Review of selected endpoints in studies evaluating the effectiveness and efficacy of topical finasteride use for androgenetic alopecia

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ABSTRACT

Androgenetic alopecia (AGA) is a disorder that worsens over time. A metabolite of testosterone called dihydrotestosterone is implicated in the pathogenesis of AGA by exerting its effect on genetically predisposed hair follicles. Oral finasteride (FNS) targets this enzymatic step and is one of the two approved medications for the condition, the other one being topical minoxidil. This paper aimed to dissect the current literature on the endpoints chosen to measure the efficacy and effectiveness of using topical FNS for managing AGA. PubMed database was searched from October to November 2021 with the following terms including (“Finasteride”[Title] OR “Finasteride”[MeSH Terms]) AND (“Local”[Title] OR “Topical”[Title]). All human studies that investigated the use of topical FNS for AGA were included. Following the initial abstract scanning, studies that only investigated animal objects were excluded. Additionally, studies that did not have at least one clinical endpoint were overlooked. This review highlighted the available tools of hair evaluation in the reviewed literature. Objective tools represent the majority. These assessment methods were inconsistently applied across the reviewed studies, which as discussed earlier led to results that are hard to combine statistically. Considering these observations, future investigators are encouraged to make use of validated and standardized methods. Despite their growing significant subjective measures of hair growth on the other hand were not included in all the investigations.

Keywords: Androgenetic alopecia, hair loss, finasteride, topical, hair assessment, hair evaluation.

Introduction

Androgenetic alopecia (AGA) is a disorder that worsens over time. Hence, the prevalence of the disease at age of 70 years is approximately two and half times the prevalence at age of 30 years. It is the commonest form of hair loss [1-3]. As hair quality and quantity decline with time, a reduction in diameter, length, and pigmentation of the hair begins to manifest [1-4]. A metabolite of testosterone called dihydrotestosterone (DHT) is implicated in the pathogenesis of AGA by exerting its effect on genetically predisposed hair follicles [5,6]. Oral finasteride (FNS) targets this enzymatic step and is one of the two approved medications for the condition, the other one being topical minoxidil [7]. Using oral FNS is known to cause multiple side effects such as decreased libido, erectile dysfunction, reduced semen volume, breast enlargement, and testicular pain. For that reason, many research projects have begun to investigate the efficacy and effectiveness of using topically administered FNS. In these studies, the progression of hair condition was assessed by multiple tools falling into different categories based on invasiveness. These tools were developed to investigate treatment options for hair loss [8]. This paper aimed to dissect the current literature on the endpoints chosen to measure the efficacy and effectiveness of using topical FNS for managing AGA.

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Materials and Methods

PubMed database was searched from October to November, 2021 with the following terms including (“Finasteride”[Title] OR “Finasteride”[MeSH Terms]) AND (“Local”[Title] OR “Topical”[Title]). All human studies that investigated the use of topical FNS for AGA were included. Following the initial abstract scanning, studies that only investigated animal objects were excluded. Additionally, studies that did not have at least one clinical endpoint were overlooked.

Discussion

Anatomy and physiology of hair follicle

During the growth phase, terminal hair follicles consist of four main segments from the most superficial to the deepest namely, infundibulum, isthmus, lower segment, and the bulb [9]. The bulb contains the dermal papilla, which is surrounded by matrix cells. These cells make up the hair shaft as they differentiate ascending upward [10]. Hair follicles in the resting phase also called the telogen phase, lack the lower segment [9]. The bulge area houses stem cells necessary for the hair growth cycle and is located at the insertion of erector pili muscle to the hair follicle [11,12]. The growth phase of the hair growth cycle is also known as the anagen phase which variably lasts from 1 to 7 years. Then a 2-week, transient period called the catagen phase precedes the resting phase which lasts around 3 months.

