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Review Article

Vaginal contraception: a roadmap to women's reproductive autonomy-a narrative review

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ABSTRACT

The right to contraception information and services is one of the essential rights of every woman that guarantees access to safe, acceptable, available, and good-quality contraceptives. Contraceptive vaginal rings are a form of modern contraceptive that is user-friendly, effective, and safe to use. The present review briefs about the contraceptive vaginal ring, its composition, mechanism of action, advantages, disadvantages, and newer development of rings with added benefits. Methodology: The recent literature till December 2021 was searched from the various governmental, and non-governmental agencies including WHO, UNFPA, UNDP, UNDESA, Committee on the Rights of the Child, FDA, and many English peer-reviewed journals, including PubMed database, the regional portal of virtual health library, and scientific electronic library online using following search terms “modern contraception”, “contraceptive vaginal ring”, and “newer vaginal rings”. The contraceptive vaginal ring has emerged as an effective, safe, self-administered form of modern contraceptive, with better cycle control, compliance, and continuation rates.

Keywords: Contraception, Estrogen, Progestogen, Sexually transmitted infections, Vaginal ring

INTRODUCTION

One of the key components of the reproductive health rights of women is the right to contraception information and services. These rights guarantee access to acceptable, available, and good-quality contraceptive information and services to all women and adolescent girls free from any coercion, discrimination, and violence against them.[1] Contraceptives protect women and adolescent girls from unwanted pregnancies, their associated dangers, HIV/AIDS, and other sexually transmitted diseases.[2] The demand for modern contraceptives is increasing due to the rise in the number of reproductive-age women desiring a smaller family.[3] Furthermore, with the onset of the COVID-19 pandemic and its associated nationwide lockdowns, increased demand and a rise in the unmet need for modern contraceptives are being observed all across the globe.[4] In 2019, only 842 million out of 1.11 billion women of reproductive age requiring family planning services, used a modern contraceptive method, while 270 million still had an unmet need for contraceptives.[5,6] The unmet need for family planning services is far worse in developing countries where more than 232 million women have no access to modern contraceptives.[7] This gap in achieving the unmet need for contraceptives has been further aggravated by the COVID-19 pandemic.[8] Furthermore, in 2019 the family planning needs of only 76% of women were satisfied by modern contraceptives globally.[9] Recent global data reveals a significant rise in the modern contraceptive use rate from 2001 (22.8%) to 2016 (39.0%), leading to a rise in total demand from 54% in 2001 to 67% in 2019.[10]

The various modern contraceptive methods commonly used are hormonal pills, injectables, emergency contraception, male and female condoms, hormonal and non-hormonal intrauterine contraceptive devices, implants, vaginal rings, contraceptive patches, lactational

amenorrhea method (LAM), standard day method, and permanent sterilization procedures.[11] The present narrative review aims to brief about the contraceptive vaginal rings, their composition, mechanism of action, advantages, disadvantages, and newer development of rings with added benefits.

CONTRACEPTIVE VAGINAL RING

Contraceptive vaginal rings are effective, and safe hormonal options of modern contraception that can be easily used by women with better compliance. They are available in different shapes and sizes and based on their hormonal type can be progestin-only, or combined progestin-estrogen with varying combinations of progestins and estrogens.[12] The development of contraceptive vaginal rings started more than 40 years ago, based on the idea that steroid hormones can be easily absorbed through the vaginal epithelium and the elastomers release these hormones at a constant rate, thereby preventing excess exposure.[13,14]

TYPES, MECHANISM OF ACTION AND SIDE EFFECTS

The commonly available contraceptive vaginal rings, their mechanism of action, and side effects are as under:

Combined hormonal contraceptive rings: There are two most commonly used combined hormonal contraceptive rings:

Etonogestrel and ethinyl estradiol ring (NuvaRing®)

