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**A COMPARATIVE STUDY OF THE SAFETY, EFFECTIVENESS AND
ACCEPTABILITY OF TWO FOAMING VAGINAL TABLETS
(nonoxynol-9 versus menfegol) IN THAI WOMEN**

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Abstract

Two foaming vaginal tablets containing nonoxynol-9 (OVT-n) or menfegol (OVT-m) were studied to evaluate safety, effectiveness and acceptability. The study was conducted at the Chulalongkorn University, Institute of Health Research, Bangkok, Thailand. One-hundred-two women randomly assigned to one of the two types of tablets were scheduled for follow-up visits at 1, 3, 6 and 12 months. Although there were differences between the two groups in the gross cumulative 12-month life table rates and 12-month continuation rates, these differences were not statistically significant. Twelve-month discontinuation rates for accidental pregnancy were 31.7 per 100 women for OVT-n group and 25.3 per 100 women for the OVT-m group. Seventeen of the total 22 pregnancies occurred due to use failure. This study indicates that the regular and proper use of OVT-n or OVT-m tablets are comparable and are a safe means of birth control. Although a few product-related (burning) or medical complaints were reported by both groups of tablet users, it seems that the vaginal contraceptive is an acceptable method for fertility control in a suitable population who will use it regularly and properly.

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Introduction

Vaginal contraceptives are the oldest and simplest forms of contraception, and they are now receiving a greater amount of attention because of increasing dissatisfaction with IUDs, oral contraceptives and depo-Provera (DMPA) injections. This dissatisfaction may be due to the side effects and some contraindications; therefore, vaginal contraceptives are a useful option. Furthermore, one study (1) reports that vaginal methods provide protection against sexually transmitted disease. However, many studies on these vaginal contraceptives are characterized by widely divergent reports of their effectiveness (2-5). This may only be due to differences in study populations and the time period of the study, for the actual factors affecting compliance and successful use of vaginal contraceptives remain a matter of speculation. An international multi-center study was designed by Family Health International (FHI). The Institute of Health Research, Chulalongkorn University, Bangkok, Thailand, was one of the centers which was part of this study. The clinical trial utilized a randomized, double-blind, parallel design. This paper reports only the data for Thai women.

The objective of the study was to evaluate the safety, efficacy and acceptability of two types of contraceptive foaming vaginal tablets. Both tablets were obtained from Ortho Pharmaceutical Corporation, Raritan, New Jersey. One contained 100 mg nonoxynol-9 (OVT-n) and the other 60 mg menfegol (OVT-m).

Materials and Methods

Admissions began in July 1986 and were completed in November 1986. Follow-up visits were completed in May 1987. A total of 102 volunteers was recruited and followed at three different sites in Bangkok; a factory clinic (14 women), a university clinic (27 women), and a health center (61 women). The same physician and clinic staff were at all three sites and provided the same information on the proper use of the tablets to all users.

Volunteers had to be healthy women, 18-40 years of age, who were sexually active. They could not be pregnant, known to be sterile or infertile, nor could they have any anatomic abnormalities or allergies that might prevent successful use of the tablets. Volunteers must have had one menstrual period since termination of her last pregnancy. All women provided an informed consent. Each woman was instructed to insert the OVT-n or OVT-m into her vagina and to wait at least 10 minutes before intercourse. If intercourse did not take place within an hour after the insertion of the tablet, another tablet was to be inserted.

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Fifty-one women were randomly allocated to the OVT-n group and 51 women were randomly allocated to the OVT-m group. Four of the 102 women participating in the study were excluded from the analysis, three OVT-n users because of non-use and one renfegol user because she did not have a menses during the course of the study. Pelvic examination, Papanicolaou smears, and gonorrhea cultures were performed at the admission visit and at the 6- and 12-month visits. The women were requested to return to the clinic at 1, 3, 6 and 12 months after admission for a follow-up examination. Sufficient supplies of the assigned study product were provided to each volunteer to last until the next scheduled visit.

All data were analyzed by Chi-square, and equally unknown variance t-tests were run on all data where it was appropriate. Product safety and effectiveness was determined by gross cumulative life table rates.

