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Spironolactone and Cimetidine in Treatment of Acne

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Hatwal A, Bhatt RP, Agrawal JK, Singh G, Bajpai HS. Spironolactone and cimetidine in treatment of acne. Acta Derm Venereol (Stockh) 1988; 68: 84–87.

In an open therapeutic trial, 50 patients with acne vulgaris were randomly allocated to one of two groups. One group received spironolactone 100 mg daily and the other cimetidine 1.6 g daily for 12 weeks. Clinical severity of acne and sebum excretion decreased significantly at the end of the trial with both drugs, but significantly more with spironolactone. Mean serum levels of testosterone, androstenedione and dehydroepiandrosterone-sulfate decreased significantly with spironolactone but showed no change with cimetidine. Our data suggest that spironolactone may be useful as antiandrogen in the short term therapy of acne vulgaris. *Key words: Sebum; Antiandrogen; Testosterone; Androstenedione and dehydroepiandrosterone-sulfate.* (Received June 12, 1987.)

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As androgenic hormones increase sebaceous gland activity and predispose to acne vulgaris, antiandrogens have been used in the treatment of acne (1, 2). However, drugs like estrogens and cyproterone-acetate are limited by their side effects. The aldosterone antagonist spironolactone and the H2-receptor blocker cimetidine have antiandrogen effects (3, 4) and both have relatively very few side effects. There are only isolated studies of their use in acne (5, 6). This study was done to evaluate the efficacy of these drugs in short term treatment of acne.

MATERIAL AND METHODS

A total of 50 patients with moderate to severe acne vulgaris (30 females, 20 males) entered the trial after giving their informed consent (age range 14–25 years; peak age incidence 20–22 years). A history of partial or no response to conventional treatment for acne was present in all the patients.

The patients were randomly allocated to one of two therapeutic groups. 25 patients (15 females, 10 males) received oral spironolactone 100 mg/day while the other 25 (16 females, 9 males) received oral cimetidine 1.6 g/day in divided doses for a period of 12 weeks. These dosages were elected as 1.6 g and 100 mg are the usual safe average daily doses of cimetidine and spironolactone in their use as H2

Table I. *Acne severity index, sebum excretion rate (SER) and serum androgen levels in male and female patients of acne before and after 12 weeks treatment with spironolactone (mean ± SD)*

	Females (n=14)			Males (n=9)		
	0 week	12 weeks	p	0 week	12 weeks	p
Acne Severity Index	74±28.1	32.4±22.4	<0.001	103±38	47.7±30	<0.001
SER (μg/cm²/min)	0.5±0.18	0.19±0.11	<0.001	1.02±0.2	0.56±0.1	<0.001
Testosterone (nmol/l)	3.8±2.0	2.6±1.7	<0.05	20.9±3.0	19.4±3.1	NS
DHEA-S (μmol/l)	8.7±1.7	6.8±1.3	<0.001	8.0±1.7	6.1±1.3	<0.001
Δ^4A (nmol/l)	8.4±2.2	6.4±2.4	<0.02	7.6±1.6	6.0±2.1	<0.05

receptor blocker and diuretic respectively. Before starting therapy, the patients were told to discontinue any form of local or systemic therapy for acne. No patient had received any hormonal treatment earlier and was not receiving any other drug or oral contraceptive concurrently.

The grading of acne severity was done before and after the trial by the objective scoring method of Michaëlsson et al. (7) by the same observer in the morning in natural light.

Sebum excretion rate (SER) was measured before and after therapy by the method of Strauss & Pochi (8) as modified by Cunliffe & Shuster (9), using cigarette paper over a defined area on the forehead. The results were expressed in micrograms per centimeter square per minute (μg/cm²/min).

Venous blood samples were collected between 0800–0900 hours for assay of serum testosterone, androstenedione (Δ^4A) and dehydroepiandrosterone-sulfate (DHEA-S) and for measurement of serum creatinine and electrolytes before and after the trial. Immediately after collection the sera were separated and stored at −20°C till assay. In females the hormone samples were taken only in the first half of the follicular phase of the menstrual cycle, at which time the trial was also begun.

All hormones were determined by radioimmunoassay using standard techniques (Table I) with commercially obtained kits. For testosterone and Δ^4A the kits were obtained from RSL Laboratories, Denville, NJ, USA and for DHEA-S from Biotec Inc., Minneapolis, Minnesota, USA. The inter- and intraassay co-efficients of variation were: 4.2% and 6.0% for testosterone, 10.4% and 8.0% for Δ^4A and 8.7% and 5.5% for DHEA-S.

Serum creatinine was measured by alkaline picrate method (10) and serum potassium by flame photometry (10) using Corning 400 flame photometer.

The results of serum measurements and SER were compared by Student's t-test.

RESULTS

Out of the 50 patients included in the trial, 47 completed the trial protocol and were included in the analysis of the results. Three patients dropped out for unknown reasons. No significant side effect was reported with either drug.

All patients had moderate to severe acne. Pustules and nodules were the commonest lesions; 8 patients had cystic acne while 32/47 patients also had lesions on the trunk. The acne severity index decreased significantly with either drug in males and females (Tables I and II). The mean ± SD per cent reduction in acne severity was significantly greater with spironolactone than with cimetidine in males (55.0±5.5% vs. 32.0±10.0%; p<0.001) and also in females (63.2±17.6% vs. 47.7±19.9%; p<0.05).

