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Therapy of Androgenetic Symptomatology with Cyproterone Acetate and Ethinyl Estradiol

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Die Behandlung des androgenetischen Symptomenkomplexes mit Cyproteronazetat und Äthinylöstradiol

Zusammenfassung. Der Therapieerfolg einer Kombination von Cyproteronazetat und Äthinylöstradiol wurde bei 103 Frauen untersucht. Akne und Seborrhoe sprachen in 91,7 bzw. 93,3% am besten an. Beim Hirsutismus wurde eine komplette Remission oder teilweise Verbesserung in 75,3% beobachtet. Unter Therapie änderte sich das Körpergewicht in 51,9% nicht, während 24,7% der Patientinnen eine Gewichtszunahme und 23,4% eine Gewichtsabnahme aufwiesen. Die Zykluslänge war vor und nach Therapie in 35,8% unverändert, eine Verbesserung wurde in 54,7% festgestellt. Nur in 3,2% traten Zyklusunregelmäßigkeiten auf. Entsprechend den geführten Basaltemperaturkurven kam es bei 32,9% der Frauen zu einer Verbesserung des Zyklusablaufes. Nur bei 3,2% trat eine Verschlechterung auf. Die 17-Ketosteroidausscheidung war nach Therapie bei 37,3% geringer als vor der Therapie und bei 64,7% der Frauen blieb sie unverändert. Dosis und Anwendungsdauer erwiesen sich als günstig und eine gute Zykluskontrolle wurde erreicht.

Schlüsselwörter: Akne – Hirsutismus – Seborrhoe – Cyproteronazetat – Zyklus.

Summary. The effectiveness of therapy with cyproterone acetate and ethinyl estradiol was studied in 103 women. Acne and seborrhea responded best with 91.7 and 93.3% respectively, including complete and partial therapeutic success. For hirsutism complete remission and partial improvement were found in 75.3% of the treated women. Under therapy, body weight did not change in 51.9%, while 24.7% of the patients gained weight and 23.4% lost weight. The cycle length remained normal after therapy in 35.8%. Normalization or improvement was found in 54.7%. In 6.3% no improvement was noted after therapy and in

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3.2% cycle irregularity developed in women with previous undisturbed pattern. According to BBT, improvement of the functional capacity of the reproductive system was found in 32.9% of the patients. Only 3% of the women studied demonstrated a deterioration. The 17-ketosteroid excretion was diminished in 35.3% after therapy and remained unchanged in 64.7%. The therapeutic regimen used for the study was well tolerated and good cycle control was obtained.

Key words: Acne – Hirsutism – Seborrhea – Cyproterone acetate – Menstrual cycle.

The development of potent antiandrogens has created new possibilities to treat androgen induced symptomatology (acne, seborrhea, hirsutism) in women effectively (Gräf et al., 1974). Among a variety of antiandrogenic substances cyproterone acetate appears to be very suitable since this compound exhibits a number of actions (progestative, antigonadotropic, antiandrogenic, anticorticotropic) which are all very useful for the treatment of androgenetic symptoms in women (Schindler, 1977). Up to the present time only a limited number of reports have been published regarding the clinical application of cyproterone acetate in combination with ethinyl estradiol (Schindler, 1977). It is the purpose of this report to present results on antiandrogen treatment with a modification of the treatment regimen suggested by Hammerstein (1969). Particular attention was directed towards the function of the reproductive system before and after therapy.

Material and Methods

The study includes 103 hirsute women between 16–30 years of age. The data were obtained by means of a specially prepared evaluation sheet. Details are described elsewhere (Mangold, 1978).

Prior to therapy each patient was clinically and endocrinologically studied in order to exclude ovarian or adrenal tumors. For therapy the following treatment schedule was used: starting on day 5 of the cycle with 100 mg cyproterone acetate (2 tablets of Androcur® daily in the morning up to day 14) and 0.04 mg ethinyl estradiol (2 tablets of Progynon C® daily in the evening up to day 24 of the cycle).

Results

Among the 103 patients the length of therapy was as follows: 13 patients (12.6%) were treated up to 3 months, nine patients (8.8%) were treated up to 6 months, 78 patients (75.7%) were treated up to 9 months and three patients (2.9%) were treated more than 10 months.

In 77 patients body weight was followed and the results are listed in Table 1.

The therapeutic effects on acne (60 patients), seborrhea (30 patients) and hirsutism (97 patients) are listed in Table 2.

