Hormonal Therapy For Suppressing Lactation

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SUMMARY

In recent years, hormonal suppression of undesired lactation has been widely employed. A review of the literature confirms the efficacy of this method, at first with estrogen alone and later with progestogen-estrogen combinations. The authors also discuss retrospective studies of the incidence of thromboembolism in such patients, and report on a new double-blind study of the successful use of norethynodrel and mestranol as a suppressant.

FOR PERHAPS 30 YEARS, it has been medically fashionable to prescribe medication to suppress lactation in patients unwilling or unable to breast-feed their infants. Before hormones became available, routines including breast binders, fluid restriction, and saline laxatives had been employed for generations in the belief that lactogenesis could be discouraged by pressure or deprived of necessary fluids by competing organs. These methods survived so long, because no really effective therapies were available, and because they gave the patient something to do. Moreover, the physician could prescribe an impressive, complicated, time-consuming and highly unpleasant routine with suitable insistence on meticulous compliance.

Stilbestrol was hailed as the first real advance in suppression therapy, and its arrival coincided with the general trend away from breast-feeding in Western countries. A combination of scientific, artificial feeding and working mothers in wartime resulted in a demand for freedom from feeding schedules by a majority of mothers.

Patients Expect Medication

The use of drugs for this purpose is not universally accepted, and probably never will be, unless it is demonstrated that medication prevents more serious sequelae than discomfort and inconvenience. But patients expect medication, and many physicians do prescribe drugs to prevent the misery of breast engorgement. (A widespread survey of the therapies employed by parous female physicians would be most enlightening in this regard). Frequently the efficacy of a therapy is assessed only after it has been widely used for some years. Hodge,[1] for instance, found it valuable to study the suppression of lactation by stilbestrol as late as 1967, and reported then that 45 mg. daily for three days is indeed effective in suppressing lactation. Although rather more than a third of his placebo group required no analgesic, even the fairly heavy dose of stilbestrol used resulted in a failure rate of 12 percent.

In this study (as in some others) a thiazide diuretic alone was found unsatisfactory. Hodge comments on the difficulty of such a study, depending on many observers and on both subjective and objective responses. His double-blind technique at least excluded personal bias. It is significant that by the time 50 patients were recorded in each of his groups, he felt that there was no justification for prolonging the sometimes severe discomfort experienced by those not receiving stilbestrol, and the trial was terminated.

In recent years the combination of an estrogen and a progestin has proven valuable in the therapy of numerous gynecological disorders, and as early as 1957 Holmstrom[2] reported its use in a patient with amenorrhea and persistent lactation of four years' duration. Initially, methallenestril plus a progestin resulted in bleeding but had no effect on lactation. The patient was then given norethynodrel 9.85 mg. and mestranol 0.15 mg. daily for 24 days, and lactation ceased. One other similar patient could not tolerate the medication.

In 1963, Toaff and Jewelwicz[3] reported a study on the inhibition of lactogenesis by progestogens and estrogens in which four different regimens were employed. They noted that while estrogens had been used first on a wide scale for this purpose, they often caused rebound phenomena, persistence of lochia and withdrawal bleeding; that much use had also been made of androgens with or without estrogens, and that the rationale of these therapies was questionable. They review theories of lactogenesis, and conclude that because a fall in progesterone at parturition allows estrogen to exert its lactogenic effect by stimulating secretion of prolactin or the lactogenic complex, progesterone or potent orally active progestogens alone or in combination with estrogen in optimal ratios should be more effective than either estrogens or androgens in inhibiting lactogenesis.

Toaff and Jewelwicz conducted a clinical trial with oral progestogens, with and without added estrogen, in 96 healthy women who were unable or unwilling to nurse. Treatment was begun not later than one hour after expulsion of the placenta. Patients were carefully monitored for subjective symptoms and observed for objective signs. Progestogen dosage (norethynodrel or medroxyprogesterone acetate) was 30 mg. initially; 30 mg. per day for five days; 20 mg. per day for one day; 15 mg. per day for two days, and 10 mg. per day for two days – a total of 250 mg. This was given either alone or combined with an estrogen. One group was given ethynyl estradiol alone; a total of 2.5 mg. over 10 days. About one third of the patients were followed for two weeks after discharge from hospital. The usual hospital stay was seven days.

In the final evaluation, the combination of norethynodrel with mestranol appeared to inhibit lactogenesis most strongly. The combination of

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medroxyprogesterone with ethynyl estradiol was almost as potent; progestogen alone was definitely inferior and ethynyl estradiol alone did not prevent lactogenesis, although it did prevent pain and engorgement. No rebound lactation or withdrawal bleeding was observed.

