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Experience of more than 3000 cycles of Brazilian women using the contraceptive vaginal ring (nuvaring®)

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ABSTRACT

Objective: To evaluate the profile of the Brazilianvaginal ring user, reasons for choosing it, satisfaction, menstrual pattern, tolerability, efficacy, side effects and reasons for discontinuation. Methods: We reviewed the files of 148 users who attended the Hospital de Jacarepaguáand private clinics, between 2005 and 2011, in a total of 3107 cycles. Kaplan-Meier survival curves and regression models were used in statistical analysis. Results: The profile was: single, nulligravida, 30 years (mean) and with university education. The previous contraception used was mostly the oral hormonal contraception (75.7%). Women chose the ring for: practicality (32.4%), forgetting the pill (32.4%) and irregular vaginal bleeding (13.5%). The satisfaction degree was 80.5% (119). There were good cycle control and no pregnancies. Thirty-eight patients discontinued the use (25.7%). The main reasons were wish for pregnancy (6%), spotting (3.4%) and increased vaginal discharge (2.7%). At the end of the first year, use of the greatest reduction of continuity probability was observed (19.3%). Women with side effects were 68% less likely to be satisfied with the method than those without (p-value <0.0001). Conclusion: Nuvaring® is an excellent contraceptiveoption due to its sefficacy, cycle control, tolerability, practicality and safety.

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KEYWORDS

Vaginal Ring; Hormonal Contraception; Efficacy; Tolerability

1. INTRODUCTION

The combined oral contraceptive pill (COC) is the mostly used method of contraception, especially by younger women with good level of education and no children [1]. However, the literature shows a high prevalence of women making irregular use of the pill, which interferes with its efficacy [2]. Some articles report failure to take 3 to 5 pills per cycle in 30% to 50% of the women [3].

The possibility of other routes of administration can benefit women who want safe contraception adapted to their profile and needs. There are few works evaluating the criteria of choice and the satisfaction degree with the contraceptive method [4,5]. However there is already evidence of higher satisfaction amongst women who switched from the COC to a non-oral route [6]. Furthermore, there are less side effects and problems related to the use of the vaginal ring than that with the transdermic hormonal contraceptive (patch) [6].

The advantages of the non-oral route are that the products have a longer lasting action (no need for daily dosing) and therefore they eliminate the forgetfulness issue; and that they avoid the hepatic first-pass effect, gastric intolerance and the serum hormonal fluctuations, providing a better control of the bleeding pattern [7].

The vaginal ring is made of a transparent evatane core and sheath, with an external diameter of 54 mm and thickness of 4 mm. It contains 11.7 mg of etonogestrel and 2.7 mg of ethinylestradiol, with the average daily release of 120 mcg and 15 mcg, respectively, for a period of three weeks. It was first approved for market release in the Netherlands (2001), followed by the EU and USA (2002) [8].

The aim of this study is to establish the profile of the Brazilian women who chose the vaginal contraception and to evaluate their satisfaction degree, menstrual bleeding pattern, tolerability, efficacy, side effects and the reasons for discontinuing the method. This information should help the health professionals counsel patients who seek a birth control method which is safe, efficient and does not require daily dosing.

2. METHODS

This was a retrospective study, based on the analysis of the files of 148 women who attended either the Ministry of Health's Hospital de Jacarepaguá (Rio de Janeiro, Brazil) or private clinics, between 2005 and 2011, reaching 3107 cycles of use of the product. The inclusion criteria were: to use the vaginal ring for at least one cycle, to have no known contraindication to the use of estrogen, no use of drugs that interfere with the metabolism of contraceptive hormones, not to be breast feeding, not to be in the postpartum or post abortion period (2 months) andto have a normal smear test on the recruitment visit.

At the first appointment, all the subjects underwent clinical and gynecological examinations, including a cervical smear test. They also answered a questionnaire about their general medical and gynecological history, including any previously used contraceptives and the reason why they had chosen the vaginal ring. The anamneses and exams were thoroughly registered on the medical files. All the patients started the use of the vaginal ring with the sole objective of contraception. Before starting the use all the women were taught how and when to insert and remove the ring. For women on each kind of contraceptive, the manufacturer's prescribing information leaflet was observed. The vaginal ring was self-inserted into the vagina and was left in place for 21 days per cycle followed by a 7 day ring-free interval. In all the follow up appointments the weight and blood pressure (BP) measurements were added to their files, as well as all the information about the periods, the use of the method (satisfaction or interruption), the side effects and the use of other medications. The efficacy of the vaginal ring was determined by the incidence of pregnancy while using the method. The level of satisfaction was evaluated by a simple scoring system ranging from 1 to 4, in which (1) meant the patient was dissatisfied, (2) not very satisfied, (3) satisfied and (4) very satisfied. "Satisfaction" was also analyzed as a binary variable in the survival analyses and the categories were regrouped in: dissatisfied (scores 1 and 2); and satisfied (scores 3 and 4).