It is the once-a-month method of hormonal contraception, approved by the FDA in 2001 and consists of a small (54 mm×4 mm), flexible, transparent, soft ring made up of ethylene-vinyl acetate copolymers and magnesium stearate.[15] It contains hormones ethinyl estradiol (EE) 2.7 mg and etonogestrel (ENG) 11.7 mg, which is an active metabolite of the progestin desogestrel. The ring releases a steady amount of 15 µg EE and 120 µg ENG daily which is then absorbed through the vaginal epithelium. The women have to wear the ring for three weeks followed by one week of ring-free intervals during which withdrawal bleeding occurs.[16] The mechanism of action includes suppression of gonadotrophins leading to inhibition of ovulation, changes in the cervical mucus consistency, and endometrium histology.[17] Common side effects include headache, vaginitis, leukorrhea, breast tenderness, nausea, vaginal discomfort, vaginitis, ring-related adverse effects, and irregular bleeding.[16]

Segesterone acetate (previously called Nestorone) and ethinyl estradiol ring (Annovera™)

It is the most recently approved contraceptive-vaginal ring.[18-20] It was approved by the United States FDA on 10th August 2018.[21] It is a one-year contraceptive vaginal system consisting of a silicone-based ring containing a total of 103 mg segesterone acetate and 17·4 mg ethinylestradiol that releases around 0·15 mg segesterone acetate and 0·013 mg ethinylestradiol daily.[22] Segesterone acetate is a new potent nonandrogenic progestin and a derivative of 19-norprogesterone.[23] It is not absorbed orally but is effective when administered vaginally.[24] Segesterone acetate binds specifically to the progesterone receptors and not to androgen or estrogen receptors, thus reducing unwanted androgen, antiandrogen, or estrogenic side effects.[23] This new progestin has the highest anti-ovulatory action amongst all the available progestins and hence acts by inhibiting ovulation.[25] The contraceptive vaginal system has to be inserted for 21 consecutive days followed by 7 days of removal during which bleeding occurs in a 28-day cycle. The same system can be used for up to 13 cycles (1 year).[26] Side effects are usually mild and include nausea, vomiting, headache, vaginal discharge, breast tenderness, uterine spasm, urinary tract infections, genital pruritis, mood swings, decreased libido, acne, vaginal candidiasis, irregular bleeding, dyspareunia, the expulsion of the ring and rarely venous thromboembolism.[22,26]

Combined hormonal contraceptive vaginal rings have the same contraindications as combined oral contraceptives including age ≥35 years, postpartum for <21 days with risk factors for venous thromboembolism, breastfeeding, smoking ≥15 cigarettes/day, hypertensive with systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥100 mmHg, vascular disease, history or acute deep vein thrombosis/pulmonary embolism, migraine, cirrhosis, hepatocellular adenoma, malignant liver tumors, breast cancer, current and history of ischemic heart disease, stroke, complicated valvular heart disease, systemic lupus erythematosus.[27,28]

Progesterone-only ring for lactating women

The most commonly used progesterone-only ring is Progering®. It is made up of a silicone-elastomer ring having an overall diameter of 58 mm and contains micronized progesterone. It releases progesterone at an average rate of 10 mg/day over three months period.[29,30] It can be continuously used for 3-4 months in lactating women and it prolongs lactational amenorrhea to 10 to 12 months.[31] With proper use, an average plasma concentration of 20 nmol/l progesterone is achieved, which is well above the critical progesterone threshold (10 nmol/l) required to inhibit ovulation during breastfeeding.[29] It also causes the thickening of cervical mucus, thereby preventing sperm penetration into the uterus.[30] Furthermore, the risk of exposure to progesterone in the infant is insignificant (<4.2 mcg), quite below the recommended maximum intake of 150 mcg/day as per the European Medicines Agency.[12,32] Hence, it is safe for both mother and infant and does not interfere with lactation. Other newer progesterone-only vaginal rings are under trial including levonorgestrel containing intravaginal rings, and nestorone vaginal ring, delivering 50 micrograms of nestorone per day.[31,33]

The common reasons for discontinuation of the progesterone-only ring include decreased efficacy in weaning mothers, less effectiveness in comparison to rings containing both progestin and estrogen, bleeding disturbances, and it does not provide protection against HIV and sexually transmitted infections.[34] To make these rings effective in protecting against HIV and to provide contraception also, newer rings combining antiretroviral and contraceptive drugs are being developed. These include a vaginal ring releasing both dapivirine and levonorgestrel, and another ring releasing a combination of tenofovir (at ~10 mg/day) and levonorgestrel (~20 µg/day) for 90 days that provides protection against HIV and pregnancy both.[35,36]

