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Effect of butoconazole nitrate cream and wax insert on the barrier property of contraceptive devices

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A new method was developed to assess the quality of the barrier property of several types of commonly used contraceptive devices (diaphragm, cervical cap, and condom). Our data showed that butoconazole nitrate cream and wax inserts did not affect the barrier property of the contraceptive devices when the products were placed in contact with the devices for up to 72 hours at 37° C. (AM J OBSTET GYNECOL 1988;158:1011-3.)

Key words: Cream and wax inserts, contraceptive devices, butoconazole nitrate cream

Recently, regulatory agencies from the United Kingdom and New Zealand expressed concerns about the possible effects of imidazole-based antifungal products on the barrier property of contraceptive devices. Since no reports on the subject had appeared in the literature, this study was initiated to address these concerns. Butoconazole nitrate cream and wax insert were used to evaluate their effects on the barrier properties of several contraceptive devices marketed in the United Kingdom.

Material and methods

Although the testing of condoms is well established, no previous work has been done to test the barrier properties of diaphragms and cervical caps. In this study we developed a method that could be applied to different types of contraceptive devices. Two brands of diaphragm (Ortho and Durex), one brand of condom (Durex), and one brand of cervical cap (Prentif) were evaluated with this method. All three types of devices were purchased in the United Kingdom. Disks were cut from each device, smoothed, and attached with a commercial cyanoacrylate-based glue to the sawed-off ends of 10 ml syringes. Four disks from each device were used.

The exposed surfaces of the disks were dipped into a beaker containing either the butoconazole nitrate cream or a molten wax insert. These were then placed in an oven set at 37° C to simulate physiologic temperature. The devices were taken out of the oven and checked for barrier damage at 24, 48, and 72 hours.

The test consisted of cleaning the disks with tissue paper and filling the syringes with about 10 ml of water. After the syringes were mounted in a syringe holder (Fig. 1), an appropriate weight was placed on the plunger handle. The disks were then examined for leaks. The choice of the weights used varied according to the device and was based on the minimum weight required to cause leakage through a puncture created by a 27-gauge hypodermic needle. The pressures used for testing the devices are listed in Table I.

A scanning electron microscope was also used to examine the devices. Device samples were left in contact with the cream or the wax insert for 72 hours. Before microscopic examination for signs of deterioration, these samples were first cleaned with a mild detergent, dried, and then coated with palladium-platinum in a vapor chamber.

Results

Barrier property. During the experimental time (up to 72 hours) no leakage was observed in any of the devices placed in contact with the butoconazole cream. With the wax insert, the Ortho diaphragm and the Prentif cervical cap showed no signs of leakage. How-

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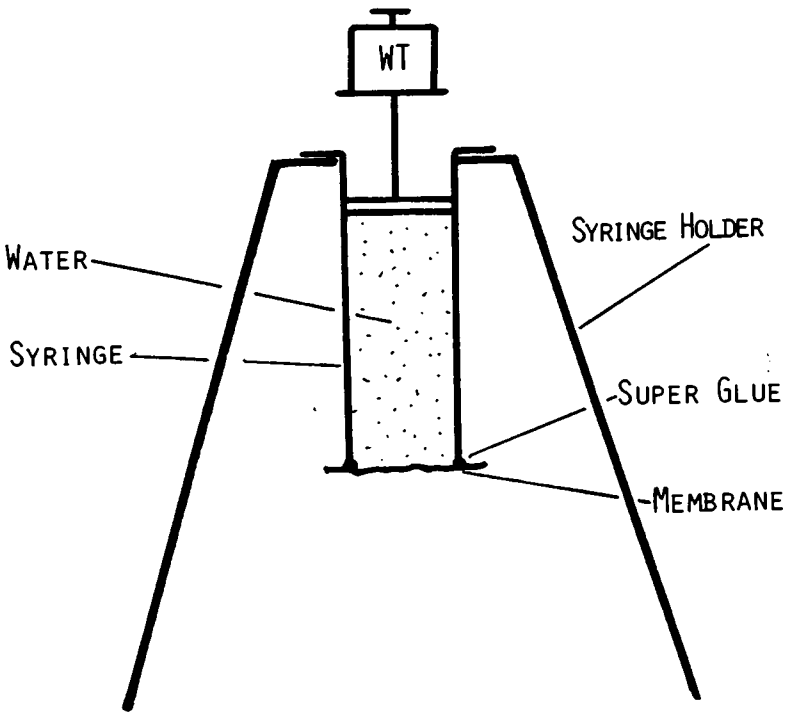

Fig. 1. Apparatus for the barrier property test.

