



**COMPARISON OF EFFICACY, COMPLIANCE, ACCEPTABILITY AND TOLERABILITY OF HORMONAL CONTRACEPTIVE VAGINAL RING (NUVARING) VERSUS COMBINED ORAL CONTRACEPTIVES (COCS) - A PROSPECTIVE RANDOMIZED CONTROLLED STUDY IN A DISTRICT LEVEL HOSPITAL IN EAST DELHI**

**Gynaecology**

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**ABSTRACT**

**Background and objectives:** NuvaRing is a novel nonoral combined hormonal contraceptive. Present study aims to compare the efficacy, compliance, acceptability and tolerability of NuvaRing with COCs.

**Method:** Prospective randomized, controlled study. Total 430 women fulfilling inclusion and exclusion criteria enrolled for study, randomly divided in two groups of 215 each. Women in NuvaRing group were given NuvaRing for 12 cycles and women in COC group were given Mala N tablets for 12 cycles. Two groups were compared for efficacy, acceptability, compliance and tolerability by filling questionnaires.

**Results:** There was no significant difference in efficacy, compliance and acceptability. NuvaRing group had more complaints of vaginal discharge and incidence of nausea was significantly higher in COC group. None of the women discontinued use due to side effects.

**Conclusion:** NuvaRing has comparable efficacy, compliance, acceptability and tolerability as compared to COCs with the advantage to once a month dosing.

**KEYWORDS**

NuvaRing; RCT; Contraceptive; Compliance; Efficacy; Tolerability

**INTRODUCTION**

The prevalence of modern contraceptive methods in India is reported to be 48.5 %; out of which, majority is constituted by permanent irreversible methods i.e. sterilization (male and female) 38.3 % (1), condoms 5.2 %, combined oral contraceptives (COCs) 3.1 %, intra-uterine devices (IUD) 1.7%, injectable 0.1 %.

Among the reversible methods, COCs are highly effective for contraception (failure rate 0.1% with correct and consistent use). There are various advantages of COCs use including cycle stabilization, cure of menstrual disorders like dysmenorrhea and menorrhagia, protection against malignancies specially ovarian and endometrial cancers, amongst others. Additionally, there is no effect on future fertility.

However, the usage of COCs is low due to various shortcomings, the most important being an obligation for daily dosing, which may lead to missed pills, resultant failure and noncompliance. The other major disadvantage is the hepatic first-pass metabolism, and any interference with gastrointestinal absorption (others drugs, malabsorption, etc) leading to fluctuations in the hormone levels and resultant decrease in efficacy.

To overcome these limitations, various non oral hormonal contraceptive methods were investigated. Majority of non oral hormonal methods are progestogen-only methods which also require a trained personnel's assistance and some kind of procedure (injectables, implants). NuvaRing is a once a month combined hormonal contraceptive vaginal ring. It was approved by FDA in 2001 and marketed in 2002. Used by over 1.5 million women worldwide, it is a soft, flexible clear plastic ring of 54mm diameter and 4mm thick, comes in a reclosable aluminum foil sachet and is stored at 2-8 °C. It contains ethinyl estradiol (EE) 2.7mg and etonorgestrel (ENG) 11.7 mg. It is inserted between day 1 and day 5 of the menstrual cycle in the vagina, after insertion, it releases 15 µg of EE and 120 µg of ENG daily. Each ring is used for three weeks and then removed for one week for withdrawal bleeding. The mechanism of contraception, like COCs, is inhibition of ovulation (2).

In the last decade, various studies conducted in Europe and North America have demonstrated excellent contraceptive efficacy, tolerability, and acceptability of NuvaRing (3-5). NuvaRing has various advantages including use of lower doses of hormones in a controlled drug delivery system, avoidance of hepatic first-pass metabolism and gastrointestinal interferences, and most importantly, once-a month use. Since NuvaRing was introduced in India in 2009, there was little information available for use of NuvaRing in Indian clinical practice. A multicenter study performed in India

(published in 2014) to understand the real-life usage of the ring in daily clinical practice (6).

Although large randomized studies done abroad had shown very good patient compliance with the monthly vaginal ring as compared to COCs (7), an Indian study in the population which attends our hospital was not available, hence it was intended to do this study in our institution.

