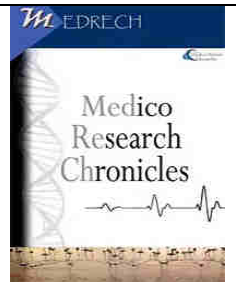




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HIRSUTISM

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ABSTRACT

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INTRODUCTION:

One of the most psychosocially distressing conditions to appear in women is Hirsutism. Hirsutism is defined as the occurrence of coarse/terminal hairs in a female with a distribution pattern that is typically associated with the adult male (Tülay and Metwally, 2015; Kalu, and Gilling-Smith, 2008; Ali and Dawber, 2006). The word "Hirsutism" is derived from the Latin word "hirsutus" which means 'hairy' or 'shaggy'. Broadly, hairs are classified into three types (Kalu and Gilling-smith, 2008)-

- **Lanugo:** These are the soft hairs that cover the body of a newborn that is eventually shed off by the age of 4-5 months.
- **Vellus:** These are the soft, non-pigmented, short hairs that cover the areas that appear to be hairless. These hairs are present on the face and body of females.
- **Terminal:** These are the long, pigmented and coarser hairs that appear on the eyebrows, eyelashes, scalp hair, pubic and axillary hairs in both sexes, and on the body of adult males.

Hirsutism is the result of the conversion of Vellus hair to Terminal hair due to androgenic stimulation of the hair follicles, thereby resulting in the appearance of the terminal hairs on the female face and body. The transformation of hairs depends on the androgen amount as well as exposure duration along with the local 5- α -reductase enzyme activity, and the intrinsic sensitivity of the hair follicle to androgen action (Mihailidis et al. 2017). Different body parts demonstrate varying levels of androgen sensitivity (Kini and Ramalingam, 2018). 5 α -reductase in the hair follicle converts testosterone, the principal circulating androgen, to the more potent dihydrotestosterone. Collectively, testosterone and dihydrotestosterone, induce the dermal papilla to generate terminal hair in the areas covered by vellus hair (Kalu and Gilling-smith, 2008). Thus, exposure to high levels of androgens results in terminal hair growth in androgen-sensitive areas such as upper lip, chin, chest, back and upper abdominal area (Mihailidis et al., 2017). Though the androgen-stimulated transformation of vellus hair is a

reversible condition, however, it becomes irreversible once termination is complete. The key trigger for the Hirsutism is thus, Hyperandrogenaemia. Hirsutism affects almost 5-10 % of the female population, affecting them psychosocially and is often a sign of a more serious underlying condition.

ETIOLOGY OF HIRSUTISM

Metabolism pattern of androgens in females helps to determine the cause of Hirsutism, which can be one or more of the following condition (Tülay and Metwally, 2015; Kalu and Gilling-smith, 2008)-

- Higher production of androgen due to Polycystic ovarian syndrome or PCOS. Although, the diagnosis of PCOS does not necessarily mean the occurrence of Hirsutism.
- Higher production of androgen due to Adrenal disorders, viz., Cushing syndrome and adult-onset congenital adrenal hyperplasia.
- Higher production of androgen in the cases with XY gonadal dysgenesis or Swyer syndrome i.e. females with functional testicles. Such cases can be identified by karyotyping.
- Androgen-producing ovarian and adrenal tumors may also result in excessive androgen production.
- Increased free androgen levels due to reduced levels of sex hormone-binding globulin. The majority of the circulating androgen binds to sex hormone-binding globulin and thus becoming inactive. However, higher insulin concentration can result in lower levels of sex hormone-binding globulin, thereby increasing the free androgen levels.
- Increased insulin and insulin-like growth factor (IGF) concentrations result in an amplified activity of 5- α reductase enzyme.
- Certain drugs viz., such as danazol, sodium valproate or anabolic steroids and androgen therapy may also result in Hirsutism.