NON-CONTRACEPTIVE VAGINAL RINGS

Dapivirine vaginal ring

On 26th January 2021, WHO recommended dapivirine vaginal ring as an additional prevention choice for women at substantial risk of HIV infection. This silicone-based ring containing 25 mg of dapivirine has to be worn for a period of 28 days. It releases the antiretroviral drug dapivirine into the vagina slowly over 28 days and protects high-risk women from acquiring HIV infection during vaginal sex.[37] Dapivirine, is a diarylpyrimidine derivative that binds irreversibly to and inhibits HIV reverse transcriptase enzyme, thereby stopping the conversion of viral RNA to proviral DNA.[38,39] Trials are underway to develop vaginal rings where dapivirine can be combined with other hormones to be used as contraceptive rings in addition to preventing HIV infection, without affecting the efficacy of antiretroviral drugs.[40]

Rings for menopausal symptoms

The vagina can be used as an alternative site for the delivery of hormone replacement therapy in menopausal women. These rings have the added advantage of producing consistent serum levels that can be maintained for up to 3 months and produce fewer adverse effects as compared to systemic therapy.[41] Some of the commonly available vaginal rings for hormone therapy are Femring® available in doses of 50 µg/day or 100 µg/day estradiol acetate, Estring® containing 2 mg estradiol and releases 7.5 µg/day, and a combined estradiol/progesterone ring.[42]

ADVANTAGES OF CONTRACEPTIVE VAGINAL RINGS

The major advantages of using a contraceptive vaginal ring are that it provides effective contraception, can be self-administered and easy to use, requires less frequent dosing as compared to other forms of contraception, and provides low doses of hormones with a nearly constant release rate, serum levels of steroids are steadier and estrogenic exposure is lower leading to decreased estrogen-related side-effects, greater bioavailability, efficacy almost comparable to combined hormonal pills, good cycle control, independent of sexual act, and newer ones can be designed to provide protection from HIV and sexually transmitted infections.[14,20,37,43,44]

CONCLUSION

Hence, the contraceptive vaginal ring is an effective, safe, self-administered form of modern contraceptive, with better cycle control, compliance, and continuation rates. Because of its easy use, control of initiation and discontinuation by the user, steady release rate of hormones, lesser side effects, and better bioavailability, it is now emerging as a promising contraceptive for women. Many more rings with added benefits and different hormonal compositions are under trial which can be of great benefit for women in the future.

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REFERENCES

1. UNFPA. Briefing paper. The right to contraceptive information and services for women and adolescents. 2010 Center for Reproductive Rights. Available at: https://www.unfpa.org/sites/default/files/resource-pdf/Contraception.pdf. Accessed on 2 September 2023.
2. Committee on the Rights of the Child, General Comment 4: Adolescent health and development in the context of the Convention on the Rights of the Child, para. 28, U.N. Doc. CRC/GC/2003/41 July 2003. Available at: http://docstore.ohchr.org/SelfServices/FilesHandler.ashx. Accessed on 2 September 2023.
3. Kebede A, Abaya SG, Merdassa E, Bekuma TT. Factors affecting demand for modern contraceptives among currently married reproductive age women in rural Kebeles of Nunu Kumba district, Oromia, Ethiopia. Contracept Reprod Med. 2019;4:21.
4. Riley T, Sully E, Ahmed Z, Biddlecom A. Estimates of the potential impact of the COVID-19 pandemic on sexual and reproductive health in low- and middle-income countries. Int Perspect Sex Reprod Health. 2020;46:73-6.
5. Kantorová V, Wheldon MC, Ueffing P, Dasgupta ANZ. Estimating progress towards meeting women's contraceptive needs in 185 countries: A Bayesian hierarchical modelling study. PLoS Med. 2020;17(2):1003026.
6. United Nations. Department of Economic and Social Affairs, Population Division. Family Planning and the 2030 Agenda for Sustainable Development. New