Dosage Not Excessive

Toaff and Jewelwicz note that their dosage was not excessive, since the secretion of placental progesterone at about term is estimated to be 190 to 280 mg. per 24 hours. Thus conclude that a pharmacological action is thus unlikely.

The work of Toaff and Jewelwicz was confirmed in a double-blind trial by Gillibrand and Huntingford,[6] employing a slightly lower dosage (210 mg. over nine days). Compared to a tapered course of stilbestrol (total dose 105 mg.), the norethynodrel/mestranol combination was superior.

The importance of early administration in order to suppress lactation was emphasized by Garcia and Pincus[4], who stated that studies of norethynodrel with mestranol show that even 10 mg. per day given in the fifth to eight week postpartum had no effect on lactation. Treatment in the third week may cause some lessening of lactation. The same combination was reported as successfully terminating pathological lactation following pituitary surgery, by Levitt[9] in 1966.

A lower dose of the norethynodrel and mestranol combination (10 mg. daily for five days) was chosen by Billingsley[5] for a study published in 1969. He had previously experimented with total dosages from 30 to 140 mg. He treated 150 consecutive patients, followed by 75 consecutive controls given placebo. The hospital staff rebelled against a larger number of control patients because of the increased care required for breast engorgement. Billingsley reports 98.7 percent effectiveness for the combination. In two patients where the first dose was delayed about 12 hours, pain, engorgement and secretion were observed in spite of norethynodrel therapy. Billingsley confirms the figure of 30 percent natural suppression of lactation without medication, which has been reported by others. Because of the incidence of rebound lactation, the period of administration of norethynodrel was later increased to six days; the necessity for administering the first dose in the delivery room is stressed.

The efficacy of norethynodrel and mestranol in preventing lactation therefore appears to be established, although there is a considerable variation in total dosage employed, and in duration of therapy.

Thrombosis-Age Relationship

The recent emphasis on the relationship between oral contraceptives and thromboembolism naturally leads one to look at this aspect of similar therapy to suppress lactogenesis, especially since the drugs are given in a situation where thromboembolism is not rare. In 1967, Daniel, Campbell and Turnbull[7] reported on nearly 10,000 women. The drug commonly used to suppress lactation was diethylstilbestrol (total nine-day dose, 210 to 330 mg.). Even after making allowance for age and parity, there was a significantly higher incidence of thromboembolism in patients who had lactation suppressed; the increase was tenfold in low-parity women who were not lactating. These authors further state that there is recurrence of lactation in 70 percent of cases where diethylstilbestrol is used.

As a result of this paper, Gunther and Kohorn[8] were prompted to examine their hospital records for an 11-year period. The standard of recording was said to be high, with all estrogen therapy reported. The same relationship between thrombosis and age or difficulty of delivery was noted. A system of matching provided controls. Although about 5,000 women received estrogens in the first week for suppression of lactation, the number of women developing superficial thrombosis after estrogen therapy was too small to show any effect compared with matched controls. There was no measurable effect of estrogens on the thrombosis rate. There were no deaths. The total dosage of estrogen, however, was only one third to one quarter of that reported by Daniel et al., and administration was spread over 12 days rather than nine. Rebound phenomena were seldom seen.

In the light of findings in the papers cited, it is of interest to report a new double-blind study against placebo, carried out in the Grace Hospital, Toronto, employing an intermediate dose level of norethynodrel and mestranol. Sixty patients were given either active drug or placebo on a random basis, one tablet in the delivery room, and three per day for four days. The active drug was the combination of norethynodrel 9.85 mg. and mestranol 0.15 mg. Patients averaged 23 years of age; parity average was 1.25. Patients were observed and questioned by nurses on both day and night shifts, and their observations recorded.

On a percentage basis, patients receiving placebo were reported as having tenderness, leakage or engorgement more than 10 times as frequently as in patients receiving the norethynodrel/mestranol combination. No adverse side effects were noted.

The total dosage employed (130 mg.) falls between the high and the low levels reported in publications cited above. Undoubtedly there is a fairly broad, effective dose range, although it has been suggested that there is an optimal dose of hormone for lactation suppression, and that too much may be as ineffective as too little. Our small series was intended merely to confirm the effectiveness of the medication at a medium dose level for a relatively short period of time. The question of thromboembolism as an adverse side effect can be even tentatively answered only by studying a very large number of cases; the variation in dose used and the fact that medication to suppress lactation may be given because thromboembolism has developed, make any retrospective study difficult to interpret. The substantial number of published reports of the successful and uncomplicated use of norethynodrel and mestranol, together with our own small series, leads us to feel that the medication as used is both safe and effective, with the additional advantages of administration of the entire course within four days, at a reasonable cost. ◀

References

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