

Assessment of a new modified soft jelly capsule containing nonoxynol as spermicide contraceptive

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Abstract

The mean rupture time, after its vaginal insertion, of a new modified soft jelly capsule containing nonoxynol-9 (DF-486) was investigated in 40 women. The subjects were randomly allocated to 8 study groups. The capsules remained in the vagina from 2-13 minutes. Vaginal infection, vaginal dryness, and multiparity, were recorded.

Capsule rupture was not observed at minute 2; 20% of capsules that remained in the vagina 3 minutes suffered rupture, as did 80% of capsules that remained 4, 5 and 7 minutes, and 100% of those remaining 9 minutes or more. The mean rupture time of the studied capsules was 8.2 minutes with 95% confidence limits of 6.2 and 8.8 minutes. At minutes 2-7, vaginal infection, dryness and tone diminution probably accounted for lack of rupture; after minute 7, these factors did not influence capsule rupture.

Introduction

The use of spermicidal agents in developing countries has increased over the past decade [1]. New medicated vaginal contraceptives with improved carriers have been developed [1-3]. Almost all currently marketed spermicides are surfactants, surface-acting compounds, and enzyme inhibitors [3]. The most frequently used spermicides are octoxynol-9 and nonoxynol-9, which are non-ionic surfactant agents [3,4]. A great advantage of nonoxynol-9 is its ability to inhibit the growth of some organisms responsible for sexually transmitted diseases [5,6]. Nonoxynol-9 toxicity is controversial [3,7-10]; no strong evidence of systemic effects in humans has been reported [11].

Recently, we described a new spermicidal carrier (soft jelly capsule) containing nonoxynol-9 with some advantages over the conventional spermicides [12]. Several cases of spontaneous capsule rupture inside the package were reported in some cities in Mexico where humidity is high [13]. Therefore, the vehicle was changed and this

modified soft jelly capsule was studied to determine its mean capsule rupture time after vaginal insertion and to evaluate whether vaginal infection, dryness and muscle tone diminution modify the time required for capsule rupture.

Materials and methods

Description of the capsule

The modified capsules contain nonoxynol-9 168 mg, aerosil R-972 and polyethyleneglycol 400 (Figure 1). The last two compounds are slightly more hydrophobic than was the polysorbate used as a vehicle in the previous capsules studied. The capsules were manufactured and provided by PROFAM, Mexico.

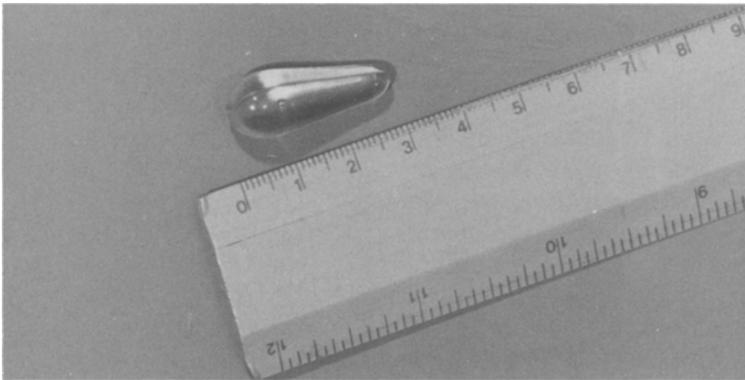


Figure 1 The modified soft-jelly capsule containing nonoxynol 9

Subjects

Forty healthy women of reproductive age attending the Family Planning Clinic of the University Hospital at Torreon volunteered to participate. A written informed consent form was obtained from each woman prior to her inclusion in the study. The mean age of the participants was 32.9 ± 10.3 years. Physical parameters among participants were similar and no statistical differences were found. The capsules were inserted into each participant at the upper vaginal portion after speculum insertion. At this time a clinical vaginal exploration was performed; thereafter, the speculum was removed and the capsules remained in for various study times. Finally, and at the end of the study time, the speculum was introduced very carefully again and the capsules were retrieved and rupture or non-rupture was recorded. The volunteers were randomly allocated to 8 study groups:

Group I	(n = 5): study time	2	minutes
Group II	(n = 5): study time	3	minutes
Group III	(n = 5): study time	4	minutes
Group IV	(n = 5): study time	5	minutes
Group V	(n = 5): study time	7	minutes
Group VI	(n = 5): study time	9	minutes
Group VII	(n = 5): study time	11	minutes
Group VIII	(n = 5): study time	13	minutes

These time intervals were selected according to our previous results [12].

Statistics

The results are expressed as arithmetic mean \pm standard deviation and 95% confidence limits. The statistical differences between groups were established using the unpaired Student's *t*-test.

