FURTHER STUDIES ON LONG-TERM CONTRACEPTION BY SUBCUTANEOUS SILASTIC[R]* CAPSULES CONTAINING MEGESTROL ACETATE

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ABSTRACT

The contraceptive effectiveness of megestrol acetate (M.A.) implants was evaluated in 126 parous young women. Each patient received 5 implants. Each implant contained 23 mg of M.A. A total of 1,560 cycles were recorded. Only one pregnancy occurred in patients observed for up to 15 months for over 1,440 cycles. Three pregnancies occurred in a group of 20 patients whose capsules were replaced by a new set at the end of the first 15-month trial period. The variation in contraceptive effectiveness and the incidence of side effects of this method compared to other methods is discussed.

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INTRODUCTION

The efficacy and acceptability of subcutaneous Silastic[R] capsules of megestrol acetate in conception control has been demonstrated in previous studies (1,2,3). Clinical evaluation of M.A. implants revealed that effective contraception, apparently without inhibition of ovulation and lasting approximately 9 to 10 months, could be obtained with 4 implants, each containing 23 mg of the compound. At the end of this period, an abrupt increase in pregnancy rate occurred indicating that the amount of progestin released was by then insufficient to prevent conception (4). Preliminary results with 5 implants suggested not only increased effectiveness--for no pregnancies were observed during the first nine months of use--but also more lasting contraception, for no pregnancies occurred in twenty patients bearing the implants for up to 13 months.

The present report extends those observations describing the effects of 5 implants of M.A., in a larger number of patients, for a longer period of time.

MATERIALS AND METHODS

Silastic capsules containing approximately 23 mg of M.A., made of silastic tubing manufactured by Glaxo Laboratories, London, were supplied by the Population Council, Inc., New York. The capsules were inserted subcutaneously in the forearm of 126 parous young women through an 11 gauge trocar following local anesthesia. All patients received 5 implants. On the basis of excretion studies (5), it has been estimated that 5 of the present size implants would be effective for 12-15 months of use. For this reason, the first set of capsules was replaced by a new set at the end of this period.

RESULTS

The patients were observed for a total of 1,560 months. One hundred patients were observed for a minimum of 10 and a maximum of 15 months with the original set of implants. Sixty-eight of these women completed 15 months of use. In 20 of these 68 women, the implants were removed at the end of 15 months and replaced by a new set. The remaining 26 patients who are still active but have not yet completed one year of treatment were observed for 4-9 months of use. Only one pregnancy was recorded in the patients observed for up to 15 months (1,440 cycles). This one pregnancy occurred at the end of 14 months of use. However, three other pregnancies were reported in the group of 20 patients who received a second set of implants at the end of the first 15-month trial period. These pregnancies occurred at the end of 4, 11, and 12 months, respectively, of the second 15-month trial period, during which a total of only 120 cycles has been recorded thus far.

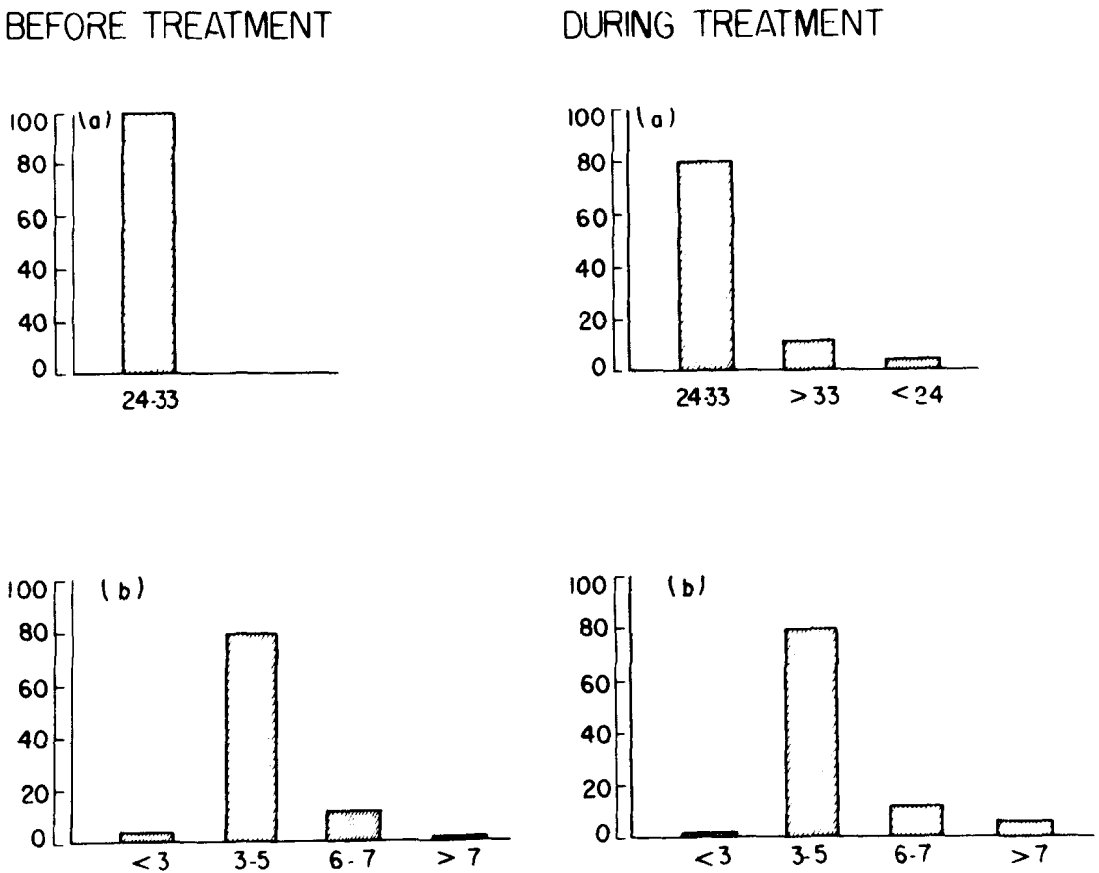

Figure 1: Comparison of (a) cycle length and (b) duration of menstrual flow, before and during treatment. The ordinate shows percentage of cycles.

Inter-menstrual bleeding or spotting was reported by 55 patients in a total of 92 cycles (approximately 6% of cycles). Hypermenorrhea was reported by 49 patients in a total of 118 cycles (7.5% of cycles), whereas amenorrhea occurred in only 29 patients for 57 cycles (3.6%). 1,163 cycles (74%) were considered normal. Only two patients requested removal of the implants before the end of the study. In both cases, the cause for discontinuation was inter-menstrual bleeding. The changes in cycle length and in duration of the menstrual flow occurring during the treatment are illustrated in Figure 1.

DISCUSSION

The present study confirms and extends the previous observations (3) that protection afforded by 5 implants of M.A. is much greater and lasts significantly longer than that provided by 4 capsules of the compound. The contraceptive effect is extended from approximately 10 months (recorded for patients bearing 4 implants) to 15 months. The occurrence of defective or incomplete filling of the capsules, of the second batch, could be the reason for the marked decrease in efficacy. When those three pregnancies are included as method failures, the new method ends up with a pregnancy rate of about 3 per 100 woman years (Pearl Index=3.1). However, when this group is excluded, the pregnancy rate for the first year drops to less than 1 per 100 woman years (Pearl Index = 0.8) which compares favourably with other methods of contraception. Further reduction in pregnancy rate and an even longer contraceptive effect may be accomplished with higher doses. Pilot studies with 6 implants are now in progress to test this assumption.

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