New Medical Treatment for Androgenetic Alopecia

reported by Dr. S. Y. Cheng

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Androgenetic alopecia is an autosomal dominant disorder with variable penetrance. It is characterized by progressive miniaturization of hair follicles, decrease in density of hair and length to which it can grow. The anagen phase is shortened so that the hair cycle is shortened with relative increased hairs in telogen phase. In early stage of hair loss, increase in shedding of hairs is apparent.

Dihydrotestosterone(DHT) has played the pathogenic role in androgenetic alopecia. Patients with genetic deficiency of 5 alpha-reductase type II enzyme, which converts testosterone to DHT, do not have androgenic alopecia. The conversion of testosterone to DHT at hair follicles leads to miniaturization. In scalp biopsy, the tissue DHT level is significantly increased in balded area than non-balded area.

Oral finasteride, a steroid analogue, is a competitive inhibitor of type II 5 alpha-reductase enzyme which are found at inner layer of outer root sheath and proximal region of inner root sheath. After administration, both serum and scalp DHT level are reduced by 70%.

In the Finasteride Male Pattern Hair Loss study, 1553 men (18 to 41 years of age), with mild to moderately severe vertical androgenetic alopecia, were recruited into a one-year double-blind, placebo-controlled, randomized multicenter study. 779 men received oral finasteride 1mg daily and 774 men received placebo for one year. After one year, 1215 men were enrolled into the extension studies for another year. They were re-randomized so that there were ultimately four groups of patients: Finasteride ® Finasteride (n=547), Finasteride ® Placebo(n=65), Placebo ® Finasteride (n=543) and Placebo ® Placebo (n=60).

Four techniques were used to assess the efficacy end points: hair count macrophotograph, patient self-assessment, investigator assessment and global photographic assessment. Hair counts were obtained from color macrophotographs of a one-inch diameter circular area of clipped hair at the anterior leading edge of the vertical thinning area. This area was centered with a dot tattoo to ensure reproducibility. Patients assessed their scalp hair growth by completing a self-administered questionnaire. The following aspects were enquired: any decrease in size of the bald spot, better or worse appearance of hair, increase or decrease of hair growth, any slowing down of hair loss and satisfaction with hair growth on frontal hairline, vertex and overall scalp. Investigators assessed patients by using a standardized 7-point rating scale of hair growth. Lastly, standardized color global photographs of the vertex scalp were taken with the head in a stereotactic positioning device. The photographs were interpretated by dermatologists, again with the use of the standardized 7-point rating scale.

At one year, the mean hair count in the Finasteride group increased from 0 (arbitrarily defined as pretreated reference point) to 86 whereas that of the placebo group decreased from 0 to -21. During the extension studies, the Finasteride ® Finasteride group demonstrated further improvement whereas the Placebo ® Placebo group showed further worsening. The effect was reversed when Finasteride group was switched to take placebo or vice versa.

The global photographic assessment showed that 50%, 49% and 1% of the Finasteride ® Finasteride group had respectively increased, no change of or decreased hair growth at one year. The corresponding results were 66%, 33% and 1% at two year. On the other hand, only 5%, 83% and 12% of Placebo ® Placebo group had respectively increased, no change of or decreased hair growth at one year. The corresponding results were 7%, 60% and 33% at two year. The false positive placebo response was only 7%.

In general, both patient self assessment and investigator assessment on scalp hair growth were superior in the finasteride group than the placebo group.

Approximately 1% or more patients experienced drug related clinical adverse effects. Finasteride-treated patients reported more sexual dysfunction events than placebo-treated patients. The sexual dysfunction was reversible and included decreased libido, erectile dysfunction, ejaculation disorder and decreased ejaculation volume. Only 11(1.4%) men in the finasteride group and 8(1.0%) men in the placebo group

discontinued the study because of sexual adverse events.

In summary, oral finasteride was effective in treatment of androgenetic alopecia. The hair count showed that 83% of patients stopped losing or gaining hairs after two-year therapy. The global photograph showed that 99% of patients stopped losing hairs or 66% of patients gained hairs after 2-year therapy. However, the effect of finasteride was slow. It took three months to decrease shedding of hairs and took six to 12 months to notice increase in scalp hair density. The benefit would lose when finasteride was stopped for 12 months. Oral finasteride was safe in men. Only less than 2% of patients had reversible sexual dysfunction. At the moment, finasteride was not approved to use in female and was contraindicated in pregnancy because of possible male foetal abnormal sexual development. Finally, it is a simple drug to use with single daily administration and there was no known drug interaction.

In the discussion, theoretical concern was raised when potentially pregnant woman touched crushed tablets of finasteride. However, the paternity of men taking finasteride was not affected because the finasteride level in semen was very low. Finasteride was found not useful in postmenopausal women. The different efficacy of finasteride in male and female patients might be related to quantitative difference in level of androgen receptors and the steroid converting enzymes in hair follicles, including Type I and II 5 alpha reductase and cytochrome P-450-aromatase. Topical therapy was ineffective because the circulating DHT was not inhibited. It was also mentioned that finasteride might be effective in treating hirsutism in women.

Learning points:

The sexual dysfunction associated with finasteride therapy is reversible and occurs in less than two percent of patients. Finasteride is not approved to be used in women and is contraindicated in pregnancy.