Results

Table I shows the selected socioeconographic characteristics of OVT-n and OVT-m users. The mean age was 26.8 for the OVT-n users and 28.7 for the OVT-m users ($t = 1.9183$, $p < 0.05$); the mean parity for OVT-n and OVT-m users was 1.2 and 1.4, respectively. The average level of formal education, however, was similar in both groups and averaged approximately 8 years.

Nearly half of all volunteer women had used oral contraceptives (Table II). Nine women (1 OVT-n user and 8 OVT-m users) had used depo-Provera. 16.7% of OVT-n users and 12.0% of OVT-m users were using no contraceptive. Only 1 OVT-m user had experience with a vaginal contraceptive method. The primary reason for participating in this study was because vaginal tablets were recommended by family, friends or the health staff, and other methods were contraindicated.

A pelvic examination was performed for each woman at her admission visit. All were generally in good health with only a few abnormal conditions reported; none was serious enough to prevent study participation. One OVT-m user with a positive gonorrhea culture at admission was successfully treated.

Acceptability is shown in Table III. Concerning the regularity of use and the reasons for irregular use of both tablets, it was found that nearly all of the women reported using their tablet at every intercourse. The most common reasons given throughout the study for irregular use were patient neglect and male discomfort. A higher percentage of women reported neglect in the last 6 months of the study,

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Table I. Selected socioeconographic characteristics of OVT-n and OVT-m users

Characteristic	OVT-n No.	OVT-m No.
Number of users:	48	50
Age (years)		
: Range	18 - 36	19-39
: Mean \pm SD	26.8 \pm 4.9	28.7 \pm 4.8
Parity		
: Range	0 - 3	0 - 3
: Mean \pm SD	1.2 \pm 0.8	1.4 \pm 0.8
Education (years):		
Range	3 - 17	0 - 19
Mean \pm SD	7.6 \pm 4.4	8.4 \pm 4.9

Table II. Prior contraceptive used among OVT-n and OVT-m users

Characteristic	OVT-n (N = 48)		OVT-m (N = 50)	
	No.	%	No.	%
None	8	16.7	6	12.0
Foam/jelly suppository tablet	0	-	1	2.0
Oral pills	23	47.9	23	46.0
IUD	1	2.1	2	4.0
Condom	12	25.0	6	12.0
Rhythm/withdrawal	3	6.3	4	8.0
Depo-Provera (DMPA)	1	2.1	8	16.0

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Table III. Regularity of use and reasons for irregular use, product-related problems at follow-up visit

	1-month		Follow-up visit 6-month		12-month	
	OVT-n (N=45)	OVT-m (N=47)	OVT-n (N=31)	OVT-m (N=35)	OVT-n (N=22)	OVT-m (N=26)
	No. %	No. %	No. %	No. %	No. %	No. %
Regularity of use						
Every intercourse	35(77.8)	35(74.5)	23(74.2)	29(82.8)	20(90.9)	25(96.2)
Occasional non-use	8(17.8)	6(12.8)	5(16.1)	5(14.3)	2(9.1)	1(3.8)
Frequent non-use	2(4.4)	5(10.6)	2(6.5)	1(2.9)	0(0)	0(0)
Not used	0(0)	1(2.1)	0(0)	0(0)	0(0)	0(0)
Unspecified	0(0)	0(0)	1(3.2)	0(0)	0(0)	0(0)
Total	45 100.0	47 100.0	31 100.0	35 100.0	22 100.0	26 100.0
Reason for irregular use**						
Female discomfort	1	4	2	1	0	1
Male discomfort	2	1	0	2	1	0
Male & female discomfort	3	1	1	0	0	0
Too troublesome	1	2	1	0	0	0
Patient neglect	3	1	2	2	1	0
Out of supplies	0	1	1	0	0	0
Thought she was safe	0	0	0	1	1	0
Unspecified	0	1	1	0	0	0
Product-related problems						
None	27(60.1)	24(51.2)	21(67.8)	26(74.2)	17(77.4)	25(96.2)
Burning, stinging, itching	10(22.2)	15(31.9)	5(16.1)	7(20.0)	3(13.6)	1(3.8)
Inconvenient/messy	5(11.1)	1(2.1)	2(6.5)	1(2.9)	0(0)	0(0)
Male discomfort/irritation	0(0)	2(4.3)	1(3.2)	1(2.9)	1(4.5)	0(0)
Tablet did not dissolve	2(4.4)	1(2.1)	0(0)	0(0)	0(0)	0(0)
Abdominal or pelvic pain	0(0)	1(2.1)	1(3.2)	0(0)	0(0)	0(0)
Prefers to douche after intercourse	1(2.2)	0(0)	0(0)	0(0)	0(0)	0(0)
Dislikes taste	0(0)	1(2.1)	0(0)	0(0)	0(0)	0(0)
Vulvar rash	0(0)	0(0)	0(0)	0(0)	1(4.5)	0(0)
Unspecified difficulty with insertion	0(0)	1(2.1)	0(0)	0(0)	0(0)	0(0)
Unspecified	0(0)	1(2.1)	1(3.2)	0(0)	0(0)	0(0)

