "natural" alternative to conventional treatments for male androgenetic alopecia as well as for other hair disorders. Telogen effluvium is a form of alopecia characterized by abnormality of hair cycling, resulting in excessive loss of telogen hair. We report the case of an 11-year-old girl presenting hot flashes that appeared after treatment of telogen effluvium with a food supplement containing S repens that lasted for ~2 months. When use of the product was discontinued, the hot flashes no longer occurred. Four months after the start of S repens intake and 45 days from the cessation of therapy, the girl experienced menarche at the age of 11 years. The Naranjo adverse drug reaction probability scale indicated a probable relationship (score of 6) between the appearance of hot flashes and the intake of S repens. A correlation between exposure to S repens and the onset of menarche is not certain, but it cannot be excluded. Medicinal products or food supplements containing S repens are generally well tolerated in male adults, but we believe that their use in pediatric patients should be better evaluated. Pediatrics 2012;130:e1374–e1376

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KEY WORDS

Serenoa repens, hot flashes, menarche, alopecia, adverse drug reaction

ABBREVIATIONS

BPH—benign prostatic hyperplasia
GnRH—gonadotropin-releasing hormone
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The use of herbal medicines has increased worldwide during the past decades. In most cases, products containing herbal medicines as ingredients are available as food supplements in health food stores in Europe and the United States, and only in the past years have efforts to change market rules been engaged.1 Serenoa repens L., a small palm native to the American Southeast, is popularly known as Saw palmetto, and the extract of its berries (containing fatty acids and phytosterols) is commonly used in male adults for the treatment of benign prostatic hyperplasia (BPH). Although the effect of this plant is thought to be limited, S. repens is unquestionably most widely used for the care of BPH.2 S. repens has also shown antiestrogenic action and is believed to decrease available sex hormone-binding globulin.3 Because S. repens extract has been considered suitable for the care of androgenetic alopecia, it is believed, similar to finasteride, to have inhibitory effects against 5α-reductase enzyme activity, which is responsible for the conversion of testosterone to dihydrotestosterone.3 Treatment of alopecia with S. repens has been considered a "natural" alternative to conventional treatments.4 Telogen effluvium is one of the most common causes of hair loss in children and is prevalent among women.5 It is characterized by a condition in which stress prematurely pushes hair roots into the resting state. In ∼33% of cases of acute telogen effluvium, no trigger can be identified,6 but chronic telogen effluvium can be associated with chronic medical conditions and/or medication exposure.7 Recommendations for treatment of primary chronic telogen effluvium are poor and include topical or systemic corticosteroids, topical minoxidil, and dietary supplements.8 In the present article, we highlight an adverse reaction possibly correlated with the intake of S. repens tablets in a young girl.

**CASE REPORT**

We report the case of an 11-year-old white girl, weighing 37 kg, presenting hot flashes. The hot flashes occurred after oral treatment with a food supplement containing S. repens marketed in Italy. Medical history was collected by answers provided by the girl and her mother. The girl had been given 1 tablet of the product per day for 3 months to treat “telogen effluvium,” as diagnosed and prescribed by a dermatologist. Early signs of telogen effluvium, characterized by relevant hair loss, appeared about 3 months before the diagnosis. The girl was not taking other prescription medications or over-the-counter medicines. Each tablet of the product contained 30% S. repens hydrosterolic extract, 120 mg fatty acids, 50 mg sulfonyl methane, green tea, zinc, biotin, copper, and tocochelenols. Serenoa in the product was titled in 95% of phytosterols. After a consecutive month, she quit the therapy for some days, then she restarted taking a tablet a day for another consecutive 30-day period. During the second month of treatment the girl experienced hot flashes several times during a day for many days. Because of the recurrence of hot flashes, after a total period of 60 days of therapy, the girl stopped her intake of S. repens. When use of the product was discontinued, the hot flashes no longer occurred. Four months (114 days) after starting the S. repens intake and 45 days after stopping, the girl experienced menarche at the age of 11 years. The menstruations showed abnormal features concerning duration and the volume of blood loss: the cycles were of 15 days (polymenorrhea) and the losses were abundant (hypermenorrhea). Polymenorrhea was present for ∼1 year after the menarche. Because the mother suspected a connection between the intake of S. repens, hot flashes, and the onset of menarche, she submitted her daughter to examination by both a specialist pediatrician and a gynecologist, with the aim to understand if the appearance of menarche could be considered normal or not for the age. At this time the girl was 156 cm tall. She was submitted to a pelvic echography, which reported the uterus as normal without any follicle in maturation and ovaries immaturity for the age.

