

## THERAPEUTIC EVALUATION OF SPIRONOLACTONE AND CIMETIDINE IN HIRSUTISM —A COMPARATIVE STUDY

by

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### SUMMARY

The study was conducted on two groups (20+20) of hirsute women to evaluate and compare the beneficial and side effects of Spironolactone and Cimetidine. There was a steady and significant decline in hair growth in 60% (12/20) subjects with Spironolactone ('S') as opposed to only 30% (6/20) with Cimetidine ('C'). Hair became lighter in 65% (13/20) with 'S' and 55% (11/20) with 'C'. Coarse hair became softer in 65% (13/20) with 'S' and 55% (11/20) with 'C'.

Face was the most responsive site showing improvement in maximum number of patients with 'S' and 'C'. Beneficial effects were evident within 2-6 months and maximum response was achieved within 9-12 months of initiation of therapy with 'S' and 'C'. Adverse effects were mild and transitory in most of the cases with both the above drugs.

### Introduction

Treatment of hirsutism is a therapeutic dilemma. A variety of methods and drugs for control of hirsutism have been tried but none has proved to be consistently successful. Thus a drug interfering at the glandular and peripheral level would appear to be the ideal agent. Spironolactone, an aldosterone antagonist inhibits androgenic action of testosterone by occupying the binding sites of cytosol and nuclear receptors in target cells in-

cluding hair follicles (Cumming *et al* 1982). Cimetidine, a H<sub>2</sub> receptor blocker has only recently been found to possess anti-androgenic action by occupying androgen receptors. (Funder and Mercer, 1979). Thus the present study was initiated to evaluate and compare the therapeutic and side effects of these two drugs in hirsute women.

### Material and Methods

Forty hirsute women (12-40 years) were enrolled for the study. Patients with adrenal/ovarian tumour were not included in the study. An assessment of the severity of hirsutism was done before, during and after the treatment by using total body hair scoring method of

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Ferriman and Gallaway (1961). A detail history, clinical examination, relevant biochemical and biophysical (ultrasound) investigations were done to establish the diagnosis and to exclude ovarian/adrenal tumour. Patients were advised to avoid pregnancy during the treatment cycles. During the first 3 months patients were given a placebo. They were then switched over to either Spironolactone (S) (100 mg) or Cimetidine (C) (1400 mgm) from the 5th-25th day of the menstrual cycle in patients with regular cycles and for 21 days with 7 days' gap in patients with irregular cycles. Patients were given (alternatingly) Spironolactone or Cimetidine (20 + 20). Evaluation of treatment was done by noting change in total body hair score, improvement in quality of hair, frequency of hair removal, changes in menstrual pattern, improvement in acne and oiliness of the skin. Response was considered to be significant when decrease in hair score was  $\geq 6$  points.

#### Results

The mean age of the hirsute patients was 21.8, range being 12-40 years and mean age of onset of hirsutism was 18.1 range being 12-30 years. The mean duration of hirsutism was 3.8 range being 3-16 years. A positive family history of hirsutism could be elicited in 50% (20/

40). Menstrual cycles were irregular in 40% (16/40), Obesity was present in 31% (12/40) and ovarian enlargement was observed (by ultrasonography) in 87.5% (35/40).

Total body hair score of the hirsute women (20 + 20) is depicted in Table I. Clinical response to Spironolactone and Cimetidine is depicted in Table II.

TABLE I  
Total Body Hair Score

Score	Hirsute N = 20 + 20
$\leq 10$	2 — 5%
11-20	18 — 45%
21-30	17 — 42.5%
$\geq 30$	3 — 7.5%
Mean	20.7
Range	9-32

Decline in hair growth was significant in 60% (12/20) with Spironolactone as opposed to 30% (6/20) subjects with Cimetidine. Face was the most responsive site showing improvement in all patients who showed improvement in total body hair score with Spironolactone and Cimetidine. The least responsive sites were chest, upper abdomen and back. It was further observed that beneficial effects were first evident over the face, and later over the chest, upper abdomen and back. The quality of hair

