Vaginal Contraception With NuvaRing Decreases Symptoms and Uterine Features of Adenomyosis: A Prospective Evaluation

Anjeza Xholli, Francesca Oppedisano, Mattia Francesco Ferraro, Isabella Perugi, Ambrogio P. Londero, and Angelo Cagnacci

Academic Unit of Obstetrics and Gynecology, IRCCS–San Martino Hospital (A.X., F.O., M.F.F., I.P., A.C.); Obstetrics and Gynecology Unit, IRCCS Istituto Giannina Gaslini (A.P.L.); and Department of Neuroscience, Obstetrics and Gynecology Unit, Rehabilitation, Ophthalmology, Genetics and Maternal and Pediatric Sciences, University of Genoa (F.O., M.F.F., I.P., A.P.L., A.C.), Genoa, Italy

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ABSTRACT

Adenomyosis occurs when ectopic endometrial glands invade the myometrium and can cause symptoms such as an enlarged uterus, heavy menstrual bleeding, pelvic pain, infertility, and pregnancy complications. It occurs in an estimated 20% of asymptomatic and 45% of symptomatic women, and risk factors for its development include age, endometriosis, multiple births, uterine surgery, spontaneous miscarriage, and cervical conditions. There is no specific guideline for the management of adenomyosis, but treatment options can include hormone withdrawal through GnRH analogs, either alone or combined with aromatase inhibitors, or progestins released through intrauterine devices. Previous studies have shown that dienogest-based hormonal contraceptives can decrease the duration of menstrual bleeding, reduce pain, and change the overall characteristics of adenomyosis on ultrasound examination. There is, however, a lack of research on the connection between adenomyosis and other contraceptives or routes of administration. This study was designed to assess the effect of a vaginal ring contraceptive on the ultrasound features and symptoms of adenomyosis.

This was a prospective, self-controlled observational study of patients diagnosed with adenomyosis who used vaginal ring contraception. Inclusion criteria were premenopausal women between the ages of 21 and 45 years requiring a vaginal ring for contraception and were diagnosed with adenomyosis. Exclusion criteria were contraindications to hormonal contraceptives, desire for contraceptive other than the vaginal ring, absence of adenomyosis, and use of hormonal contraceptives. Follow-up was conducted at or after 6 months of use.

Final analysis included 42 patients with a mean age of 30.0 ± 4.5 years and a mean body mass index of 22.8 ± 1.8 kg/m^2. Of these 42 patients, 29 had concomitant endometriosis. Most of those in this sample had adenomyosis affecting their entire uterus or localized at the anterior or posterior wall. Most experienced moderate to severe menstrual pain, intermenstrual pain, or pain during intercourse, and all experienced heavy menstrual bleeding, except the 6 who were already being treated with dienogest.

Reduced uterine volume was observed in 39 patients, with an average decrease of 7.2 ± 7.7 cm^3 ($P = 0.0001$). The mean number of direct signs of adenomyosis also declined significantly ($P = 0.003$), as well as indirect signs including wall asymmetry ($P = 0.002$), fan-shaped shadowing ($P = 0.004$), and heterogeneous myometrial echogenicity ($P = 0.002$). The mean number of indirect signs per individual patient also decreased significantly ($P = 0.001$). Significant decreases were observed in pain scores for menstrual pain, intermenstrual pain, and pain during intercourse ($P = 0.001$ for all). Decreases in uterine volume were directly associated with decreased pain ($R^2 = 0.299$, $P = 0.003$).

These results indicate that vaginal ring contraception is effective at reducing uterine volume in adenomyosis, thus resulting in a reduction of adenomyosis-associated pain. This shows potential superiority to treatment with dienogest, which does not decrease uterine volume. Future research should focus on samples of women with confirmed histological diagnosis of adenomyosis, as well as implementing longer follow-up periods to assess long-term effects of vaginal ring contraception. In addition, future studies should compare the effectiveness of treatment across a spectrum of severity of adenomyosis to determine benefits and efficacy for different adenomyosis subpopulations.

