CLINICAL TRIAL OF E. P. FORTE IN SECONDARY AMENORRHOEA

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Secondary amenorrhoea is a problem commonly met with in gynaecological practice. Secondary amenorrhoea is due to the distrubance in the hypothalamo - hypophysio - ovario - uterine axis. Secondary amenorrhoea may also be produced by disorders of thyroid and adrenals. If the endometrium is refractory or removed by vigorous curettage or affected by tuberculous infection, secondary amenorrhoea may be the end result.

It is essential that in every case of secondary amenorrhoea the cause should be determined by detailed history and clinical examination. Endometrial biopsy should be invariably done in all cases before any therapy.

Between December 1966 and January 1968, in the Department of Obstetrics & Gynaecology, Government General Hospital, Guntur the therapeutic value of E.P. Forte in secondary amenorrhoea was studied. Each tablet contains hydroprogesterone acetate 5 mg. ethinyl oestradiol 0.06 mg and hydroxyzine hydrochloride N.F. 10 mg.

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Material and Methods

A study of 178 cases of secondary amenorrhoea was made. The age of menarche was normal in these cases. Women in the age group of 15 to 40 years, who had amenorrhoea of more than 3 months following more or less regular menstrual cycles were included. All patients who showed on clinical examination any obvious general or local diseases to account-for the secondary amenorrhoea were eliminated.

Sixty-five patients (36.5%) of the 178 cases were in the age group of 26-30 years; 59 (33.4%) were between 15 and 20 years and the rest above 30 years. (Table I).

TABLE I

Showing the age incidence of secondary amenorrhoea in 178 patients studied

Age group	No. of cases	Percentage
15-20 years	59	33.4%
21-25 years	36	20.2%
26-30 years	65	36.5%
31-35 years	10	5.4%
36-40 years	8	4.5%
Total	178	

Ninety-seven cases were nulliparae. Of the parous women, 32 had only one child.

The duration of amenorrhoea ranged from 3 months to 10 years; and of these 178 cases, 102 (57.3%) cases were of 3 to 6 months, duration.

After taking a detailed history, every patient was examined thoroughly. A routine blood examination i.e., Hb%, total leucocyte count, differential count and erythrocytic sedimentation rate were done. If the E.S.R. was found to be high, x-ray of the chest was taken. Blood sugar, blood cholesterol and B.M.R. were done whenever indicated. In all cases endometrial biopsy was done after determining the size of the uterus. Forty cases of this series had undersized uterus. In those who received hormonal treatment the biopsy was repeated after a course of 3 cycles.

The nature of endometrium in secondary amenorrhoea is shown in Table II.

TABLE II

Showing the endometrial histology in secondary amenorrhoea before E. P. Forte

Type of endometrium	Before E. P. Forte	Percentage
Proliferative	79	44 %
No endometrium	64	36 %
Atrophic	9	5 %
Secretory	7	4 %
Tubercular	13	7.5%
Cystoglandular hyperplasia	6	3.3%
TOTAL	178	

In 44% of cases it was in the proliferative phase; in 36% no endometrium could be obtained and in 13 cases (7.5%) tuberculous endometritis was detected. In India Bhasker Rao *et al* have reported 18 cases of tubercular endometritis in 80 cases of secondary amenorrhoea. When compared to this our incidence of tuberculous endometritis is rather low.

Treatment

Of 178 patients thus investigated, 165 were given the hormones. Thirteen of them were treated for endometrial tuberculosis.

The following was the scheme adopted:

Amenorrhoea up to 6 months: E. P. Forte, three tablets, one for three days were given.

Amenorrhoea of 6 months to 1 year—One intramuscular injection of 1 ml (E.P. Forte, one ampoule,) was given. (1 ml of an oily solution containing 3 mg of oestradiol benzoate and 50 mg progesterone).

When amenorrhoea had lasted for over 2 years and in those cases where no endometrium was obtained during curettage and also in those showing atrophic endometrium—1 ml of E. P. Forte intramuscularly was given for 2 consecutive days.

Results

One hundred and forty-five cases, or 87.7%, had withdrawal bleeding after the first course of hormones and 20 cases failed to respond. These 20 cases showed no endometrium on endometrial biopsy prior to the hormonal administration as shown from Table III. Of the 165 cases who had hormones only 133 cases could be followed up for a minimum period of 4 months.

