

# THE EFFICACY OF FLUTAMIDE, AN ANTIANDROGEN IN IDIOPATHIC HIRSUTISM

**V K Somani, V Sucharita, V K Sharma, VNVL Sita, Fatima Razvi,  
Ramesh Bang**

The efficacy of flutamide, an antiandrogen in idiopathic hirsutism was studied. The long term effects of treatment with low doses of flutamide on clinical and hormonal parameters were investigated. Nine patients with idiopathic hirsutism were studied basally and during treatment with 125mg flutamide thrice daily for a period of 9 months. Safety parameters were assessed throughout the study. Hirsutism was graded by Ferriman and Gallwey score and hormones were evaluated basally and later quarterly. After three months of therapy, flutamide had caused a significant alleviation of hirsutism and this continued during the subsequent months. No clinical significant side effects were observed during the period of the study. Biochemical and hormonal parameters remained unchanged after 9 months of flutamide.

**Key words : Flutamide, Hirsutism, Antiandrogen**

## Introduction

Hirsutism is a common clinical condition characterised by abnormal growth and male distribution of hair in women. It is a singularly distressing condition, in that it is not only psychologically disturbing but also exposes them to ridicule and social rejection. Excess androgen production by either ovaries or adrenals or heightened sensitivity of hair follicles to normal androgen levels can lead to hirsutism. Other features of increased androgenism include acne, seborrhoea, alopecia etc. Even

partly successful therapy would be extremely welcome and has much to offer in terms of psychological and cosmetic benefits.

Therapeutic intervention in the treatment of increased androgenic clinical state may be directed at the source of androgens or at the level of their target tissue. The antiandrogen drugs have either a steroidal structure, such as cyproterone acetate (CPA) and spironolactone or a non steroidal structure such as flutamide.

CPA is a progestogen having an antiandrogenic and antigonadotrophic activity and is ideal for hyperandrogenic hirsutism.<sup>1</sup> Spironolactone is an aldosterone antagonist but it also inhibits testosterone synthesis and increases conversion of tes-

---

From the Department of Skin and VD, Deccan College of Medical Sciences, Princess Esra Hospital, Shah Ali Banda, Hyderabad, A.P, India

**Address correspondence to:**  
Dr. V K Somani, 'Sanskar', 2-1-438/A  
Nallakunta, Hyderabad 500 004

---

tosterone to oestradiol. Flutamide is the only antiandrogen that blocks specifically androgen receptors without glucocorticoid, progestational, androgenic or oestrogenic activity. Flutamide appears to exert its antiandrogenic effects by inhibiting uptake and / or by suppressing nuclear binding of androgen in the target tissue where it seems to form inactive complexes with androgen receptors.<sup>2</sup> A recent study indicates that flutamide decreases cytochrome P 450 content in testicular microsomal fraction in male rats.<sup>3</sup> It has also been found to suppress biosynthesis by inhibiting rat testicular microsomal 17-20 hydroxylase and 17 - 20 lyase activity.<sup>4</sup> Several dosage schedules have been used in various studies from 250mg thrice daily to 125mg twice daily.<sup>1</sup> The objective of the present study was to evaluate the safety and efficacy of a pure antiandrogen, flutamide alone, in an uncontrolled open label study in the treatment of hirsutism. Another aim in this study was to devise a dosage schedule for Indian women as there have been no reports of flutamide usage in Indian patients.

## Materials and Methods

Nine consecutive patients between 18 - 30 years with idiopathic hirsutism were studied. Written informed consent was obtained. Each patient underwent a complete medical and gynaecological examination besides endocrine, haematological, hepatic and renal pro-

file. Pelvic ultrasonography was done to rule out polycystic ovarian disease. Hirsutism scores were determined according to the "Ferriman - Gallwey" scoring system.<sup>5</sup> Eleven body sites were studied - lip, chin, chest, upper abdomen, arm and back of the forearm, thigh and the leg. Only terminal hair growth was considered and five grades were determined (0,1,2,3,4), zero grading indicating absence of terminal hair. Definitions of gradings are shown in **table.I**. Hair growth was scored according to the sum of gradings obtained. A score of >10 was taken as the threshold for hirsutism. The patients had not received hormonal therapy prior to this study.

