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Effects of hormonal contraception on vaginal flora☆,☆☆

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Abstract

Background: The sector of the market that deals with contraception offers a long list of different contraceptive methods. Within the estroprogestinic choice, the routes of administration are oral, transdermic and vaginal one. Even though efficacy is comparable with these methods, secondary and adverse effects are directly involved in the acceptability of the method.
Study Design: This was a prospective comparative study. During 1 year, we enrolled 60 asymptomatic women who voluntarily requested combined oral contraception (COC) or combined contraceptive vaginal ring (CCVR group). After a baseline study of vaginal milieu prior to starting hormonal contraception, we performed a follow-up. For each woman, we examined vaginal pH; quantification of leukocytes, lactobacilli, *Candida* and cocci on saline microscopy fluid; Gram stain with Nugent score and the presence of vaginal infection [culture for *Trichomonas vaginalis*, albicans and nonalbicans *Candida*, Group B *Streptococcus* (GBS)].
Results: At the end of follow-up, there was a little change of vaginal milieu in both groups. We noted an increase of lactobacilli in the CCVR users and an increase of GBS in COC users.
Conclusion: CCVR compared to COC users showed an increase of the number of lactobacilli in vaginal flora. It means that an increase of leukorrhea in that group could be protective in terms of prevention of vaginal imbalance/infection.

Keywords: Vaginal ring; Lactobacilli; Oral contraceptive; Vaginal flora; Leukocytes

1. Introduction

In 2001, the American Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products approved the use in the United States and in Europe of a vaginal contraceptive ring that releases 120 mcg of etonogestrel and 15 mcg/day of ethinylestradiol (EE). This combined contraceptive vaginal ring (CCVR, NuvaRing®, Organon Int., Oss, the Netherlands) is well tolerated, but there are few randomized trials that evaluate long-term adverse events [1–3]. A recent Cochrane study [4] comparing different formulations of hormonal contraception shows that women using the patch have more discontinuation rate and fewer adverse events and that the CCVR users have less adverse effects than the COC users, but more vaginal irritation and discharge. This finding is in agreement with other studies in the literature [5–7]. In particular, Oddson et al. [8] report that, in women using vaginal ring, there is an increase of local symptoms such as vaginitis, leukorrhea, vaginal discomfort and ring-related events (expulsion, feeling a foreign body sensation and coital problems). The only study showing that there could be a protective effect on vaginal flora in CCVR users is published by Veres et al. [9]. This study showed an increase of H_20_2 producing lactobacilli in women with CCVR than in COC users [9]. This is an important consideration because we know from the literature how crucial the role of H_20_2 is for producing lactobacilli to maintain a physiologic vaginal milieu and to prevent the bacterial vaginosis (BV) [10,11].

The aim of the present study is to evaluate the effects of CCVR versus COC on vaginal flora.

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2. Materials and methods

This prospective comparative study of vaginal flora in CCVR users versus COC users has been conducted in the Department of Obstetrics and Gynaecology of IRCCS Burlo Garofolo University of Trieste, Italy, from January to December 2010. After institutional review board approval, written informed consent and collection of medical and gynecological data, we enrolled 60 consecutive asymptomatic women between 18 and 45 years old who voluntarily requested oral or vaginal contraception and did not plan to use condoms, with sexual activity and with a negative Pap test in the last 12 months.

Exclusion criteria were abnormal or unknown Pap test in the last 12 months, any contraindications for contraceptive steroids, pregnancy, chronic illness such as hypertension or diabetes, current use of a contraceptive implant or intrauterine device, use of an injectable hormonal method of contraception within a period of 6 months before the recruitment, presence of microscopic or cultural diagnosis of *Trichomonas vaginalis*, current symptomatic candidiasis, previous history of recurrent vulvovaginal candidiasis or cervical dysplasia, any subjective report of symptomatic leukorrhea. According to the choice of contraception, we differentiated two groups: CCVR users (N=30) and COC users with the same steroids (desogestrel 150 mcg+EE 20 mcg) (N=30). At the time of enrolment and during a follow-up at 3 and 6 months of treatment, a gynecologic evaluation was performed concerning the vaginal objective environment (value of pH, presence of vulvovaginal infection, quantification of leukocytes and lactobacilli) and considering subjective symptoms from the patients like leukorrhea as vaginal subjective discharge (spontaneously reported from the women as an increased amount of cervicovaginal mucous).

In fact, applying directly a pH indicator paper into the vaginal sidewall, a color change was recorded as a numeric pH result. Then, a sample of vaginal discharge from the posterior vaginal fornix was collected using a sterile and single use swab for Gram stain. All slides were evaluated for lactobacillary presence by one trained technician at 1000× magnification; Gram-stained slides were classified according to the Nugent criteria, being scored as negative (score 0–3), intermediate (score 4–6) or consistent with BV (score 7–10). Lactobacilli were identified by the characteristic morphology on Gram stain and quantified as "+" (presence of <1 *Lactobacillus* cell per field), "++" (1–4 cells per field) and "+++" (5–30 cells per field) [12]. A second swab was performed for saline wet mount preparation to perform a microscopy observation for the detection of *T. vaginalis*, *Candida albicans* and/or aerobic vaginitis. Two other swabs were used to carry out Group B *Streptococcus* (GBS) on the first and yeast, *Trichomonas* or bacteria on the second. The presence of leukocytes was determined and recorded as the main number of leukocytes counted per 400 fields. Data were tabulated into a database (Microsoft Access), and descriptive statistics were performed. We calculated contingency tables in order to evaluate the collected data. χ^2 test was used to compare from a cross-sectional point of view, i.e., separately at baseline and after 3 and 6 months, the modification in the vaginal flora between the two groups. Generalized estimating equations (GEEs) were applied to evaluate the treatment effect longitudinally, i.e., on the relative change in the vaginal flora from baseline to 3 and 6 months taking into account the correlated nature of the data. In the GEE estimation, lactobacilli were treated as a unique ordinal variable, as well as the Gram stain slide for Nugent score. The analysis was performed using the SPSS package, version 13.0 (SPSS Inc., Chicago, IL, USA) and the R statistical software version 2.12.2, library "geepack."

Table 1
CCVR vs. COC: comparison of vaginal milieu at baseline and at 3 and 6 months

		Baseline				3 months				6 months			
		CCVR N=30/60		COC N=30/60		CCVR N=30/60		COC N=30/60		CCVR N=30/60		COC N=30/60	
		N	%	N	%	N	%	N	%	N		%	
Leukorrhea		8	27	8	27	10	33	5	17	10	33	5	17
pH≤4		24	80	24	80	29	97	25	83	29	97	25	83
Gram-stained slide for	Negative	21	70	22	74	26	87	24	80	26	87	24	80
Nugent score	Intermediate	3	10	3	10	1	3	2	7	1	3	2	7
	BV	3	10	3	10	0	0	0	0	0	0	0	0
Aerobic vaginitis		1	3	1	3	0	0	3	10	0	0	3	10
Candida		2	7	1	3	3	10	1	3	3	10	1	3
Trichomonas		0	0	0	0	0	0	0	0	0	0	0	0
GBS		0	0	0	0	0	0	3	10	0	0	3	10
Leukocytes		2	7	1	3	3	10	1	3	3	10	1	3
Lactobacilli +		17	57	22	73	3	10	24	80	3	10	24	80
Lactobacilli ++		5	17	3	10	11	37	4	13	11	37	4	13
Lactobacilli +++		0	0	0	0	16	53	1	3	16	53	1	3