*N is number of women with follow-up data.

**Irregular use includes occasional non-use and frequent non-use.

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while male discomfort was primarily reported in the first 6 months.

Twenty-four women, 12 OVT-n and 12 OVT-m users, indicated use of other contraceptive methods at one or more follow-up visits. Seven of these women began using depo-Provera or oral contraceptives and were discontinued from the study. The remaining 17 women used withdrawal, rhythm or condoms as alternative or additional methods of contraception at isolated instances during the course of the study.

Product-related problems are defined as those problems associated with use of the product, e.g., insertion difficulties, or those which result from product use, e.g., complaints of discomfort or messiness. Occurrence of such problems adversely affects the product's acceptability. Such problems reported at the follow-up visits (Table III) show that burning, stinging and itching were reported most often by both groups of tablet users. Although infrequent, other reported problems with the product included inconvenience/messiness and male discomfort or irritation. At 12 months, more OVT-n users reported method-related complaints than OVT-m users ($X^2 = 3.88$, $p < 0.05$); it was a statistically significant difference.

Medical complications are defined as clinically significant conditions that develop during use of the assigned method. In both groups, very a few medical complications were reported at follow-up visits. The most common was cellular atypia on Papanicolaou (Pap) smear. There were few reports of monilia or amenorrhea. One exception was an OVT-n user who presented at admission with a dysplastic Pap smear, and after cervical biopsy and conization of the cervix, there was indication of mild cervical dysplasia; this woman discontinued the study 2 months later due to dysplasia.

Discontinuation during the study was analyzed by reasons for discontinuation and gross cumulative life table rates per 100 women at 6 and 12 months (Tables V and VI). Twelve-month continuation rates were 45.4 per 100 women in the OVT-n and 55.3 per 100 women in the OVT-m group. Women discontinued for various reasons including pregnancy, vaginal/penile discomfort, medical, product-related, and other personal reasons. The most common reason for discontinuation was accidental pregnancy due to use failure.

At 12 months, discontinuation rates due to accidental pregnancy were 31.7 per 100 women for the OVT-n group and 25.3 per 100 women for the OVT-m group. A total of 22 accidental pregnancies, 12 among the OVT-n group and 10 among the OVT-m group, was reported. Seventeen of the 22 total pregnancies were attributed by the physician to be

Table IV. Distribution and rates of pregnancies

Event	OVT-n (N = 48) No.	OVT-m (N = 50) No.
Pregnancy		
Method failure	3	1
Use failure	8	9
Planned pregnancy	1	0
Pearl pregnancy rates*	37.7	30.0

*Pearl pregnancy rates are calculated on 12-month data and include all pregnancies and total woman-months of use.

Table V. Reasons for discontinuation

Discontinuation reasons	OVT-n (N = 48) No.	OVT-m (N = 50) No.
Pregnancy	12	10
Vaginal/penile discomfort reasons		
Burning, stinging, heat	5	6
Penile irritation	0	1
Medical reasons		
Moniliasis	0	1
Vulvovaginitis	1	0
Cervical dysplasia	1	0
Dysuria	0	1
Product-related reasons		
Messy, inconvenient	1	1
Other personal reasons		
Desires another method	0	1
Partner objects	2	0
Partner had vasectomy	1	0
Unable to continue		
follow-up visits	1	1
Lost to follow-up	5	4
Completed 12 months of use	19	24

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Table VI. Gross cumulative life table rates per 100 women