Cycle length could be evaluated in 95 patients before and after therapy. The pattern remained unchanged before and after therapy in 34 patients (35.8%). Nor-

Table 1. Weight changes in patients treated with cyproterone acetate and ethinyl estradiol

Weight change (kg)	Number of patients		Weight gain (%)	Weight loss (%)	No change	
	Weight gain	Weight loss			Number	%
2–3	11	13	14.3	16.9	–	–
4–5	7	2	9.1	2.6	–	–
> 5	1	3	1.3	3.9	–	–
Total	19	18	24.7	23.4	40	51.9

Table 2. Effects of treatment on acne, seborrhea and hirsutism

	Acne		Seborrhea		Hirsutism	
	n	%	*n*	%	*n*	%
Complete success	9	15.0	3	10.0	4	4.1
Partial success	46	76.7	25	83.3	69	71.2
No effect	2	3.3	2	6.7	23	23.7
Worsening	3	5.0	0	–	1	1.0

malization or improvement was noted in 52 patients (54.7%). In six patients (6.3%) no improvement occured and in three patients (3.2%) cycle irregularities developed after therapy.

In 67 patients BBT was recorded for 1 month before and for 3 months after treatment. In 32 patients (47.7%) BBT remained biphasic after therapy. In 15 patients (22.4%) a monophasic BBT before therapy changed to a biphasic pattern after therapy. Five patients (7.5%) who had a changing pattern of BBT before therapy exhibited biphasic cycles after the treatment, and in two patients (3.0%) the monophasic BBT turned after therapy into an alternating pattern. A changing pattern was present in two patients (3.0%) before and after the drug application. In another two patients monophasic BBT remained. Two patients developed for the first time monophasic BBT after discontinuation of therapy.

The 17-ketosteroid excretion was measured before and after treatment in 17 patients. In 11 patients the excretion remained unchanged, while in six patients reduction of the 17-ketosteroid excretion was found between 20–50%. None of the patients demonstrated an increase of the 17-ketosteroid excretion after therapy.

Discussion

Since the first clinical report by Hammerstein and Cupceanco (1969) on experiences with a combined oral application of cyproterone acetate and ethinyl estradiol for the treatment of androgenetic symptomatology in women, only a limited number of publication have followed (Schindler, 1977). The present study reports on results

obtained in 103 women using a modified treatment schedule when compared with the regimen suggested by Hammerstein (Hammerstein and Cupceanco, 1969). The changes included a decrease of the estrogen dose to 0.04 mg ethinyl estradiol daily and a decrease of the length of treatment to 20 days. In accordance with other authors the therapeutic effect was best for acne and seborrhea (Braendle et al., 1974; Hammerstein et al., 1975; Nardi et al., 1975). However, one should keep in mind that complete remission could only be achieved in 10—15% (Table 2). In hirsutism a satisfactory therapeutic effect needs a longer period of treatment. Complete success (4.1%) as well as partial therapeutic effect (71.2%) is less pronounced. This is an agreement with data published so far (Schindler, 1977).

In view of the known effect of estrogen/gestagen combinations on the menstrual pattern (e.g. after the use of oral contraceptives), it appears of particular interest that BBT remained biphasic before and after therapy in 47.7%, while in 32.9% improvement was seen after discontinuation of medication. Only in 3% anovulation occured. So far, improvement of the menstrual pattern after therapy with cyproterone acetate has been reported by Nardi et al. (1975). Hammerstein et al. (1975) mentioned a rapid resumption of spontaneous menstruation after discontinuation of cyproterone acetate/ethinyl estradiol medication. Possible explainations for these findings have been discussed elsewhere (Schindler, 1976).

The data demonstrates that the reduction of the estrogen dose from 0.05 to 0.04 mg daily and the length of treatment to 20 days is possible without loss of treatment efficiency or cycle control. It appears noteworthy that in more than 50% of the patients body weight did not change under therapy. And the number of patients gaining or loosing weight while on therapy was nearly equal. This moderate effect on weight gain noted in the study could be due to the decreased estrogen dosage. Although satisfactory treatment results have been recently published using a combination of 2 mg cyproterone acetate and 0.05 mg ethinyl estradiol (Kaiser et al., 1976), the overall effectiveness of the present treatment regimen and that of Hammerstein and Cupceanco (1969) will be not obtained. Therefore, it appears appropriate to use the latter treatment regimens for initial therapy and to preserve the therapeutic effect by continuation with the preparation containing 2 mg cyproterone acetate. According to recent reports, this lower-dose-formula can be effectively used if treatment is aimed primarely at acne and seborrhea alone (Aydinlik and Lachnit-Fixon, 1977; Schmidt-Elmendorff and Steger, 1977).

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