- Exponentially high level of activity of peripheral 5 α -reductase, androgen receptor polymorphisms, and altered androgen metabolism are some of the postulated causes of Idiopathic hirsutism. (Idiopathic hirsutism is a condition of hirsutism in a subject with normal ovary functioning and circulating androgen levels)

MANAGEMENT OF HIRSUTISM

Traditionally, mild or moderate hirsutism does not necessitate treatment. However, in 2008, Endocrine Society guidelines suggested to include patients' perception to initiate the treatment under the term "patient-important hirsutism" (Martin et al., 2008). Prior to the initiation of treatment, the cause for hirsutism should be identified (Mihailidis *et al.*, 2017). Estimation of total testosterone levels gives the best preliminary evaluation of androgen levels in the hirsute women. Estimation of dehydroepiandrosterone sulfate (DHEAS) levels is also an important indicator of androgen levels. Testosterone level greater than 150 ng.dl⁻¹ is suggestive of an ovarian or adrenal testosterone-secreting tumor or ovarian hyperthecosis. While DHEA-S levels greater than 700mcg.dl⁻¹ are suggestive of hormone-secreting adrenocortical carcinoma (Brodell and Mercurio 2010). Cosmetically, hirsutism can be corrected using electrolysis, laser epilation, and photoepilation. Lifestyle management viz., diet, exercise, behavioral changes, or combined treatments leading to weight loss are also suggested for the management of hirsutism especially in patients with PCOS. The pharmacological management of hirsutism includes the following therapies-

1. Oral contraceptives

Combination oral contraceptive pills are the first-line approach for the treatment of hirsutism. This therapy aims to suppress or reduce androgen production and increase the production of sex hormone-binding globulin via the reduction of gonadotropins /luteinizing hormone production. Estrogen-progestin combinations are the most widely used oral contraceptives for the management of

hirsutism. Estrogen levels promote the production of sex hormone-binding globulin thereby reducing the free testosterone levels. Therapy is most commonly initiated using a combination having low androgenic or antiandrogenic properties, viz., Ethinyl estradiol (0.03 to 0.035 mg) with a progestin (Mihailidis *et al.*, 2017; Kini and Ramalingam, 2018).

2. Antiandrogen Therapy

This therapy is beneficial for idiopathic hirsutism or as adjuncts to androgen suppressive therapies. Antiandrogen molecules prevent the androgen to exhibit its activity at the target organ. Spironolactone, Cyproterone acetate, Finasteride, Flutamide are few of the antiandrogen candidates. Spironolactone is a structural analog of progestins while, Finasteride is a 5- α reductase inhibitor, Flutamide is a nonsteroidal antiandrogen and Cyproterone is a 17-hydroxyprogesterone acetate derivative with strong progestogenic effects (Mihailidis *et al.*, 2017). However, Flutamide is generally not a recommended therapy due to possible hepatotoxicity.

3. Insulin-sensitizing agents

Metformin and Thiazolidinediones reduce hyperinsulinemia thereby reducing the androgen production. However, insufficient clinical trials for the usage of Metformin and Thiazolidinediones in hirsutism limit their usage (Brodell and Mercurio 2010).

4. Topical treatment

Eflornithine hydrochloride, an ornithine decarboxylase inhibitor, available as a topical preparation (13.9%) has been found to reduce hair growth. Eflornithine hydrochloride irreversibly inhibits ornithine decarboxylase thereby inhibiting hair growth. Although, it does not remove the existing hairs, however, it slows the hair growth. This can be used alone or in conjunction with other therapies (Kini and Ramalingam, 2018).

5. Glucocorticoids and Gonadotropin-releasing hormone analogs (GnRHa)

Glucocorticoids can suppress adrenal androgen production while GnRHa inhibits

gonadotropins thereby reducing ovarian androgen production. However, GnRHa also induces lower estrogen levels, hence; it is preferred to use it in combination with low-dose estrogen-progestin pills rather than monotherapy. The use of glucocorticoids, however, is not recommended for the routine management of hirsutism (Mihailidis *et al.*, 2017).

CONCLUSION

Hirsutism is perceived to be a cosmetic problem however; it is the manifestation of an underlying endocrinological disorder, that is psychosocially distressing for the patient. An interdisciplinary approach is required for the management of hirsutism. A team of endocrinologists, gynecologists, dermatologists, psychologists, and cosmeticians are often required for the successful management of hirsutism. It is pertinent for the healthcare providers to recognize the pathophysiology and its cause, to rule out underlying disease or tumors. Also, healthcare providers need to educate the patient regarding the timeframe and the success rate of the therapy.

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