



THE EFFECT OF SPIRONOLACTONE IN IDIOPATHIC HIRSUTE WOMEN

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ABSTRACT

Idiopathic hirsutism also defined as peripheral hirsutism is a consequence of modified androgen metabolism at the peripheral level. An attempt has been made in the present work to study the clinical efficacy of spironolactone in diagnosed cases of idiopathic hirsutism, attending Endocrinology clinic, at Government Rajaji Hospital Madurai. The study has also been extended further to correlate its clinical efficacy to the plasma level of 3α AdG as an easier and reliable diagnostic as well as prognostic approach to judge the androgenic activity in hirsute women. Spironolactone was administered in the dosage of 100 mg/day for 30 days in selected cases of idiopathic hirsute women and the plasma level of 3α AdG is estimated before and after medication. The Study reveals an increase in 3α AdG levels in the plasma after spironolactone therapy. It is found to be well correlated with the clinical improvement. During the study period of one month no disturbing side effects have been noticed.

KEYWORDS: Hirsutism, 3α AdG (Androstenediol Glucoronide), Spironolactone.



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INTRODUCTION

Hirsutism is a male pattern of hair growth in women. Androgens are the principle determinants of hirsutism. These androgens are converted into testosterone or dihydrotestosterone (DHT). These metabolites bind to androgenic receptor including hair follicles, and induce an androgenic response. The conversion of testosterone to DHT is mediated by the enzyme 5 α reductase in the skin. Dihydrotestosterone is further reduced to 3 α androstane diol and further into 3 α androstane diol glucuronide (3 α AdG). 3 α AdG has been estimated as a marker of target tissue cell action [1]. The level of 3 α androstane diol glucuronide is found to be elevated in Idiopathic hirsutism [2]. Management of Hirsutism has been strikingly influenced by the introduction of anti-androgen besides local/cosmetic treatment. Spironolactone, an antiandrogen appears to act by increasing the metabolic clearance rate of Testosterone. Its efficacy in Idiopathic hirsutism has been evaluated by several workers. An attempt has been made in the present work to study the clinical efficacy of spironolactone in diagnosed cases of Idiopathic hirsutism attending Endocrinology clinic at Government Rajaji Hospital, Madurai

MATERIALS AND METHODS

The study was undertaken in Hirsute women diagnosed as Idiopathic Hirsutism attending the Department of Endocrinology, Government Rajaji Hospital, Madurai, with the approval of the Hospital Ethical-committee and patients informed consent. Ten Volunteers, 5 men and 5 women of the age group (19-50) were included in the study as control. Twenty Idiopathic hirsute women of 19-50 years age group, body weight (40 to 60 kg) were included for the study after getting informed consent. Patients with adrenal or ovarian malignancies, renal and hepatic

diseases, Grade '0' Hirsutism were excluded. Pregnant and lactating mothers were also not included. The procedure follows the basic principles of radio immuno assay. Tablet spironolactone 25 mg Arvind Remedies Ltd. Company available in the hospital were used for the study. Patients were treated with a dose of 100 mg administered as 2 tablets twice daily for 30 days. Blood samples were taken before and 30 days after medication for estimation of plasma level of 3 α androstane diol glucuronide. Patients were directed to attend the outpatient department every week, and efficacy was evaluated clinically with improvement in symptom and sign of Hirsutism, frequency of local cosmetic therapy as well as biochemically with the value of plasma 3 α androstane diol glucuronide. Observations were tabulated, investigation reports recorded and statistical analysis of results were made using students 't' test.

RESULTS

Twenty cases of idiopathic hirsute women were chosen for this study. The estimation of 3 α androstane diol glucuronide in the plasma of these patients were studied by Radio-immuno Assay method using DSL 9200 kit. The level of 3 α AdG is noted in these patients before and after treatment with spironolactone administered in the dosage of 100 mg daily for 30 days.