Spironolactone as well as cimetidine reduced the SER significantly after 12 weeks (Tables I and II). However, the mean per cent reduction in SER was significantly greater with spironolactone than with cimetidine in males (45.3±5.7% vs. 21.4±12.8%; p<0.001) as well as in females (59.6±18.8% vs. 24.7±11.6%; p<0.001).

After 12 weeks, the mean ± SD serum levels of testosterone, DHEA-S and Δ^4A decreased significantly in patients receiving spironolactone (Table I), except in males in

Table II. *Acne severity index, sebum excretion rate (SER) and serum androgen levels in male and female patients of acne before and after 12 weeks treatment with cimetidine (mean ± SD)*

	Females (n=15)			Males (n=9)		
	0 week	12 weeks	p	0 week	12 weeks	p
Acne Severity Index	81.4±32.2	44.0±29.0	<0.001	91±32	60±18	<0.01
SER (μg/cm^2/min)	0.63±0.21	0.45±0.1	<0.001	0.91±0.23	0.73±0.27	<0.001
Testosterone (nmol/l)	3.7±1.0	3.5±0.8	–	21.4±3.1	21.5±4.5	–
DHEA-S (μmol/l)	8.1±1.1	8.2±1.3	–	7.9±2.2	8.1±1.8	–
Δ^4A (nmol/l)	8.5±3.3	8.6±3.5	–	7.6±1.9	7.0±2.8	–

whom the fall in testosterone levels was not significant. In the cimetidine group there was no appreciable change in the serum levels of either of the androgens (Table II).

There was no significant change in serum creatinine and potassium levels in either treatment groups.

DISCUSSION

The significant reduction in sebum secretion with either drug is in accordance with the clinical remission of acne observed in our patients. Spironolactone was significantly more effective than cimetidine in reducing SER and improving acne clinically.

Since cimetidine acts as a peripheral antiandrogen (3), and causes no significant change in serum testosterone levels (11), it may be offsetting its own antiandrogenic effect by causing a marginal increase in androgen secretion through negative feedback. On the contrary, spironolactone has been shown to inhibit androgen biosynthesis and decrease serum testosterone levels (4). This difference of action may explain the greater effectiveness of spironolactone in reducing SER in our study.

There was no significant change in serum potassium levels with the dosage of spironolactone used which is to be expected with normal renal function. No male patient developed gynaecomastia or decreased libido. However, long term studies are required to evaluate the side effects and remission of acne after drug withdrawal. We suggest that spironolactone may be safely used as short term therapy to tide over a severe phase of acne and perhaps to aid the conventional methods of therapy to act better.

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Axillary Hyperhidrosis. Local Treatment with Aluminium-chloride Hexahydrate 25 % in Absolute Ethanol with and without Supplementary Treatment with Triethanolamine

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Glent-Madsen L, Dahl JC. Axillary hyperhidrosis. Local treatment with aluminium-chloride hexahydrate 25% in absolute ethanol with and without supplementary treatment with triethanolamine. Acta Derm Venereol (Stockh) 1988; 68: 87–89.

In a randomized, double-blind, half-sided experiment, 30 volunteers were treated in both armpits with aluminium chloride hexahydrate 25% in ethanol. In order to neutralize pH and thus reduce the skin irritation, post-treatment was performed in one armpit with triethanolamine 50% in ethanol. The sweat production was measured after physical labour by means of a combined colorimetric/gravimetric method. The combined treatment with aluminium chloride hexahydrate and triethanolamine was found to be statistically significantly ($p<0.01$) less irritating to the skin, but also statistically significantly ($p<0.01$) less effective than treatment with aluminium chloride hexahydrate alone. However, the reduction in the effect of the treatment was not of a sufficient extent as to be noticed by the volunteers themselves. *Key words: Antiperspirant; Sweating.* (Received January 26, 1987.)

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The best medicinal treatment for axillary hypertridrosis is aluminium-chloride hexahydrate (ACH) dissolved in ethanol (1–2). In a double-blind, controlled experiment, aluminium chloride 20% in ethanol was thus found to have a beneficial effect in 24 out of 38 patients whose sweat problems were so great that they were referred for plastic surgery (3). 19 patients found the topical treatment so satisfactory that they avoided the operation.

A frequent cause of discontinued treatment was unacceptable skin irritation, which has also been recorded by other authors (2). Furthermore, there has been a tendency towards decomposition of clothes near the armpits. For this reason, the American Food and Drug Administration has recommended that alcoholic solutions with aluminium chloride should only be dispensed on doctor's prescription (4). There is thus need to avoid or at least reduce skin irritation during treatment. Triethanolamine (TEA) is assumed to neutralize the hydrochloric acid developed on the surface of the skin without substantially affecting the aluminium chloride solution which has penetrated into the sweat glands.

The purpose of the test was to establish whether skin irritation following treatment with ACH 25% in ethanol is reduced by post-treatment with TEA 50% in ethanol, and whether the sweat-reducing effect is influenced by this combination treatment.

MATERIALS AND METHODS

The test was carried out as a randomized and double-blind half-sided experiment. The volunteers were treated in the evening every 48 h during the course of 3 weeks. The persons had been instructed