York: United Nations. https://www.un.org/en/development/desa/population/publications/pdf/family/familyPlanning_DataBooklet_2019.pdf. Accessed on 2 September 2023.
7. UNDP. Costing the Three Transformative Results. 2019. Available at: https://www.unfpa.org/sites/default/files/pub-pdf/Transformative_results_journal_23-online.pdf. Accessed on 2 September 2023.
8. Kumar N. COVID 19 era: a beginning of upsurge in unwanted pregnancies, unmet need for contraception and other women related issues. Eur J Contracept Reprod Health Care. 2020;25(4):323-5.
9. United Nations, Department of Economic and Social Affairs, Population Division (2019). Contraceptive Use by Method 2019: Data Booklet (ST/ESA/SER.A/435). Available at: https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2020/Jan/un_2019_contraceptiveusebymethod_databooklet.pdf. Accessed on 2 September 2023.
10. Tetui M, Baroudi M, Ssekamatte T, Birabwa C, Kibira SP, Atuyambe L, et al. Total demand, use and unmet need for modern contraceptives among women living in informal settlements in Kira Municipality, Wakiso District, Uganda. Implications for Urban Health. Front Glob Womens Health. 2021;2:655413.
11. Ethiopian Public Health Institute (EPHI) [Ethiopia] and ICF. 2021. Ethiopia mini demographic and health survey 2019: Final report. Rockville, Maryland, USA: EPHI and ICF.
12. Brache V, Payán LJ, Faundes A. Current status of contraceptive vaginal rings. Contraception. 2013;87(3):264-72.
13. Mishell DR, Lumkin ME. Contraceptive effect of varying dosages of progestogen in silastic vaginal rings. Fertil Steril. 1970;21(2):99-103.
14. Temmerman M. A new woman-controlled contraceptive vaginal ring: a global step forward. Lancet Glob Health. 2019;7(8):986-7.
15. FDA approves NuvaRing contraceptive implant. J Gend Specif Med. 2002;5(2):6.
16. Roumen FJ. Review of the combined contraceptive vaginal ring, NuvaRing. Ther Clin Risk Manag. 2008;4(2):441-51.
17. Wieder DR, Pattimakiel L. Examining the efficacy, safety, and patient acceptability of the combined contraceptive vaginal ring (NuvaRing). Int J Womens Health. 2010;2:401-9.
18. Brache V, Faundes A. Contraceptive vaginal rings: a review. Contraception. 2010;82(5):418-27.
19. Monteiro I, Guazzelli CF, Bahamondes L. Advances in contraceptive vaginal rings: what does the future hold? Expert Opin Pharmacother. 2018;19(15):1685-91.
20. Delvaux T, Jespers V, Benova L, van de Wijgert J. Acceptability and satisfaction of contraceptive vaginal rings in clinical studies: a systematic review and narrative synthesis. Front Glob Womens Health. 2021;2:799963.
21. U.S. Food and Drug Administration. FDA News Release. FDA approves new vaginal ring for one year of birth control, 10th August 2018. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-vaginal-ring-one-year-birth-control. Accessed on 2 September 2023.
22. Archer DF, Merkatz RB, Bahamondes L, Westhoff CL, Darney P, Apter D, et al. Efficacy of the 1-year (13-cycle) segesterone acetate and ethinylestradiol contraceptive vaginal system: results of two multicentre, open-label, single-arm, phase 3 trials. Lancet Glob Health. 2019;7(8):1054-64.
23. Kumar N, Koide SS, Tsong Y, Sundaram K. Nestorone: a progestin with a unique pharmacological profile. Steroids. 2000;65(10-11):629-36.
24. Kumar N, Fagart J, Liere P, Mitchell SJ, Knibb AR, Petit-Topin I, et al. Nestorone® as a novel progestin for nonoral contraception: structure-activity relationships and brain metabolism studies. Endocrinology. 2017;158(1):170-82.
25. Nelson AL. Comprehensive overview of the recently FDA-approved contraceptive vaginal ring releasing segesterone acetate and ethinylestradiol: A new year-long, patient controlled, reversible birth control method. Expert Rev Clin Pharmacol. 2019;12(10):953-63.
26. Gemzell-Danielsson K, Sitruk-Ware R, Creinin MD, Thomas M, Barnhart KT, Creasy G, et al. Segesterone acetate/ethinyl estradiol 12-month contraceptive vaginal system safety evaluation. Contraception. 2019;99(6):323-8.
27. Gruber CJ. The combined contraceptive vaginal ring (NuvaRing): evaluation of the clinical and pharmacological evidence. Womens Health (Lond). 2006;2(3):351-6.
28. Medical Eligibility Criteria for Contraceptive Use. 5th ed. Geneva: World Health Organization; 2015.
29. Carr SL, Gaffield ME, Dragoman MV, Phillips S. Safety of the progesterone-releasing vaginal ring (PVR) among lactating women: A systematic review. Contraception. 2016;94(3):253-61.
30. Nath A, Sitruk-Ware R. Progesterone vaginal ring for contraceptive use during lactation. Contraception. 2010;82(5):428-34.
31. Massai R, Díaz S, Jackanicz T, Croxatto HB. Vaginal rings for contraception in lactating women. Steroids. 2000;65(10-11):703-7.
32. EMEA Committee for Veterinary Medicinal Products Progesterone: Summary Report. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Maximum_Residue_Limits_-_Report/2011/07/WC500108427.pdf (1999). Accessed on 2 September 2023.
33. Nave R, Höchel J, Mellinger U, Kohnke A, Elliesen J, Schmitz H. Pearl Index study with levonorgestrel-releasing intravaginal rings: using pharmacokinetic results to investigate treatment compliance as a potential contributor for contraceptive failure. Hum Reprod. 2020;35(11):2515-23.