For the statistic analysis the categorical predictors were: age (<30; ≥30 years), level of schooling (secondary; higher), marital status (single; married), previous contraceptive method (COC; condom; patch; implant; injection; IUD and diaphragm), length of use (less than 2 years; from 2 to 3 years; more than 3 years), side effects, reasons why the vaginal ring was chosen and reasons for quitting.

The categorical variables were described as proportions with a confidence interval of 95% (CI95%). Means and standard deviations were used to describe the numeric variables. Kaplan-Meier survival curve was plotted to describe discontinuity probability of method along the time. Bivariate log-binomial regression models were used to assess the association between the characteristics of the patients (age, schooling, marital status, previous contraceptive method and side effects) and the satisfaction with the vaginal ring. Age adjusted models were applied to assess user satisfaction with the vaginal ring in relation to side effects and previous contraceptive method. The softwares Epi Info/version 3.5.3, R-Project 2.15.2 and Stata/SE 8.0 for Windows were used for the statistical analyses. The research was approved by the Ethics Committee of the Hospital de Jacarepaguá.

3. RESULTS

The mean age of the users was 29.5 years (16 to 42 years). The method was chosen by adolescents in 8.1% (12; CI95% 4.3 - 13.7) of cases; patients were between 20 and 29 years in 44% (65; CI95% 35.8 - 52.3); from 30 to 39 in 41.2% (61; CI95% 33.2 - 49.6) and from 40 to 42 in 6.7% (10; CI95% 3.3 - 12.1).

Regarding marital status, 52.7% (78) were single, 41.2% (61) married and 6.1% (9) divorced. Patients had either university 79% (117) or high school level of education 21% (31). Menarche had occurred from 8 to 16 years (mean = 12.4) and the first intercourse from 12 to 25 (mean = 17.1). Roughly half of the patients (50.7%, 75) were null igravidae, 29.7% (44) had one previous pregnancy and 19.6% (29) had two to four previous pregnancies. Prior miscarriages were reported by 11% (16).

Most women had used COC before (75.7%). The other previously used methods were condom (10.8%), patch (3.4%), implant (4.1%), injection (2.7%), IUD (1.4%), diaphragm (0.7%) and none (1.4%). The main reasons for choosing the vaginal ring were: practicality for 32.4% (48) of the women, forgetfulness to take the oral contraceptive for 32.4% (48) and irregularvaginal bleeding for 13.5% (20) (**Table 1**).

Table 1. Distribution of the reasons for switching to the contraceptive vaginal ring.

Reasons	N	%	CI 95%
Forgetting the oral contraceptive	48	32.4	25 - 40.6
Practicality	48	32.4	25 - 40.6
Irregular bleeding/Metrorrhagia	20	13.5	6.8 - 22.5
Nausea/heartburn	6	4.0	1.5 - 8.6
Breast tenderness	6	4.0	1.5 - 8.6
Safety	5	3.4	1.1 - 7.7
Migraine/headache	4	2.8	0.4 - 5.8
Weight gain	4	2.8	0.4 - 5.8
Decreased libido/PMS/Acne	3	2.0	0.4 - 5.8
Hepatitis/hepnodular hyperplasia/↑AST	3	2.0	0.4 - 5.8
Patch fell off	1	0.7	0 - 3.7
Total	148	100	

A total of 3107 cycles of use were achieved and during this period there were no pregnancies. The patients reported well controlled menstrual cycles, with a mean of 3.4 days of bleeding. Periods lasted one day in 0.7% (1) of the women, three days in 60.8% (90), four days in 27.7% (41) and five days in 9.5% (14). Two patients had amenorrhea (1.4%) but in one of them it was induced by the continuous use of the method. The satisfaction degree was 80.5% (n = 119). The specific results were: very satisfied (71%, n = 105), satisfied (9.5%, n = 14), not very satisfied (9.5%, n = 14) and dissatisfied (10%, n = 15).

Side effects were reported by 21% (31) of the users, the most frequent were spotting (8%, 12), increased vaginal discharge (4%, 6) and breast tenderness (3.4%, 5). One patient had a deep vein thrombosis (DVT) and on the subsequent diagnostic investigation it was found that she was homozygous for the C677T mutation of the MTHFR gene (**Table 2**).