Results

The results obtained in the study show that 77.5% of all capsules ruptured. The minimum time required for capsule rupture was 3 minutes, and, by minute 9, 100% of the capsules had ruptured (Table 1). The mean rupture time was 8.2 ± 3.3 minutes, with 95% confidence limits of 6.2–8.8 minutes. Statistical differences ($p < 0.05$) were found only when groups II and III were compared. After minute 11, disintegration of the capsule wall was seen.

Table 1 Number of cases of rupture and non-rupture capsule and rupture percentage

Group (n = 5)	Time (min)	Rupture	Non-rupture	Rupture (%)
I	2	0	5	0
II	3	1	4	20
III	4	4	1	80
IV	5	4	1	80
V	7	4	1	80
VI	9	5	0	100
VII	11	5	0	100
VIII	13	5	0	100

Vaginal infection with leucorrhoea was observed in ten (25%) of the forty participants; of these 10 subjects, 2 were in group III, 2 in group IV, 2 in group V, 1 in group VI, 1 in group VII and 2 in group VIII.

Vaginal dryness was observed only in one participant (2.5%), a woman in group II.

Diminution of the vaginal muscle tone due to multiparity was found in one subject (2.5%) in group VIII.

Distribution of the active compound was observed in the vaginal fundus in all cases.

Discussion

This study demonstrates that most of the capsules ruptured (77.5%). When the percentage of ruptured capsules was compared with that of our previous study (61%) [12], we found statistical differences ($p < 0.05$). In the present study, however, a slightly more hydrophobic vehicle was used, although the components of the capsule wall were not modified. This modification may account for the slight delay in the minimum time required for capsule rupture (3 minutes), compared with our last study (2.5 minutes) [12]. The mean time for capsule rupture was 8.2 minutes, less than the dissolution time required for conventional spermicides with an oil base widely used in Latin America [12]. Therefore, the intercourse delay period will be minimal.

As in our previous study [12], vaginal infection, dryness and diminished muscle tone due to multiparity were observed in the subjects from groups II–V whose capsules did not rupture. However, these phenomena did not influence capsule rupture in groups VI–VIII.

Conclusion

This study provided more definitive data on capsule rupture than those provided by our previous trial. To eliminate the problem of capsule rupture in the package, we suggest the use of a hermetic package for future distribution of this contraceptive capsule.

Acknowledgements

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Resumé

Le temps de rupture moyen de la nouvelle capsule modifiée gélifiée molle contenant du nonoxynol-9 (DF-486) après son insertion dans le vagin a été étudié sur 40 femmes. Les patientes ont été divisées au hasard en 8 groupes d'étude. Les capsules sont restées dans le vagin pendant 2 à 13 minutes. On a enregistré les infections vaginales, le degré de sécheresse du vagin et le nombre d'enfants.

On a observé la rupture des capsules 2 minutes après l'insertion: 20% des capsules retenues dans le vagin pendant 3 minutes se sont rompues, de même que 80% des capsules retenues pendant 4, 5 et 7 minutes et 100% de celles qui avaient été retenues pendant 9 minutes ou plus. Le temps de rupture moyen des capsules étudiées était de 8,2 minutes, les limites de fiabilité de 95% correspondant à 6,2 et 8,8 minutes. De la 2^{ème} à la 7^{ème} minute, la non rupture était probablement attribuable à une infection vaginale, à la sécheresse et une réduction de tonus; après la septième minute, ces facteurs n'avaient plus d'influence sur la rupture des capsules.

Resumen

El tiempo medio de ruptura de la nueva cápsula de jalea blanda modificada que contiene nonoxynol-9 (DF-486) después de su inserción en la vagina fue estudiado en 40 mujeres. Estas fueron divididas al azar en 8 grupos de estudio. Las cápsulas permanecieron en la vagina durante un lapso de 2 a 13 minutos. Se registraron las infecciones vaginales, el grado de sequedad de la vagina y el número de hijos.

Se observó la ruptura de las cápsulas 2 minutos después de su inserción: el 20% de las cápsulas retenidas en la vagina durante 3 minutos se rompieron, así como el 80% de las cápsulas retenidas durante 4, 5 y 7 minutos y el 100% de las retenidas durante 9 minutos o más. El tiempo medio de ruptura de las cápsulas estudiadas fue de 8,2 minutos, con límites de fiabilidad del 95% correspondientes a los 6,2 y 8,8 minutos. Del 2^o al 7^o minuto, la no ruptura fue probablemente atribuible a una infección vaginal, a la sequedad y a una reducción del tono; después del 7^o minuto, estos factores ya no influyeron sobre la ruptura de las cápsulas.