**Materials and Methods**

It was a Prospective Randomized Controlled Questionnaire based Analytical study to assess the efficacy, tolerability, compliance, and user acceptability of combined hormonal vaginal ring (NuvaRing) with combined oral contraceptives (COCs).

Ethical clearance was obtained from Institutional Ethics Committee prior to starting the study. A complete written and informed consent was taken from all patients included in the study.

The inclusion criteria were women attending gynecology out patient department, aged 18-40 years, at risk of pregnancy, seeking contraception and are willing to participate in study.

The exclusion criteria were women with contraindications for contraceptive steroids i.e. current or past history of ischemic heart disease, stroke, valvular heart disease, migraine, known or suspected breast carcinoma, diabetes with vascular disease, thrombophlebitis or thromboembolic disorder, history of deep vein thrombosis, hypertension, symptomatic gall bladder disease, past history of COC related cholestasis, acute viral hepatitis, cirrhosis, liver tumors- hepatocellular adenoma, malignant hepatoma, recent major surgery with prolonged immobilization. Also, breastfeeding women less than six months postpartum, women who used injectable hormonal contraceptive use within last six months, abnormal cervical smear diagnosed during screening, women currently using or used within last two months of drugs that interfere with the metabolism of contraceptive hormones were excluded from the study.

A total of 450 women fulfilling inclusion and exclusion criteria were enrolled for the study. A complete history was taken and routine physical and gynaecological examination was performed in all women at time of enrolment in the study. In addition, complete blood count, random blood sugar, lipid profile, liver function test, kidney function test, ultrasonography of lower abdomen and pelvis and pap smear was done in all women. Women were randomly divided into two groups (n=225 each) using a random number table chart.

Group 1 (NuvaRing group) was offered NuvaRing

Group 2 (COC group) was offered Mala D tablets containing 30 µg of EE and 150 µg of Levonorgestrel per tablet.

Both groups received NuvaRing /COC for twelve consecutive cycles. The duration of each cycle was 28 days, with 21-day ring/pill treatment period followed by 7-day ring or pill-free period.

Women in Nuva Ring group were instructed about ring use at the beginning of first cycle, including how and when to insert and remove NuvaRing. All women in the group were advised to insert the ring between day 1-5 of menstrual cycle.

Women in COC group were advised to start taking pill on first day of menstrual cycle.

Assessment was done for following parameters at the start of study and after cycle 1, 3, 6, 9 and 12.

**Contraceptive efficacy:** It was determined by the occurrence of pregnancy during the study.

**Compliance:** Women were instructed to use a diary to record ring/pill use, and this data was used to determine compliance. In the COC group, compliance was defined as a cycle in which all scheduled pills were taken. For NuvaRing group, a cycle was considered compliant if the period of ring use did not deviate by 48 hours from the scheduled 3 weeks and the ring-free period did not deviate by 24 hours from the scheduled 1 week.

**Acceptability:** User acceptability was assessed using a questionnaire.

**Tolerability:** Any adverse effect in both groups was recorded at each assessment.

At the end of twelve cycles, all the data was compiled and statistical analysis was using SPSS. P value less than 0.05 was considered significant.

## Results

A total of 447 women were recruited and randomly divided in two groups. In the NuvaRing group, six women discontinued the use during the study period due to no further need of contraception, and four women were lost to follow up. In the COC group, four women stopped pill use due to no further need of contraception and three were lost to follow up. Hence a total of 430 women (NuvaRing=215, COC=215) were randomized and treated.

The two study groups were similar with respect to age, BMI, parity, duration of menstrual flow.

**Table 1: Baseline characteristics of two study groups.**

	NuvaRing (n= 215)	OCP (n= 215)	P value
Age (mean ±S.D.) (years)	27±3.36	26.7±3.39	0.345
Weight (mean± S.D.) (kg)	62±7.25	65±5.46	0.463
BMI (mean±S.D.) (kg/m <sup>2</sup> )	22±3	23.3±4.5	0.484
Parity	2.32	2.37	0.747
Usual duration of menstrual flow( mean ±S.D.)(days)	5±3	5.6±2	0.496

**Efficacy:** No pregnancy occurred in any of the two groups. Hence efficacy was 100% in both the groups.

**Compliance-** Compliance was high in both groups (more than 90%).  
**Acceptability-** Satisfaction with the method during use was high in both groups (more than 90%). Questions regarding ease of use showed that majority of women never had a problem with insertion or removal of NuvaRing during the trial. None of the women felt NuvaRing during the use. One of the partners felt NuvaRing during intercourse but did not object for the use of the ring. Ring use was not bothersome to any of the users or their partners.