The method was interrupted by 25.7% (38) of the users. The main reasons were: wish to get pregnant in 6% (9), spotting in 3.4% (5) and increased vaginal discharge in 2.7% (4). The discontinuation of the method due to side effects happened in 8.8% (13) of cases (**Table 3**).

Figure 1 shows the continuity probability of the use of the vaginal ring over time. There is a significant decrease (19.3%) at the end of the first year of treatment. From this point on it becomes less pronounced 7.3% from the first to second year, 3.9% from the second to third year and 6.1% from the third to fourth year. The probabilities of continuity after the first, second, third and fourth years of use of the ring correspond to 0.81 (95% CI 0.74 - 0.88), 0.73 (95% CI 0.66 - 0.82) 0.70 (95% CI 0.61 - 0.80) and 0.63 (95% CI 0.53 - 0.76), respectively.

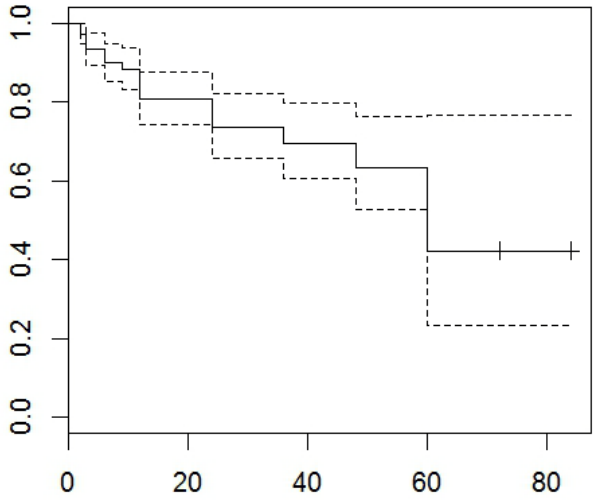

Figure 1. Continuity probability of use of the vaginal ring over time (months).

Table 2. Side effects of the contraceptive vaginal ring.

Effects	Freq.	%	CI 95%
None	117	79	71.6 - 85.3
Spotting	12	8.1	4.3 - 13.7
Increased vaginal discharge	6	4.0	1.5 - 8.6
Breast tenderness	5	3.4	1.1 - 7.7
Discomfort	2	1.3	0.2 - 4.8
Partner felt the ring	2	1.3	0.2 - 4.8
Patient felt the ring	1	0.7	0 - 3.7
Migraine	1	0.7	0 - 3.7
Amenorrhea	1	0.7	0 - 3.7
DVT (trombophilia)	1	0.7	0 - 3.7
Total	148	100	

Table 4 shows the relationship between the main characteristics of the patients and the satisfaction with the vaginal ring. Bivariate analysis (left side of the table) showed that patients with previous use of condom had a greater probability of satisfaction with the vaginal ring than those using COC or other contraceptive method. It also found an inverse association between the incidence of side effects and the user satisfaction. After adjusting the models by age group (right side of the table), this findings remained statistically significant, indicating that both "previous method of contraception" and "side effects" play an important role in determining user's satisfaction with the vaginal ring. Women who had previously used COC or other contraceptive methods were less

Table 3. Distribution of the reasons for discontinuing the method.

Reasons	Freq.	%	CI 95%
Still using the ring	110	74.3	66.5 - 81.1
Discontinued due to side effects:			
Spotting	5	3.4	1.1 - 7.7
Increased vaginal discharge	4	2.7	0.7 - 6.8
Amenorrhea	1	0.7	0 - 3.7
Migraine	1	0.7	0 - 3.7
Breast tenderness	1	0.7	0 - 3.7
DVT (trombophilia)	1	0.7	0 - 3.7
Discontinued due to other reasons:			
Wish to get pregnant	9	6.0	2.8 - 11.2
Discomfort	2	1.4	0.2 - 4.8
Insecurity	2	1.4	0.2 - 4.8
No sexual activity	3	2.0	0.4 - 5.8
Wish for amenorrhea	3	2.0	0.4 - 5.8
Partner felt the ring	2	1.4	0.2 - 4.8
Ring came out spontaneously	2	1.4	0.2 - 4.8
Difficult to remove	1	0.7	0 - 3.7
Price	1	0.7	0 - 3.7
Total	38	25.7	

likely to be satisfied with the ring than the ones who had used condoms 15% (p-value < 0.001) and 32% (p-value < 0.02), respectively. The incidence of side effects also reduced the probability of satisfaction (68%, p-value < 0.0001).