**DISCUSSION**

Because early menarche is generally considered only when it appears before the age of 7, it is not possible to declare that its appearance was the result of the intake of the herbal preparation. The girl was 11 years old at the time of first menstruation, and this age is compatible with her puberty stage.2 However, it is not possible to exclude the possibility that the intake of S. repens could have anticipated the menarche in this specific case. Otherwise, it is more plausible that the hot flashes could be linked with intake of the product containing S. repens. The girl had a history of S. repens consumption but no exogenous hormone intake, and no thyroid disease or other endocrinological diseases were present. Hot flashes are generally a phenomenon appearing in women who are becoming or have become menopausal. Some premenopausal women describe having hot flashes, and these can occur in both men and women after acute gonadal steroid withdrawal, as in an ovarioctomy in young women or an orchioctomy in men, in men or women who are hypogonadal, or in those who take gonadotropin-releasing hormone (GnRH) agonists, antagonists, or other antigonadal agents that cause estrogen (in women) or testosterone (in men) levels to fall.10 The story told by the girl’s mother and an analysis of the patient’s clinical data suggested the possibility of a correlation between

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the consumption of S repens tablets and the onset of hot flashes. To investigate the relationship of causality, we used the Naranjo probability scale and obtained a score of 6, indicating that the relationship of causality as probable.11 Blood tests measuring hormonal status in the girl were not performed, even though they would have helped the causality discussion. S repens is well tolerated by most users, but mild and serious adverse effects have been reported after its intake.5 Among the serious adverse reactions linked to S repens intake, pancreatitis has been reported in 2 case reports; one of the cases was associated with acute hepatitis.12,13 A case of intraoperative hemorrhage and a coagulopathy have been associated with the use of S repens extracts14,15 (Table 1). Only 1 case report has been published about contact dermatitis (Table 1). Only 1 case report has been published about contact dermatitis produced, albeit without certainty, by a saw palmetto topical preparation used to treat androgenetic alopecia.4 This is the first report of hot flashes in a girl that can be related to S repens. A search in more widely used databases (PubMed, Medline, Embase) found no reports of similar reactions with vasomotor symptoms linked to the plant. We have taken into account the possibility that the hot flashes could be linked to incipient puberty, but menarche is not generally associated with vasomotor symptoms. Several studies have tried to explain how estrogens and GnRH (even GnRH analogs) cause vasomotor reaction among women in the pre-, post-, and perimenopausal states and even pregnant women, but hot flashes in puberal girls have not been observed.10

**CONCLUSIONS**

S repens extracts are generally well tolerated, but their safety profile generally results from the analysis of clinical data obtained by studies on the effects on male adults affected by lower urinary tract symptoms or BPH.16 Limited information exists on what occurs after the use by other subgroups such as females and, in particular, the pediatric population. It remains unclear how S repens can cause vasomotor symptoms, but we believe that the relationship between Serenoa and the onset of hot flashes is plausible and could be explained by the antiestrogenic effects and the reduction of available sex hormone-binding globulin. Moreover, the description of the case also suggests that the age of appearance of menarche could be influenced. Thus, we believe that, even though medicinal products or food supplements containing S repens are generally well tolerated in adults, their use in pediatric patients should be better evaluated. Although S repens is almost exclusively used for BPH, our concern is strengthened by the ready availability of S repens products in health food stores.

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