These patients were given 125mg of flutamide three times a day for a period of 9 months. Married women liable to get pregnant were advised against it by using non hormonal methods. Patients were followed up for clinical and hormonal parameters quarterly. The hormonal assay included FSH, LH, serum testosterone and dihydroepiandrosterone sulphate (DHEAS). Effort was made to collect blood samples in the same week of the menstrual cycle (luteal phase) in all the patients. Hepatic and renal status was reassessed at the end of 9 months. Patients were seen monthly and evaluated for hirsutism, acne and seborrhoea. During follow up any untoward effects of treatment were recorded in each patient. The patients were advised not to use any mechanical depilatory methods during the study period.

## Results

Clinical improvement in the degree of hirsutism was observed in all the patients treated with 375mg of flutamide daily. The Ferriman - Gallwey scores for hirsutism decreased significantly, first noted after 3 months of therapy, which continued throughout the study period and were back to normal values for premenopausal women in most of the patients after 9 months of therapy. Two of the 9 patients developed menstrual irregularities, one oligomenorrhoea and one amenorrhoea. One patient complained of worsening of her acne, which later responded to topical antiacne therapy. Dry skin was observed in 3 patients but no other side effects were observed in any of the nine patients.

Renal and hepatic parameters were unchanged at the end of the therapy. Basal level of LH and FSH were normal before and after the end of treatment. Serum testosterone and DHEAS levels showed no significant change at the end of the therapy (Table II).

## Discussion

Of the various antiandrogen drugs available, flutamide appears to be the best because it inhibits hair growth without any significant side effects such as disturbances in menstruation and dry skin. Long term flutamide therapy has no effect on ovarian and adrenal androgen levels in women.<sup>6</sup> It acts solely by blocking andro-

gen receptors. Moreover cessation of antiandrogen therapy at nine months was associated with a much slower return of hirsutism in flutamide, when compared to spironolactone.<sup>7</sup>

Oral contraceptives are generally prescribed along with flutamide, for they not only prevent pregnancy to preclude the possibility of feminization of a male foetus but also have an additive effect in combating hirsutism.<sup>2</sup> Patients intolerant to oral contraceptives and unmarried women reluctant to take oral contraceptives are ideal candidates for flutamide therapy alone. Since the efficacy of low dose of flutamide (125mg twice daily) was comparable to higher dose (500 mg to 750mg),<sup>1</sup> and considering the economic constraints and smaller body mass of Indian women, we decided to use slightly higher than the minimum effective dose as flutamide was used alone. As there does not seem to be any study regarding flutamide in Indian women to the best of our knowledge, we also wanted to arrive at a dosage schedule for Indian women. The optimum duration of treatment was kept at nine months as most of the earlier studies indicated the same.

The patients began showing significant improvement by third month of therapy as noted in earlier studies,<sup>1,7,8</sup>. There was reduction in the hirsutism grading and the diameter of hair decreased in accordance with an earlier study.<sup>9</sup> The effect was most obvious initially on the face followed

Table I. Ferriman and Gallewey score

Definition of hair gradings at each of 11 sites(Grade - 0 at all sites indicates absence of terminal hair)

Site	Grade	Definition
1. Upper lip	1	A few hairs at outer margin
	2	A small moustache at outer margin
	3	A moustache extending halfway from outer margin
	4	A moustache extending to mid-line
2. Chin	1	A few scattered hairs
	2	Scattered hairs with small concentration
	3 & 4	Complete cover, light and heavy
3. Chest	1	Circum areolar hairs
	2	With midline hair in addition
	3	Fusion of these areas with 3/4th cover
	4	Complete cover
4. Upper back	1	A few scattered hairs
	2	Rather more, still scattered
	3 & 4	Complete cover
5. Lower back	1	A sacral tuft of hair
	2	With some lateral extension
	3	Three quarter cover
	4	Complete cover
6. Upper abdomen	1	A few mid - line hairs
	2	A mid - line streak of hair
	3 & 4	Half and full cover
7. Lower abdomen	1	A few mid -line hairs
	2	A mid - line streak of hair
	3	A mid-line band of hair
	4	An inverted V-shaped growth
8. Arm	1	Sparse growth not more than 1/4th limb surface
	2	More than this; cover still incomplete
	3 & 4	complete cover, light and heavy
9. Forearm	1,2,3,4	Complete cover of dorsal surface; 2 grades of light and 2 of heavy growth
10. Thigh	1,2,3,4	As for arm
11. Leg	1,2,3,4	As for arm