34. Massai R, Miranda P, Valdés P, Lavín P, Zepeda A, Casado ME, et al. Preregistration study on the safety and contraceptive efficacy of a progesterone-releasing vaginal ring in Chilean nursing women. Contraception. 1999;60(1):9-14.
35. Bashi YH, McCoy CF, Murphy DJ, Boyd P, Spence P, Kleinbeck K, et al. Towards a dapivirine and levonorgestrel multipurpose vaginal ring: Investigations into the reaction between levonorgestrel and addition-cure silicone elastomers. Int J Pharm. 2019;569:118574.
36. Thurman AR, Schwartz JL, Brache V, Clark MR, McCormick T, Chandra N, et al. Randomized, placebo-controlled phase I trial of safety, pharmacokinetics, pharmacodynamics and acceptability of tenofovir and tenofovir plus levonorgestrel vaginal rings in women. PLoS One. 2018;13(6):0199778.
37. World Health Organization. WHO recommends the dapivirine vaginal ring as a new choice for HIV prevention for women at substantial risk of HIV infection. 26 January, 2021. Available at: https://www.who.int/news/item/26-01-2021-who-recommends-the-dapivirine-vaginal-ring-as-a-new-choice-for-hiv-prevention-for-women-at-substantial-risk-of-hiv-infection. Accessed on 2 September 2023.
38. Garg AB, Nuttall J, Romano J. The future of HIV microbicides: challenges and opportunities. Antivir Chem Chemother. 2009;19(4):143-50.
39. Nuttall JP, Thake DC, Lewis MG, Ferkany JW, Romano JW, Mitchnick MA. Concentrations of dapivirine in the rhesus macaque and rabbit following once daily intravaginal administration of a gel formulation of [14C] dapivirine for 7 days. Antimicrob Agents Chemother. 2008;52(3):909-14.
40. Balkus JE, Palanee-Phillips T, Reddy K, Siva S, Harkoo I, Nakabiito C, et al. Brief report: dapivirine vaginal ring use does not diminish the effectiveness of hormonal contraception. J Acquir Immune Defic Syndr. 2017;76(2):47-51.
41. Ballagh SA. Vaginal rings for menopausal symptom relief. Drugs Aging. 2004;21(12):757-66.
42. Krause M, Wheeler TL, Snyder TE, Richter HE. Local effects of vaginally administered estrogen therapy: a review. J Pelvic Med Surg. 2009;15(3):105-14.
43. Edwardson J, Jamshidi R. The contraceptive vaginal ring. Semin Reprod Med. 2010;28(2):133-9.
44. Roumen FJ, Mishell DR. The contraceptive vaginal ring, NuvaRing(®), a decade after its introduction. Eur J Contracept Reprod Health Care. 2012;17(6):415-27.

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