Efficacy and Safety of Topical Antiandrogen Fluridil in Hirsutism: a Pilot Study

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INTRODUCTION

Hirsutism is defined as an excessive male-pattern hair growth in women caused by androgen excess or hypersensitivity of hair follicles to androgens. In idiopathic hirsutism the serum androgen levels are normal and no other clinical syndromes, or an identifiable endocrine imbalance such as in the polycystic ovary syndrome is present. Idiopathic hirsutism belongs to the hyperandrogenic skin syndromes.
Although certain treatments can improve hirsutism, most medical therapies do not significantly reduce the unwanted hair growth and the treatments often turn out to be more palliative than curative.
Systemic therapy of hirsutism always requires a long-term treatment and the recurrences are frequent. Systemic therapy includes estrogens, antiandrogens and/or agents such as finasteride, corticosteroids, gonadotrophin-releasing hormone agonists, or insulin sensitizing agents.
Local therapy of hirsutism includes shaving, plucking, bleaching, depilatory creams and waxes, electrolysis, electrocoagulation and laser removal. Other possibility is eflornithine hydrochloride cream which directly affects the cell growth cycle of the pilosebaceous unit.
Fluridil (F) was developed as a topical antiandrogen for use in hyperandrogenic skin syndromes. Fluridil is formulated in isopropanol ("rubbing alcohol") which allows for solubility in the sebum to entry into the hair follicles, where F suppresses cutaneous androgen receptors. F is not systemically resorbed, and neither F nor its catabolites could be found in the serum of the test subjects by the HPLC method with a detection limit of 5 ng/ml. As a safety feature, should F accidentally enter the gastrointestinal tract or the circulation, its molecule was designed to be hydrolytically degradable into non toxic fragments BP-34 and trifluoracetic acid, both devoid of antiandrogenic activity ***(Fig. 1)***.

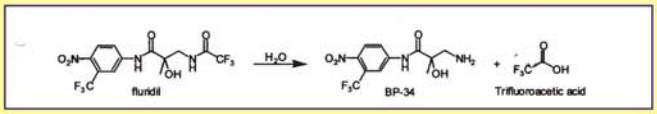

Fig.1. Fluridil and its hydrolytic decomposition

In a previous clinical study conducted by us, F has been shown effective and non-irritating safe in the treatment of men with androgenetic alopecia. We conducted a three-month pilot study to evaluate the efficacy and safety of F formulated as a gel, in female patients with idiopathic facial hirsutism.

MATERIAL AND METHODS

The test substance contained 2% fluridil, 5% Carbopol ETD 2050, and 93% isopropylalcohol.
The study included 10 females 25 to 68 years old with idiopathic facial hirsutism, selected from the outpatient population. On the day 0 photographic documentation and blood samples were obtained for total testosterone and sex hormone binding globulin (SHBG). 3 baseline photographs of the affected area ***(Fig. 2)*** were taken (front view, and right and left profile views). The subjects applied the test substance (about 1 g/day) over the affected area daily, in the evening for three months (i.e. a total of 100 g fluridil gel). On day 90 efficacy and tolerance of the preparation were assessed by a question-naire and physician and subject observation and a series of photographs was obtained ***(Fig. 3).***

RESULTS

1. Evaluation of efficacy:
a) by the subject:
Nine out of ten subjects observed and reported reduced rate of hair growth (7 patients), thinning of the hair stem (9 patients) and occasionally a loss or reduction of dark hair color (9 patients).
B) by physician:
Comparison of the photographs taken before and after fluridil use confirmed the subjective findings and showed reduced hair count in 9 subjects.
2. Evaluation of tolerance:
None of the 10 subjects reported undesirable effects over the course of treatment such as skin irritation, burning sensation, etc. Two subjects found the odor of isopropanol too intense immediately after the application.
All initial and final laboratory values were within normal range not with standing changes which however did not suggest any correlation between testosterone and/or SHBG levels, and the response to the treatment.

No fluridil nor its metabolites or products of decomposition were found in the serum using the HPLC method with detectability limit of 5ng/ml (Sovak et al., 2002).

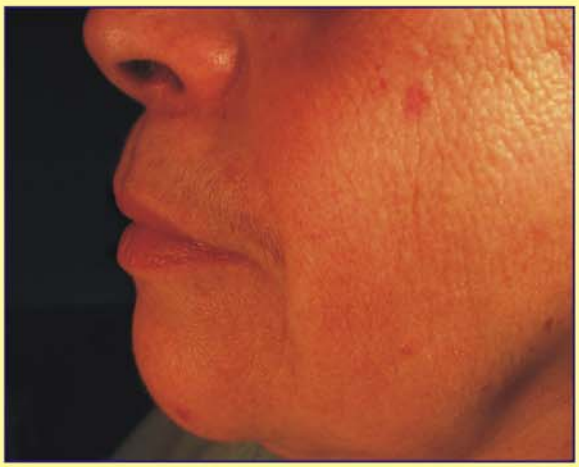

Fig. 2 Patient with facial hirsutism before fluridil treatment

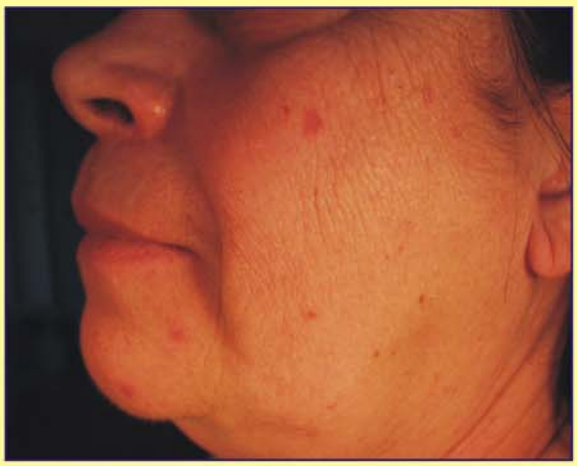

Fig. 3 Patient with facial hirsutism after 3-month fluridil treatment

CONCLUSION

Since hirsutism represents for most women a serious psychological problem, more efficacious alternatives to the current treatment methods should be developed.
The present pilot clinical study indicates that 2% fluridil is a safe and effective treatment method of hirsutism. Compared to systemic antiandrogens, the topical fluridil has no systemic effects, especially it does not affect the libido and/or sexual functions. None of the subjects experienced any local side effects such as skin irritation. In terms of its efficacy, fluridil appears to be a candidate for development for the hirsutism indication, both as monotherapy and possibly in combination with other treatment modalities.

REFERENCES

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