Journal of Pakistan Association of Dermatologists 2009; **19**: 90-94.

Original Article

Treatment of idiopathic facial hirsutism with medroxyprogesterone acetate iontophoresis

Muneeza Rizwan*, Ahsan Hameed

* Dermatology Department, Pakistan Aeronautical Complex Hospital, Kamra
** Dermatology Department, Shifa International Hospital, Islamabad

Abstract

Background Hirsutism is a major psychosocial problem amongst young girls and women. Medroxyprogesterone acetate (MPA) is a progestational agent with antiandrogen effects, and has a role in the treatment of hirsutism, but very little research has been done to utilize this therapeutic effect of the drug.

Objective The aim of the present study was to evaluate the safety and efficacy of iontophoretically administered MPA on idiopathic facial hirsutism independent of reduction in serum androgen levels.

Patients and methods The study was conducted in Military Hospital Rawalpindi for 2 years. Thirty women aged 18-30 years (mean age 24 years) having idiopathic facial hirsutism between Ferriman Gallwey grade 2-3 were recruited in the trial. 1 ml of 7.5% aqueous solution of MPA was applied iontophoretically twice weekly for 16-weeks. The target areas were right and left cheeks, while the chin was taken as control. The response to treatment was evaluated by the assessment of hair density, thickness of hair, and rate of hair growth at baseline and end of the study. Blood samples were also taken, at baseline and the end of the study, to measure serum testosterone (T) and dehydroepiandrosterone sulphate (DS) levels.

Results MPA iontophoresis significantly reduced the hair length, manifesting as reduction in the rate of hair growth, without any significant local side effects or effects on serum androgen levels.

Conclusion MPA iontophoresis is a safe, effective and well-tolerated therapy in idiopathic facial hirsutism.

Key words
Hirsutism, iontophoresis, medroxyprogesterone acetate.

Introduction

Hirsutism is characterized by an excessive growth of terminal hair in women on androgen dependant areas of the body.[1] It results from an excess production of androgens from either adrenal[2] or ovarian sources, or from constitutional increase in sensitivity of hair follicles,[3] or from both. By far the commonest cause is idiopathic where there is an increased 5α-reductase activity in hair follicles.[4,5] Treatment of hirsutism is very challenging and presently available modalities like electrolysis, lasers, anti-androgens, chemical and physical epilation have many drawbacks including expense, permanence, systemic and local side effects. Therefore, there is need for a treatment

Address for correspondence
Dr. Muneeza Rizwan,
Consultant Dermatologist,
PAC Hospital, Kamra
Email: muneeza.rizwan@manchester.ac.uk,
muneezar@yahoo.co.uk

modality which can offer efficacy, safety, affordability and easy accessibility.

Medroxyprogesterone acetate (MPA) has been available for over 30 years and has achieved wide therapeutic use as a progestational agent.[6] It is basically a contraceptive agent, but also affects androgen dependant hair growth by inhibition of 5α-reductase and blocking of androgen receptors in hair follicles.[7] It also causes suppression of luteinizing hormone and testosterone (T) production, and increased hepatic clearance of T.[6] A comparative study of topical MPA ointment with systemic therapy either by intramuscular injection of MPA or subcutaneous injection has reported its beneficial effects in most patients with hirsutism.[7] Keeping in view its antiandrogen properties, we examined its potential in treatment of hirsutism by administering the drug iontophoretically. Transdermal iontophoresis provides an effective technique to deliver ions and charged molecules across the skin at an enhanced rate in a controllable manner by the use of small electric current.[8]

Patients and methods

Subjects and study design The subjects were 30 women, aged 18-30 years (mean age 24 years), with idiopathic facial hirsutism, between Ferriman-Gallwey[9] grade 2-3, who attended the outpatient department at Military Hospital, Rawalpindi between 1998-2000. Exclusion criteria were systemic antiandrogens, previous treatment of hirsutism (including hair removal in the last 3 months), eczema or rosacea on the face, pregnancy and lactation. Any identifiable underlying cause of hirsutism was excluded by evaluating the sex hormone profile and ultrasound pelvis.