Event	6-month		12-month	
	OVT-n Rates/100 women (±SE) ¹	OVT-n Rates/100 women (±SE)	OVT-n Rates/100 women (±SE)	OVT-n Rates/100 women (±SE)
Continuation rate*	66.9	66.3	45.4	55.3
Follow-rate	85.3	88.6	79.2	82.8
Discontinuation rate				
Accidental pregnancy	15.2±5.8	13.3±5.6	31.7±3.1	25.3±7.3
Planned pregnancy	0.0±0.0	0.0±0.0	4.8±4.6	0.0±0.0
Discomfort discount.	10.1±4.9	13.4±5.1	13.5±5.7	16.2±5.7
Method-related discount.	2.6±2.5	2.2±2.2	2.6±2.5	2.2±5.7
Other medical discount.	5.4±3.7	5.1±3.5	5.4±3.7	5.1±3.5
Other personal discount.	4.7±3.3	4.8±3.3	12.4±6.0	4.8±3.3
Lost to follow-up rate	10.42	8	39.58	42.0
Total woman-month of use, 12 months	-	-	350.0	400.0

¹Standard error of rate

*Includes 9 women who subsequently became lost to follow-up.

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user failures. Twelve-month Pearl pregnancy rates (Table IV) were 37.7 and 30.0 per 100 women-years for the OVT-n group and OVT-m group, respectively.

Five women in the OVT-n group discontinued for reasons of discomfort (burning/stinging) and 7 women did so in the OVT-m group. Twelve-month discontinuation rates due to discomfort were 13.5 per 100 women for the OVT-n group and 16.2 per 100 women for the OVT-m group.

There were 4 discontinuations in the OVT-n group and 2 in the OVT-m group for other personal reasons (e.g., partner objected, partner had vasectomy, desired another method). Discontinuation rates for other personal reasons at 6 months were 4.7 per 100 women among OVT-n users and 4.8 per 100 women among OVT-m users. While the discontinuation rate did not change for the OVT-m users at 12 months, it increased to 12.4 per 100 women among the OVT-n users.

Five OVT-n users were lost to follow-up and 4 OVT-m users were lost to follow-up. The follow-up rates at 12 months were 79.2 per 100 women for OVT-n users and 82.8 per 100 women for OVT-m users. A total of 19 OVT-n users (39.6%) and 24 OVT-m users (48.0%) completed 12 months of the study.

Discussion

The results from this study found differences in the foaming vaginal tablets containing nonoxynol-9 or menfegol in the gross cumulative 12-month life table, the pregnancy rates and the 12-month continuation rates; however, these differences were not statistically significant. Nearly half of the women in each group discontinued use of their assigned method, most often because of accidental pregnancy due to use failure (e.g., intercourse before 10-15 minutes after insertion of the tablet, neglect, no clock at home).

From reports of other studies (5) in different countries, accidental pregnancy occurred in a wide range from 1-31%. The study of Chi et al. (6) found that the pregnancy rate was 6.2-29.9 in 100 neo-sampoo users. The study of Youssef et al. (7) reported the rate of pregnancy as 2.8%. Our study showed a high incidence in pregnancy rates. This may be due to differences in population and methodology of the studies.

The results of this study indicate that with regular and proper use, OVT-n or OVT-m tablets are a comparable and safe means of birth control. Although few related or medical complaints were reported by both groups of tablet users, the high incidence of user failures indicates that tablets may not be suitable for Thai women.

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Furthermore, from other studies (5) concerning the safety of the product, it was found that there are arguments on the effect of spermicide use on pregnancy outcome. At present, the association of congenital abnormalities in the fetus and accidental pregnancy in users has not been resolved, though there is little absorption of these products through the vagina. A recent World Health Organization meeting concluded, however, that in neither lactating nor non-lactating postpartum women has there been any suggestion of an adverse effect on the woman's health in association with use of spermicidal creams or suppositories.

Conclusion

In our opinion, vaginal contraceptives should be used in groups of women who are highly motivated to use the tablets regularly and properly (8). Nevertheless, for women who want a reversible method of contraception but who cannot use oral contraceptives or IUDs, vaginal methods are a useful option. They are one of the many reversible contraceptive methods marketed today, are available throughout the world, and require no prescription.

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