**Tolerability-** In general both NuvaRing and OCPs were well tolerated. None of the subject discontinued treatment due to adverse event. No serious adverse event was reported in any group.

**Table2. Comparison of compliance, acceptability and tolerability of two study groups**

	NuvaRing (n=213)	COC (n=213)	P value
Compliance	200(93.02%)	197(91.62%)	0.587
Acceptability	205(95.34%)	200(93.02%)	0.303
Tolerability			
1. Headache	8(8.37%)	12(5.58%)	0.256
2. Mastalgia	2(0.9%)	4(1.8%)	0.410
3. Nausea	5 (2.33%)	24 (11.16%)	<b>0.0002</b>
4. Vaginal discharge	22(10.23%)	3(1.4%)	<b>0.0009</b>

## Discussion

The present RCT was conducted to evaluate the efficacy, acceptability, compliance and tolerability of a novel contraceptive NuvaRing and to compare it with the existing contraceptive pills. Acceptability is a very significant aspect in the success of a contraceptive method. Women found the ring use quite convenient which is consistent with the results of various international studies (4,5,8,9). The high efficacy and tolerability further makes NuvaRing close to ideal contraceptive. The advantage of once a month use is the most beneficial aspect leading to high compliance. Since the side effects were not bothersome to the users, none of the users discontinued use due to adverse effects.

## Conclusion

Based on the findings of this study, we conclude that NuvaRing is an efficacious, safe and acceptable combined hormonal contraceptive which has the advantage of once a month use and avoidance of hepatic first pass metabolism. The contraceptive pills have been in use for multiple decades and this study shows that user acceptability, compliance, efficacy and tolerability of NuvaRing is comparable with COCs.

## REFERENCES

- United Nations, Department of Economic and Social Affairs, Population Division (2011). World Contraceptive Use 2010 (POP/DB/CP/Rev2010). [http:// www.un.org/esa/population/publications/wcu2010/Main.html](http://www.un.org/esa/population/publications/wcu2010/Main.html)
- Williams obstetrics. McGraw Hill. Contraception. 23rd edition. 681-82
- Roumen FMJE, Apter D, Mulders TMT, et al. Efficacy, tolerability, and acceptability of a novel contraceptive vaginal ring releasing etonogestrel and ethinylloestradiol. Hum Reprod. 2001;16: 469-75
- Dieben TOM, Roumen FMJE, Apter D. Efficacy, cycle control, and user acceptability of a novel contraceptive vaginal ring. Obstet Gynecol. 2002;100:585-92
- Novak A, De la Loge C, Abetz L, et al. The combined contraceptive vaginal ring, NuvaRing: an international study for user acceptability. Contraception. 2003;67:187-94
- Pandit SN, Chauhan AR, Anagani M, Reddy S, Birla A, Ray SK. Multicenter Study of Contraceptive Vaginal Ring (NuvaRing®) in Normal Daily Practice in Indian Women. J Obstet Gynaecol India. 2014 Dec;64(6):409-16
- Ahrendt HJ, Nisand I, Bastianelli C, Gómez MA, Gemzell-Danielsson K, Urdl W et al. Efficacy, acceptability and tolerability of the combined contraceptive ring, NuvaRing, compared with an oral contraceptive containing 30 microg of ethinyl estradiol and 3 mg of drospirenone. Contraception. 2006 Dec;74(6):451-7
- Roumen FMJE, op ten Berg MMT, Hoomans EHM. The combined contraceptive vaginal ring NuvaRing: first experience in daily clinical practice in the Netherlands. Eur J Contracept Reprod Health Care. 2006; 11:14-22.
- Merki-Feld GS, Hund M. Clinical experience with NuvaRing in daily practice in Switzerland: cycle control and acceptability among women of all reproductive ages. Eur J Contracept Reprod Health Care. 2007;12:240-7.