The study design was single-blind and controlled. The target areas were right and left cheeks while chin was taken as control and these areas were marked with templates. Epilation by the patients was prohibited in the target and control areas. Patients underwent treatment twice weekly.

Apparatus Iontophoresis was carried out with Duffield Orthotron MK-6. Positive and negative electrodes were attached to copper plates measuring 4x3 cms. 7.5% aqueous solution of MPA was used as testing agent.

Method After obtaining informed consent, face was washed with soap and water to remove any kind of makeup. Patients were positioned supine on couch with their head elevated at an angle of 45^{o}. During the first visit target and control areas were marked with templates, and the hair shaved off. Target areas were cleaned with spirit swab. 1 ml of 7.5% aqueous solution of MPA was applied to the filter papers, fixed to the copper plates, which were then placed over the sides of the cheeks on the prefixed areas. The positive electrode was placed over the right side and negative electrode over the left side during each treatment. A constant direct current of 3 milliampere was used. Iontophoresis was performed for 20 minutes during each session and sessions were given twice weekly for 16 weeks.

Bloods Blood samples were taken at the beginning and end of the 16 week treatment period to measure serum T and dehydroepiandrosterone sulphate (DS) levels.

Evaluation procedures

Hair density Hair density of the target and control areas was determined by counting the number of hair in an area of 1 cm^2 marked with

the templates. The hair was counted with the help of magnifying lens and light.

Hair diameter 8-10 hairs were plucked from the target and control areas and their diameter was calculated in Neubaeur chamber under the microscope and average diameter determined.

Hair length (rate of hair growth) 8-10 hairs from each target and control areas were sampled to calculate the average hair length, with the help of a scale. The hair length was determined at first visit, the areas were shaved and the final length determined after 16 weeks.

Statistical analysis

Statistical analysis was performed on SPSS 13. Values expressed as means±standard deviation (SD). *p* values ≤0.05 were regarded as significant. One-way analysis of variance (ANOVA) was performed to compare the means of pre- and posttreatment values on selected parameters of hirsutism, i.e. hair length, diameter and density over the target (right and left cheek) and control sites. Student-t test applied to compare the means of pre and post treatment T and DS levels.

Results

After 16 weeks of treatment hair length was the most significantly affected parameter (F=7.54, $p<0.05$) with the noticeable change on the right cheek (positive electrode) as compared to the left cheek (negative electrode) and control site (chin), **Table 1** and **Figure 1**. Hair diameter showed an apparent reduction on right cheek after 16 weeks of treatment, however, it did not reach significance (F=0.48, $p>0.05$), **Table 2** and **Figure 2**. Hair density showed no change after MPA iontophoresis (F=0.06, $p>0.05$), **Table 3** and **Figure3**. There were no significant changes on serum T (median pre-treatment T=1.21nm/l; median post-treatment T=1.23nm/l; $p>0.05$) and serum DS levels (median pre-treatment DS=164µg/dl; median post-treatment DS=164.8µg/dl; $p>0.05$) after the treatment.

Table 1 Mean hair length, SD, CI and range of hair length on the target sites (right: R, left: L cheek) and control (C) site pre and post MPA iontophoresis, in 30 females with idiopathic hirsutism.

	Mean (mm)	*95% CI*
Pre treatment (R)	1.90±0.48	1.72-2.09
Post treatment (R)	1.28±0.64	1.04-1.52
Pre treatment (L)	1.91±0.49	1.73-2.10
Post treatment (L)	1.90±0.46	1.72-2.07
Pre treatment (C)	1.92±0.46	1.75-2.10
Post treatment (C)	1.90±0.46	1.72-2.07

CI=Confidence interval for mean

Table 2 Mean hair diameter, SD, CI and range of hair diameter on the target sites (right: R, left: L cheek) and control (C) site pre and post MPA iontophoresis, in 30 females with idiopathic hirsutism.

	Mean (mm^3)	*95% CI*
Pre treatment (R)	69.93±9.21	66.49-73.37
Post treatment (R)	66.96±9.28	63.49-70.43
Pre treatment (L)	69.81±9.15	66.39-73.23
Post treatment (L)	69.60±9.03	66.22-72.97
Pre treatment (C)	69.93±9.21	66.49-73.37
Post treatment (C)	69.83±9.22	66.38-73.27

CI=Confidence interval for mean

Table 3 Mean hair density, SD, CI and range of hair density on the target sites (right: R, left: L cheek) and control (C) site pre and post MPA iontophoresis, in 30 females with idiopathic hirsutism.