CONTROL STUDY

Plasma levels of 3 α AdG in normal men shows higher level as expected, A comparative study between normal women and Hirsute women shows a significant rise in 3 α androstane diol glucuronide in hirsute women. (Table 1 & 2 and Fig 1).

TABLE 1
LEVEL OF 3 α AdG IN CONTROL GROUP

GROUPS	LEVEL OF 3 α AdG IN PLASMA
Normal men (mean 5)	12.5 ng/l
Normal women (mean 5)	0.5 ng/l

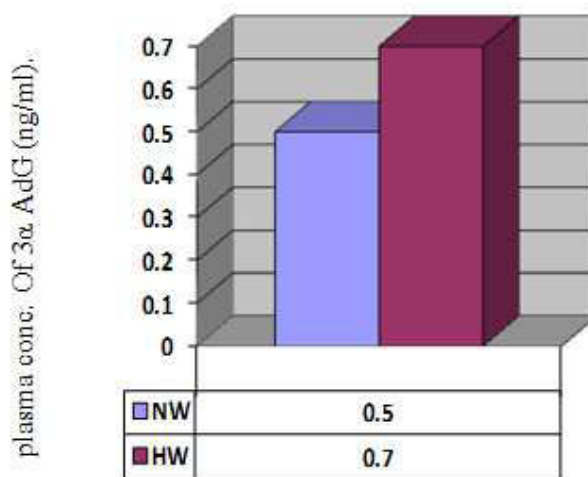
TABLE 2
LEVEL OF 3 α AdG IN HIRSUTISM

GROUPS	LEVEL OF 3 α AdG IN PLASMA
Normal Women (5)	0.5 ng/l
Hirsute women (20)	0.7 ng/l

*P** < 0.01 significant*

LEVEL OF 3 α AdG IN HIRSUTISM

FIGURE 1



The level of 3 α AdG is noted in the selected patients before and after treatment with spironolactone (Table 3 & 4). Spironolactone treatment for 30 days in selected cases of idiopathic hirsutism shows a significant increase in the level of 3 α AdG as compared to its level before treatment (Fig 2).