4. DISCUSSION

After evaluating more than 3000 cycles of Nuvaring®, the profile of the Brazilian woman who opted for the method was established. Most of the patients (85.2%) were between 20 and 39 years old, showing good acceptance throughout the reproductive age. The adolescents were the only population with a lower proportion of users (8.1%), although there is evidence of the product's safety [9]. The teenager's lack of knowledge about the ring could be due to the shortage of information, as reported by an American study, which found that even if the girls had heard about it, only 51% had been informed by a health professional [10].

There was a predominance of single and nulligravidae users, which is likely to be a consequence of the mean age and the schooling level. There is a high percentage of university students and these women are delaying wedding and pregnancy in order to pursue their higher education and career goals. The higher education prevalence probably represents a selection bias since three of the recruiting centers were private clinics.

The COC was the main method used previously to the vaginal ring (more than 75%) and the main reasons for the switch were practicality and the fear of forgetting the daily dosing of the pill, as it was also observed by Let *et al*. (2007) [11].

Our Pearl index was 0.0. In the manufacturer's prescribing information the CI ranges from 0.01 to 1.36. Ahrend *et al*. (2006) disagree as they found 0.25 in the comparison between the Nuvaring® and the oral contraceptives, for which they found 0.99 [12].

The satisfaction degree with the ring was similar to ours in several studies, with an approval rate of more than 80% [3,4,9,12,13] and a low rate of discontinuation of the method. Furthermore, the main reason for stopping the use was the wish to get pregnant (6%) rather than the incidence of side effects.

The good control of the cycle, with a low frequency of spotting (8%) and cycles of 3 - 4 days of bleeding in more than 88%, were contributing factors to the compliance. This is in agreement with the literature, in which cycle control was found to be excellent, with irregular bleeding in only 2.6% - 6.4% of cycles [14-16]. In a trial comparing the vaginal ring and a COC containing 150 µg LNG and 30 µg EE, irregular bleeding and spotting during cycles 2 to 13 was less frequent with the ring than with the COC (2% - 6% vs. 4% - 13%) [17]. The hypothesis is that the steady low-dose release of ethynilestradiol of the vaginal ring favourably affects cycle control compared with the fluctuating steroid levels between the peaks caused by the once-a-day pill intake [18]. However not only the cycle control was important, but the practicality of the method also played a crucial role, especially the monthly dosing and the easy insertion and removal of the ring reported by the patients, in opposition to their considerations regarding the oral contraceptives [14,15]. Counseling and information sharing can help to improve contraceptive compliance, continuation and user satisfaction.

5. CONCLUSION

The limitations of the study lie in its retrospective design, which could prompt an information bias due to incomplete or inaccurate clinical files. The schooling level and marital status might represent a bias because patients were recruited from both private clinics and the public hospital. But, even if not representative of the whole population, our study represents the acceptance of a new contraceptive option by different groups of women.

Table 4. Relationship between the main characteristics of the patients and the satisfaction with the vaginal ring.

Characteristics assessed	Categories	Bivariate analysis RR (CI 95%)	P-value	Multivariate[1] analysis RR (CI 95%)	P-value
Age (years)	≥30/<30	0.93 (0.79 - 1.9)	0.39		
Duration of treatment (years)	2 - 3/≤2	1.21 (1.01 - 1.45)	0.06	1.27 (0.99 - 1.62)	0.06
	>3/≤2	1.19 (1.01 - 1.40)	0.10	1.17 (0.97 - 1.40)	0.10
Marital status	Single/married	0.94 (0.79 - 1.12)	0.47		
Previous contraceptive method	COC[2]/condom	0.81 (0.74 - 0.88)	0.001*	0.85 (0.77 - 0.93)	0.001*
	Others[3]/condom	0.66 (0.48 - 0.92)	0.01*	0.68 (0.49 - 0.94)	0.02*
Side effects	Yes/no	0.29 (0.17 - 0.50)	0.0001*	0.32 (0.18 - 0.56)	0.0001*

[1]Log-binomial multivariate model (characteristics vs. satisfaction) adjusted by age; [2]COC: combined oral contraception; [3]others: patch; implant; injection; IUD and diaphragm.

The average Brazilian choosing Nuvaring® was single, nulligravida, 30 years old (mean) and with university education. It proved to be an excellent contraceptive option for them for its efficacy, good cycle control and tolerability, in addition to being a practical and safe choice.

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