	Mean (cm^2)	*95% CI*
Pre treatment (R)	29.76±3.82	28.33-31.19
Post treatment (R)	29.43±3.71	28.04-30.81
Pre treatment (L)	29.43±3.73	28.03-30.82
Post treatment (L)	29.30±3.88	27.84-30.75
Pre treatment (C)	29.43±3.73	28.03-30.82
Post treatment (C)	29.30±3.88	27.84-30.75

CI=Confidence interval for mean

Discussion

Hirsutism carries high psychosocial impact amongst young girls and women. There is range of therapeutic options available; however, they all have certain limitations including lack of permanence, systemic and local side effects and

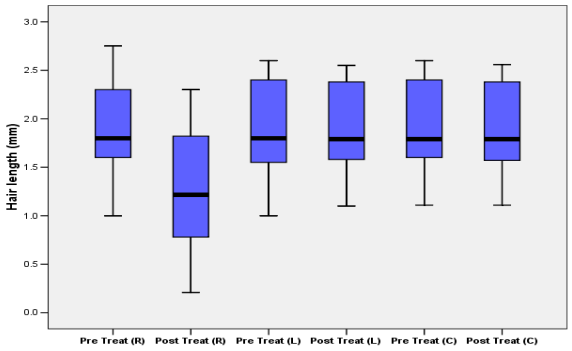

Figure 1 Median hair length on right cheek (R), left cheek (L) and chin (C) pre (pre treat) and post-iontophoresis (post treat) with MPA, showing a significant reduction in hair length post-treatment on the right cheek (p<0.05), n=30. Data are median and interquartile range (IQR). The whiskers represent a data point in the 25th and 75th centiles±1.5xIQR.

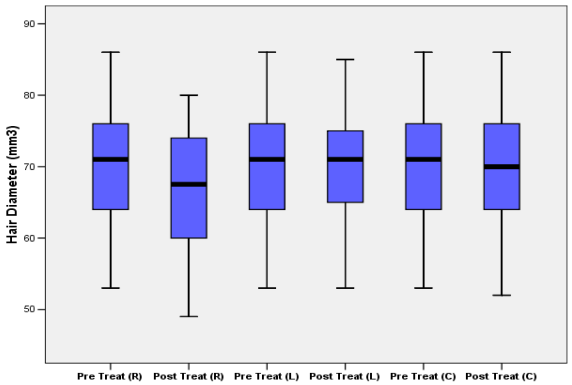

Figure 2 Median hair diameter on right cheek (R), left cheek (L) and chin (C) pre (pre treat)and post-iontophoresis (post treat) with MPA, showing apparent reduction in hair diameter post-treatment on the right cheek, but it did not reach significance (p>0.05), n=30. Data are median and interquartile range (IQR). The whiskers represent a data point in the 25th and 75th centiles±1.5xIQR.

cost. The present study was aimed to explore a treatment modality for hirsutism which can offer efficacy, safety and affordability.

MPA is a progestational agent and is mainly indicated for contraception; however literature reports its effectiveness in the treatment of hirsutism. Studies in the polycystic ovary syndrome have demonstrated reduction in blood testosterone levels by administration of 40 mg

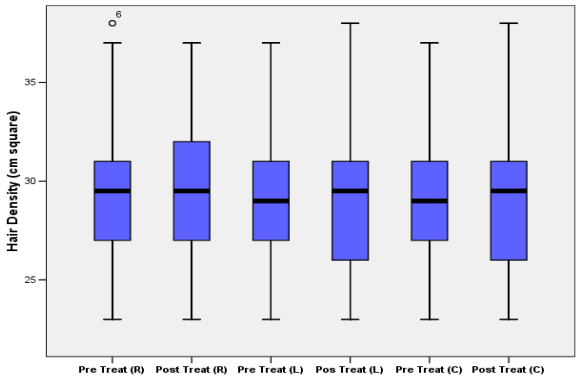

Figure 3 Median hair density on right cheek (R), left cheek (L) and chin (C) pre (pre treat) and post-iontophoresis (post treat) with MPA did not change significantly (p>0.05), n=30. Data are median and interquartile range (IQR) and outliers, where o represents a data point 1.5–3xIQR. The whiskers represent a data point in the 25th and 75th centiles±1.5xIQR.