Table II. Clinical and laboratory data of hirsute patients

Case no	Symptom duration in years	Age in years	Menses	Hirsuties Score	LH mIU/ml <sup>125</sup>	FSH MIA/ml	S.testosterone ng/ml	DHEAS ng/ml
1	5	18	S-O E-A	S-23 E-10	S-7.6 E-12	S-8 E-7.4	S-0.30 E-0.05	S-720 E-640
2	10	29	S-O E-O	S-26 E-17	S-5.6 E-9.2	S-7.9 E-6.8	S-3.3 E-2.4	S-2200 E-2500
3	4	20	S-N E-N	S-19 E-12	S-4.9 E-8.5	S-4.1 E-4.7	S-0.52 E-0.46	S-1340 E-1100
4	15	30	S-N E-O	S-22 E-10	S-6.2 E-5.7	S-8 E-7.2	S-0.39 E-0.6	S-790 E-710
5	6	19	S-O E-O	S-28 E-13	S-10 E-8.8	S-4.6 E-4.9	S-0.9 E-1.1	S-2400 E-2000
6	6	19	S-N E-N	S-30 E-14	S-10.8 E-11.4	S-6 E-8	S-1.8 E-0.8	S-3110 E-2900
7	2	18	S-N E-N	S-32 E-1	S-3.9 E-5.6	S-5.4 E-5.8	S-0.3 E-0.27	S-1220 E-1460
8	4	18	S-N E-N	S-20 E-12	S-4.8 E-4.3	S-2.9 E-2.4	S-0.6 E-0.4	S-900 E-760
9	4	18	S-N E-N	S-29 E-11	S-5.8 E-6.6	S-3.8 E-4.3	S-0.7 E-0.4	S-1600 E-1800

A-Amenorrhoea, O-Oligomenorrhoea, N-Normal menstrual cycle,  
S- At the start of treatment, E- At the end of treatment (9months)

later by trunk and lastly the limbs. Only minor side effects like menstrual irregularities, dry skin and acne were noted. Deterioration in acne on antiandrogen therapy has been noted earlier after CPA.<sup>10</sup> One case (case no.4) in our study had worsening of acne for about 3 months. This is in variance with earlier studies,<sup>8</sup> where no change in acne was noted. The hormonal parameters did not show significant change before and after the study, again implying the lack of any central effect of flutamide. This finding is in accordance with earlier studies.<sup>8,9</sup> Although a small number of patients in our study do not allow us to come to definitive conclusion, it still appears that the pure

antiandrogen flutamide is a potent therapeutic tool to fight hirsutism.

The dosage of 375mg/day is not only effective within a short period of time, but also remarkably safe and relatively economically affordable.

In conclusion, the results of this study clearly show the beneficial effect of flutamide in women with idiopathic hirsutism. Further the dosage of 375mg/day over a period of 9 months was free from any side effects. However further studies involving more number of patients over longer periods would be necessary to assess the efficacy and duration for which it lasts.

## References

1. Sylvie Dodin, Fure N, Isabelle Cedrin, et al. Clinical efficacy and safety of low dose flutamide alone and combined with an oral contraceptive for the treatment of idiopathic hirsutism. *Cli. Endocrinology* 1995;43:575-582.
2. Liliana Ciotta, Antonio Cianci, Laura Pisana, et al. Treatment of hirsutism with flutamide and a low dosage oral contraceptives in polycystic ovarian disease patients. *Fertil Steril* 1994;62:1129 - 1135.
3. Clos V, Esteve A, Jane F, et al. Microsomal effects of cyproterone acetate and flutamide in rat testis. *General Pharmacology* 1988;19:393-397.
4. Brogden RN, Clissold SP. Flutamide: a preliminary review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy in advanced prostatic cancer. *Drugs* 1989; 38: 185 - 203.
5. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrinol Metabol* 1961; 21: 1440 - 1447.
6. Cusan L, Dupont A, Tremblay R, et al. Treatment of hirsutism with pure antiandrogen flutamide. *J Am Acad Dermatol* 1990; 23: 462 - 469.
7. Cusan L, Dupont A, Gomez JL, et al. Comparison of flutamide and spironolactone in the treatment of hirsutism: a randomized controlled trial. *Fertil Steril* 1994; 61:281 - 287.
8. Marcondes AM, Minnani L, Bernardo L, et al. Treatment of hirsutism in women with flutamide. *Fertil, Steril*, 1992; 57: 513-547.
9. Franca Fruzzetti, Daniele De Lorenzo et al. Clinical and endocrine effects of flutamide in hyperandrogenic women. *Fertil Steril* 1993; 60:806 - 813.
10. Poyet P, Labrie F. Comparison of the antiandrogenic / androgenic activities of flutamide, cyproterone acetate. *Mol cell Endocrinol* 1985;42:283 - 288.