The response was seen within 10 days of the last dose. The hormonal treatment was repeated at intervals

of 21 days. After 3 such courses endometrial biopsy was repeated.

In patients with amenorrhoea of less than 6 months' duration the response was 97.9%. In amenorrhoea of over 3 years the response was 55.5%. No patient who had amenorrhoea for over 5 years had any withdrawal bleeding with hormonal therapy. It may, however, be noted that when the amenorrhoea was below 2 years' duration the prognosis was brighter and it was poor in cases over 2 years (Table III).

TABLE III

Showing the duration of Secondary amenorrhoea and response to hormonal therapy.

Duration	Number treated	Number responded	Percentage
6 months	98	96	97.9%
1 year	39	34	87 %
2 years	11	8	72.7%
3 years	9	5	55.5%
4 years	4	2	50 %
Over 5 years	4	Nil	Nil
	165	145	

The response to E. P. Forte in cases of secondary amenorrhoea of less than 6 months is very yood, 98%; of one year, it was 87% and of 2 years the response was 72.7%. In cases of 3 years' duration the response was fair and practically nil in cases of secondary amenorrhoea of over 5 years.

In all cases of secondary amenorrhoea the cause when found should be remedied. In cases of tuberculous endometritis after antituberculous treatment the response was satisfactory when hormones were given.

After 3 courses of E. P. Forte (ampoules or tablets) endometrial biopsy was done 21 days after the last withdrawal bleeding; 75% showed secretory phase, 20% showed proliferative phase, 3% no endometrium and 0.75% cystoglandular hyperplasia. (Table IV).

TABLE IV

Showing the endometrial histology in secondary amenorrhoea after E. P. Forte therapy

Type of endometrium	Response to E. P. Forte therapy. (3 courses)	Percentage
Secretory	101	75 %
Proliferative	27	20 %
Cystoglandular hyperplasia	1	0.75%
Atrophic	Nil	Nil
No endometrium	4	3 %
	133	

It is worth noting that out of 64 cases which did not show any endometrium prior to the administration of the hormones, 60 gave a good response and only 4 cases of amenorrhoea of over 5 years' duration did not respond.

Thirty-two patients had the drug only for one month and in them the response was good; 50% showed secretory phase and 35% showed proliferative phase. (Table V).

TABLE V

Showing the endometrial histology in secondary amenorrhoea after E. P. Forte therapy

Type of endometrium	Response to E. P. Forte Therapy. (1 course)	Percentage
Secretory	16	50%
Proliferative	11	35%
No endometrium	5	15%
Atrophic	Nil	Nil
	32	

Summary and Conclusions

1. One hundred and seventy-eight cases of secondary amenorrhoea with no clinically detectable aetiological factors were studied.

2. Endometrial biopsy was done in all, both before and after the E. P. Forte administration.

3. In 64 cases (36%), no endometrium was obtained during curettage prior to E. P. Forte.

4. In 13 cases (7.5%) tubercular endometritis was seen.

5. One hundred and sixty-five cases were given E. P. Forte—32 for one cycle, 133 for 3 cycles.

6. One hundred and forty-five patients (87.7%) had withdrawal bleeding with the first course of E.P. Forte.

7. The endometrium showed secretory phase in nearly 75% of cases after 3 courses of E. P. Forte.

8. The response to E. P. Forte in secondary amenorrhoea of less than 6 months was very good—98%; if the duration was less than one year the response was 87%; in cases of less than two years it was 72.7%. But in patients with 3 years' amenorrhoea the response was not quite satisfactory and practically nil in amenorrhoea of over five years.

9. No adverse side-effects were seen.

A combination of oestrogen and progesterone, E. P. Forte, is useful in the therapy of secondary amenorrhoea, either as a single intramuscular injection or as 2 injections, one daily on consecutive days, in long standing cases. If given orally, E. P. Forte, one tablet per day for 3 consecutive days should be given. This should be used only after a thorough search for the cause of secondary amenorrhoea, including the histological study of the endometrium. Asymptomatic tuberculous endometritis must always be ruled out. In those patients in whom no general or local cause is detected and endometrial biopsy suggests hormonal deficiency, E. P. Forte should be administered.

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