TABLE II  
Clinical Response of Spironolactone and Cimetidine in Hirsutism

	Spironolactone N = 20		Cimetidine N = 20	
	%	N	%	N
Decrease in hair growth	60	12	30	6
Colour lighter	65	13	55	11
Texture softer	65	13	55	11
Decrease in frequency of hair removal	75	9/12	66.7	6/9
Improvement in menstrual pattern	70	7/10	50	3/6

improved in both the groups. Hair colour became lighter in 65% (13/20) with 'S' as compared to 55% (11/20) with 'C'. Hair became softer in 65% (13/20) with 'S' as compared to 55% (11/20) with 'C'. Frequency of hair removal also showed a decline in 75% (9/12) with 'S' and in 66.7% (6/9) with 'C'. Improvement in menstrual pattern was observed in 70% (7/10) with 'S' and in 50% (3/6) with 'C'. Beneficial effects were evident within 2-6 months but a significant response was achieved with 9-12 months of therapy.

Side effects were observed in 4 patients with 'S' and in 3 patients with 'C'. The side effects observed were giddiness, weakness, lack of concentration, nausea and vomiting, lithargy, headache, blurring of vision. All these side effects disappeared on continuation of treatment except for giddiness, loss of concentration and menstrual dysfunction.

#### Discussion

Decreased testosterone formation, increased peripheral conversion of testosterone to estradiol and competitive inhibition of the binding of DHT to its receptors by Spironolactone was observed by Menard *et al* (1974), Rose *et al* (1977) and Rifka *et al* (1979).

Thus these antiandrogenic properties of Spironolactone were tested in 20 hirsute women. Hair growth decreased substantially in 60% (12/20). The quality of hair changed for better i.e. texture becoming less coarse and softer in 65% (13/20). It also became lighter in 65% (13/20). The return of cyclic pattern of menses was observed in 70% (7/10). The beneficial effects were evident within 2-6 months but maximum response was achieved after 9-12 months of the commencement of the therapy. Effect of the

treatment varied depending upon the site. Face being the most responsive site where a steady decline in hair density and improvement in quality of hair was observed among all the responders.

Shapiro and Evrons (1980) observed a progressive decrease in hair growth, improvement in quality and colour of hair and menstrual function after 13 months of the start of Spironolactone therapy in 23/30 hirsute women. Regression of hirsutism was also noted by Cumming *et al* (1982) with Spironolactone within 6 months of initiation of the therapy. The inhibition of hair growth could be registered in 57% (12/21) improvement in texture in 52% (11/21) and colour becoming lighter in 38% (8/21) by Neilson (1982).

Side effects were observed in 4 patients with 'S' and in 3 patients with 'C'. The side effects observed were giddiness, weakness, lack of concentration, nausea and vomiting, lithargy, headache, blurring of vision. All these side effects disappeared on continuation of treatment except for giddiness, loss of concentration and menstrual dysfunction.

However, periodic breaks in medication did not diminish the efficacy of the therapy. Shapiro and Evrons (1980) observed polydipsia, headache, weight gain, increase in appetite, weakness, tiredness and lassitude with Spironolactone therapy.

The results of our study divulged that Spironolactone was able to suppress androgenic activity in skin which is one of the major site of androgen metabolism. Rose *et al* (1977) state that the underlying mechanism of beneficial results of 'S' are probably because it lowers the circulating testosterone level by increasing the metabolic clearance rate of testosterone and prevents compensatory rise in ad-

renal and or ovarian androgen production.

With Cimetidine significant decline in hair score was observed in only 30% (6/20). Whereas, Vigersky *et al* (1980) found a significant decrease in rate of hair growth in 4/5 hirsute patients. Funder and Mercer (1979) state that the beneficial effects of Cimetidine are probably due to its ability to block androgen action, by inhibiting binding of dihydro testosterone to androgen receptors.

Side effects were observed less often with both the drugs in our series. Thus our study revealed that both the drugs 'S' and 'C' are effective in hirsutism but therapeutic response is much better with 'S' than with 'C' (Table II).

However, a careful clinical and biochemical monitoring of the patients is very essential to avoid, detect and treat hypokalemia, endocrinal, systemic and other serious side effects and complications. Patients are advised to avoid pregnancy

while on treatment since embryo toxicity of these drugs has not been ruled out.

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