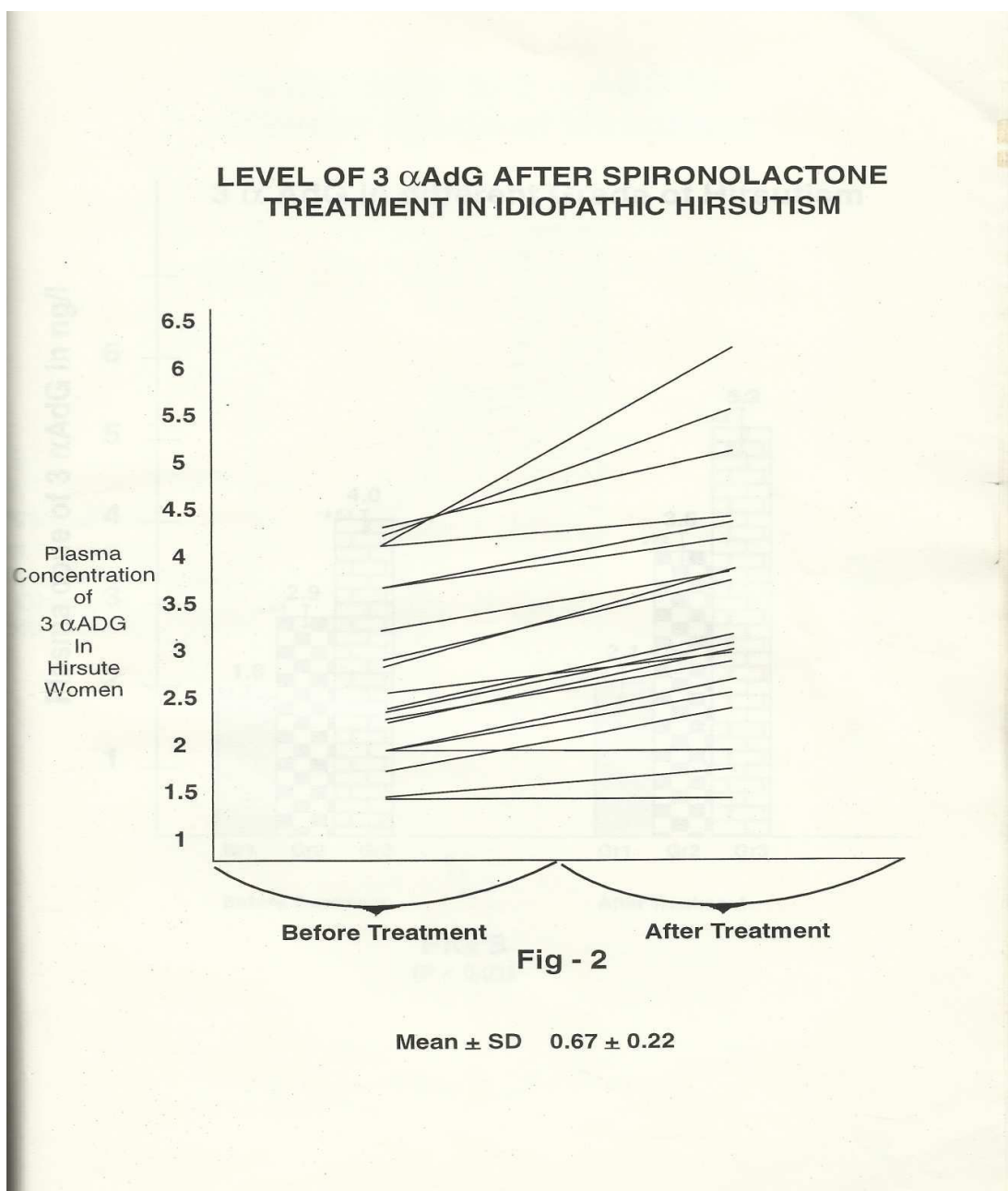
TABLE 3
CASE VALUES OF PLASMA 3 α AdG ng/l IDIOPATHIC HIRSUTE PATIENTS

Sl.No.	Before Treatment	After treatment
1.	1.90	5.57
2.	1.40	1.40
3.	4.27	4.76
4.	2.82	3.65
5.	2.51	2.67
6.	2.72	3.87
7.	4.07	5.46
8.	2.28	2.89
9.	1.90	1.90
10.	3.65	4.39

TABLE 4
CASE VALUES OF PLASMA 3 α AdG ng/l IDIOPATHIC HIRSUTE PATIENTS

Sl.No.	Before Treatment	After treatment
11.	2.25	2.63
12.	3.20	3.65
13.	1.75	2.25
14.	4.01	4.27
15.	4.01	6.26
16.	3.65	4.27
17.	1.90	2.50
18.	1.48	1.56
19.	2.38	3.18
20.	2.36	3.05

($p^{**} < 0.01$ significant) Mean + SD = 0.67 + 0.22



DISCUSSION

The present study on spironolactone has shown significant clinical improvement correlated with increased level of 3α AdG^[3] in hirsute women. A comparatively high level of 3α AdG in hirsute women than normal women suggests that there is a proportionate increase in the metabolic breakdown of circulating androgen. This metabolic abnormality becomes more severe as the disease progresses. The mechanism of action of spironolactone may be explained as inducing the metabolite turnover of testosterone, leading to elevation of 3α AdG and androgenic clearance effect in plasma^[4]. It may also act by decreasing synthesis and production of testosterone, by competitive

inhibition of testosterone binding at receptor site^[5].

CONCLUSION

Spironolactone has shown significant improvement clinically & biochemically in idiopathic hirsute women. Clinically it improved symptoms, signs & it is confirmed by the estimation of 3α AdG^[5], a prognostic index of clinical improvement. Hence circulating androgen level decreases and becomes less effective in stimulating hair growth. During the study period, no disturbing side effects have been noticed with spironolactone treatment.

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