Table I. Pressures used in tests of devices

Device	*Manufacturer*	*Test pressure (gm/cm²)*
Diaphragm	Ortho	415
Diaphragm	Durex	415
Condom	Durex	105
Cervical cap	Prentif	565

ever, one of the four Durex condoms leaked at 48 hours, while the others were intact for the 72-hour observation time. Since the condoms are expected to have only brief exposure to antifungal products during normal use, their barrier property is not likely to be compromised.

Two of the four Durex diaphragms exposed to the molten wax insert leaked at 48 hours. The Ortho diaphragms and the two other samples of the Durex diaphragm did not show any leakage for the duration of the test. In the two Durex diaphragms that showed leakage, the wax insert appeared to have diffused into the diaphragm and caused the membrane to wrinkle. Closer examination revealed that the leakage in one of the samples occurred close to the rim of attachment of the disk to the syringe, while for the other the leakage occurred at the point of attachment. In both instances the leakage appeared to have been caused either by the weakening of the bond as molten wax diffused into the membrane or by improper attachment during setup. In either case it was considered an artificial phenomenon and not a barrier failure. To test this hypothesis, five more samples were set up with the Durex product; this time the test was designed to keep the molten insert away from the vicinity of the seam. This was accomplished by carefully placing the molten wax in the depressions formed when the plungers were pulled back slightly. The samples were stored in the oven with the syringes standing on the plunger ends. There was no membrane leakage after 72 hours.

Scanning electron microscopy. During scanning electron microscopic examination, the edges and the surfaces of all the samples were carefully inspected. No deterioration or damage was observed in any of the sample products.

Gross appearance. The contact surfaces of the contraceptive devices showed some light stains after exposure to both semisolid products for about 72 hours. The cream did not change the physical property of the products; however, the wax softened the cervical cap and caused shallow wrinkles on the diaphragm. No obvious changes occurred in the physical properties of the condoms, perhaps because of the thinness and pliability of the membrane.

Comment

It can be safely predicted that no leakage should be anticipated when the tested contraceptive devices are used with the butoconazole nitrate cream. This is a

reasonable expectation because water-based semisolids usually do not cause damage to rubber latex material. With an oil-based material, such as the molten wax insert, the oil may penetrate the rubber latex, physically softening the material. Nonetheless, in our study no leakage occurred with the oil-based insert when the test was set up properly. Results with both products were excellent in terms of their lack of effect on the barrier properties of the contraceptive devices studied.

Conference compendium

At the conclusion of the conference on vulvovaginal candidiasis, Conference Chairman Dr. Eduard Friedrich and participants summarized the major points made during the presentations at the 2-day conference. Mycology and its relationship to the disease state was discussed extensively. Some of the discussion included the following:

1. Some *Candida* strains may use food sources other than glycogen.
2. By-products of fungal metabolism, such as alcohol, may trigger the symptoms associated with vulvovaginal candidiasis.
3. Ergosterol, a key component of the cell wall of *Candida*, is not present in all species. In addition not all growth phases of a single species or a single strain are equally dependent on ergosterol—hence the lack of uniform response to drugs that block the biosynthesis of this sterol.
4. High-frequency switching may be involved in pathogenesis; once studies have defined the molecular basis for this phenomenon, new strategies can be developed to combat such switching.
5. Phenotypic switching within strains of *Candida* and gene jumping may account for problems of resistance and recurrence of infection.
6. Efforts in the field of molecular biology should be aimed at the development of tools to fingerprint strains of *Candida albicans;* only then will answers emerge to fundamental questions such as, "Are commensal strains really the infecting strains?"

Problems encountered in treating women with vulvovaginal candidiasis were enumerated by several presenters. Among the important conclusions made by discussants were the following:

1. Studies show that therapy with butoconazole nitrate suppositories has good efficacy.
2. Short-term use of a topical steroid preparation for symptomatic relief administered concomitantly with a vaginal antimycotic agent does not appear to be associated with adverse side effects and the efficacy of the active agents does not appear to be reduced.
3. In a small in vitro study conducted on latex contraceptive products (condoms, diaphragms), butoconazole nitrate did not affect the barrier properties of the latex substances.
4. Compliance, always a problem in therapy, remains a significant factor in cure. Data from a small study on the use of premeasured dose, prefilled vaginal cream applicators indicate that this one-time-use applicator device may eliminate some of the complaints of patients about mess and the difficulty in cleaning refillable applicators. Acceptability and compliance during the study were high.
5. Nurse practitioners, as part of the physician's office team, substantially increase patient compliance by instruction in the proper administration of therapeutic agent, follow-up of patients to ensure length of therapy, and increasing patient confidence.