EDITORIAL COMMENT

(The contraceptive vaginal ring is a very effective form of contraception that is the least commonly used hormonal method. There are 2 types of contraceptive vaginal ring approved by the Food and Drug Administration in the United States. The NuvaRing contains etonogestrel and ethinyl estradiol. Annovera

contains segesterone acetate and ethinyl estradiol. In typical use, the ring is placed in the vagina for 3 weeks and then removed for one after which a new contraceptive ring is placed. This study looked specifically at the NuvaRing brand used continuously (a new ring was placed after every 3 weeks, without a hormone-free period of time). The hormones in the NuvaRing are highly absorbed through the mucosa of the vagina with a bioavailability of 100% for etonogestrel and 56% for ethinyl estradiol, comparable to combined oral contraceptives. NuvaRing is approved for a reduction in menorrhagia and dysmenorrhea in addition to contraception. It is considered to be less effective than other long-acting reversible hormonal methods because it is dependent on the user to remember to replace the ring monthly, rather than being user-independent as with the contraceptive implant or intrauterine device.

This study showed that the NuvaRing, when used continuously over 6 months, was effective in reducing uterine volume. It most likely has a direct effect on reducing the amount and/or activity of adenomyotic tissue. Dysmenorrhea and dyspareunia were significantly decreased along with alleviation of heavy menstrual bleeding. It is not known whether this effect would abate or continue with longer use or whether using the ring cyclically (3 weeks in place, with 1 week off between cycles) would work as well. It is also not known if the other brand of vaginal contraceptive ring, Annovera, would work just as well or how long the improvement of symptoms lasts after discontinuation of the method. Would the effect be maintained after switching to another contraceptive method?

Despite all the unknowns, the high levels of significance are impressive. Larger studies that address the longer-term impact would be helpful, but in the meantime, the data are strong enough that the NuvaRing should be considered as a potential first-line therapy for the symptoms associated with adenomyosis. It certainly should be offered to every patient with adenomyosis as an excellent option.—HZS)

Thin Endometrium Restricts Peri-ovulatory Physiological Transition Between Anti-adhesive and Adhesive Receptivity Modulators

Onder Celik, Aynur Ersahin, Nur D. Gungor, Ulun Ulug, Nilufer Celik, Meltem Yardim, Ahmet Tektemur, Semih Dalkilic, Tuncay Kuloglu, Suphan Ersahin, Sudenaz Celik, and Ramazan F. Akkoc

Department of Obstetrics and Gynecology, Private Clinic, Usak (O.C.); Department of Obstetrics and Gynecology, Bahcesehir University Goztepe Medicalpark Hospital (A.E., N.D.G.); and Department of Obstetrics and Gynecology, School of Medicine, Halic University (U.U.), Istanbul; Department of Biochemistry, Behcet Uz Children's Hospital, Izmir (N.C.); Department of Medical Biochemistry, Yerkoy State Hospital, Yozgat (M.Y.); Department of Medical Biology, Faculty of Medicine, Firat University (A.T.); Firat University, Faculty of Science, Department of Biology, Molecular Biology and Genetics Program (S.D.); and Department of Histology and Embryology, Faculty of Medicine, Firat University (T.K.), Elazig; Department of Obstetrics and Gynecology, Altinbas University Medical Faculty, Istanbul (S.E.), Turkey; Medical Faculty, University of Sofia 'St. Kliment Ohridski', Sofia, Bulgaria (S.C.); and Department of Anatomy, School of Medicine, Firat University, Elazig, Turkey (R.F.A.)

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ABSTRACT

Receptivity modulators control and facilitate cell differentiation and embryo development as well as inflammatory pathways and suppression of paternal alloantigens. Molecular changes driven by the microenvironment of the endometrium drive endometrial thickening that prepares the uterus for implantation. It is unknown, however, if endometrial thickness alone can