MPA per day for 4 to 6 weeks.[10] Inhibition of 5α-reductase, blockage of androgen receptors and lowering of androgen serum levels are all potential mechanisms which reduce androgen dependent hair growth.[7,11] A study comparing various modes of administration of MPA in hirsutism as topical cream, subcutaneous and Intramuscular injections reports its efficacy in hirsutism.[7] These various methods of administration of the drug have certain limitations including lack of penetration with topicals, risks of subcutaneous injections and the systemic side effects due to Intramuscular injections. To counteract these limitations and to restrict the beneficial antiandrogen effects of the drug to the site being treated we delivered it through iontophoresis which is a simple and economical method of transdermal delivery of drugs.[8]

Our data suggest that iontophoretic application of MPA have significant effects on the rate of hair growth observed by reduction in hair lengths. Hair diameter also showed apparent reduction, however, it did not reach significance levels. The effects on hair density were

negligible. All the significant changes were observed towards the positive electrode, which indicates that after the ionic dissociation of MPA the diffusion of drug is more at the positive electrode.

This treatment methodology is safe in terms of its local and systemic side effects. No local complications were observed in any of the case except for mild tingling during the procedure and post-iontophoresis erythema which too settled in a couple of minutes. Also there was no significant change in the serum androgen levels, i.e. T and DS, after the treatment which suggests a local action of MPA at cellular level, most likely effect on 5α-reductase activity as previously suggested.[11,7]

Hence, iontophoretic administration of MPA is a potentially simple, cost effective, safe and reasonably effective method for the treatment of hirsutism. Since this is a pilot study, results can potentially be improved by any or all of the following measures:

- by increasing the concentration of MPA
- by increasing the frequency of application of the drug
- by increasing the time duration of iontophoresis in each sitting
- by reversing the polarity of the electrodes periodically so as to benefit both the treatment sites

This relatively simple methodology can be utilized in future to treat a very common problem among the females belonging to every subset of the community.

References

1. Rittmaster RS. Hirsutism. *Lancet* 1997; **349**: 191-5.
2. Pang S, Lerner AJ, Stoner et al. Late onset adrenal steroid 3β-hydroxysteroid dehydrogenase deficiency. A case of hirsutism in pubertal and postpubertal woman. *J Clin Endocrinol Metabol* 1985; **60**: 428-33.
3. Reingold SB, Rosenfield RL. The relationship of mild hirsutism or acne in women to androgens. *Arch Dermatol* 1987; **123**: 209-14.
4. Ebling FJG. Hair. *J Invest Dermatol* 1967; **67**: 98-105.
5. Serafini P, Lobo R. Increased 5α-reductase activity in idiopathic hirsutism. *Fertil Steril* 1985; **43**: 74.
6. Schwallie PC, Assenzo JR. Contraceptive use-efficacy study utilizing medroxyprogesterone acetate administered as an intramuscular injection once every 90 days. *Fertil Steril* 1973: **24**: 331-9.
7. Schmidt JB, Huber J, Spona J. Medroxyprogesterone acetate therapy in hirsutism. *Br J Dermatol* 1985; **113**: 161-6.
8. Costello CT, Jeske AH. Iontophoresis: applications in transdermal medication delivery. *Physical Therapy* 1995; **75**: 554-63.
9. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrinol* 1961; **21**: 1440-9.
10. Gordon GG, Southern AL, Calanog A *et al.* The effect of medroxyprogesterone acetate on androgen metabolism in the polycystic ovary syndrome. *J Clin Endocrinol Metabol* 1972; **35**: 444-7.
11. Frost P, Gomez EC. Inhibitors of sex hormones: Development of experimental models. In: Montagna W, Van Scott EJ, Sloughton RB, editors. *Advances in Biology of Skin: Pharmacology and Skin*. New York: Appleton Century Crofts; 1972. p.403.