FNS effect on the metabolism of androgens

Androgens are a group of sex hormones that help develop internal and external sex organs in male fetuses. Additionally, during adolescence, their presence is essential for acquiring secondary sexual characteristics [13]. A 5-alpha reductase mediates the conversion of testosterone to the five times more potent form DHT [14-16]. Before clearance, testosterone or DHT could further get metabolized to weaker androgens or estrogenic compounds by the aromatase enzyme activity [13]. Under the influence of androgens, genetically predisposed hair follicles in AGA experience shortening in the growth phase and lose pigment overtime to finally become vellus-like hair [13]. Because 5-alpha reductase significantly produces potent androgens, it has become the target for a family of medications called 5-alpha reductase inhibitors.

These inhibitors, including FNS, are testosterone analogs that could inhibit the conversion of testosterone to DHT [13]. Notably, FNS does not have any affinity to androgen receptors. Thus, it does not interfere with the physiologic activity of testosterone. Oral administration of FNS maintains normal blood levels of testosterone; however, DHT levels get significantly reduced [17]. In contrast, locally applied FNS showed no effect on blood levels of DHT as shown in a previous investigation [18]. Since topical FNS does not pose any change to blood concentration of DHT, it’s speculated that participants would experience less side effects.

Serial photography

Comparing serial photos of hair regions of interest against each other is superior to evaluating patients while solely relying on memory, which appears to be more subjective and less consistent over time. The literature review has shown that many investigators took the advantage of this evaluation tool and included it as an endpoint in their studies. However, despite the recent efforts put to standardized this approach of documentation [19], there seems to be a lack of agreement in the specifics related to the conduct of this method. While sometimes no clinical changes of the hair status have occurred, erroneous interpretation might still take a place because of variabilities in the techniques used. Moreover, many of the studies did not delve into enough detail for the following investigations to replicate the results. The current review included studies that did not specify which type of digital cameras they used [20-22]. Let alone more details about the settings when shots were taken including but not limited to lenses used, lighting, head position, film sensitivity, etc., In contrast to the previously cited studies, two investigations led by Suchonwanit et al. [23,24] provided more descriptions, especially of the views used. The two studies also provided detailed directions that were given to the patients on how to comb the hair so consistent photos could be obtained. Instructions and guidance on hair styling should be delivered to participants since variations might make the hair appears thicker or even thinner. One more complication to mention is the varying scaling systems used to rate hair growth or loss over time which makes it even harder to combine the results later in quantitative systematic reviews.

Hair count

Hair counting might sound simple and straightforward. Nevertheless, it’s a multistep assessment that starts with an accurate localization of the area where after clipping hair tally could be carried on. One study used a dual method of identification to minimize the risk of losing a previously defined region [23]. Once the site is defined and hairs are clipped the investigator could then mark the previously defined region [23]. Once the site is defined and hairs are clipped the investigator could then mark the site permanently, an omitted step in some of the studies [21,25]. Results of hair counting, which could be done by naked eyes [25,26] or with the aid of a tricoscopy [21,23] are summarized either as means or in a frequency table with multiple categories. All these variabilities in how hair density is measured and how findings are reported bring about the difficulty of combining the results in later review studies.

Size of bald area

Of the studies, two groups of investigators used the same scoring system that included the size of the bald area to

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evaluate the effectiveness of topical FNS [25,26]. All study participants in both the studies had a maximum bald area of 10 cm as per the inclusion criteria. Participants were sorted into four different size categories. Each category had an assigned score which was summed with scores of other measures to give one final score. Besides reporting the results in the form of different classes, Hajheydari et al. [25] calculated the mean area of bald spots before and after the treatment. Despite the lack of validation and standardization of this method in the literature, these two studies described and followed the exact same method.

**Tricoscopy**

Examining the scalp with videodermoscopy allows for more detailed evaluations of the hair. In addition, videodermoscopy generates images that could be stored for later comparisons. Two studies investigating the use of topical FNS for AGA by Suchonwanit et al. [23,24], used dermoscopy to measure hair parameters like density and diameter before and after the intervention in preselected areas. These areas of interest were localized with two methods of localization ensuring reproducibility of the findings. Results of these parameters were reported as means. This technology also facilitates conducting simpler methods of evaluations such as hair count [21].

**Wash test**

Mazzarella et al. [20], who conducted the first study to investigate the effect of topical FNS in managing AGA, quantified hair loss with a standardized wash test. Participants were instructed not to shampoo or rinse their hairs for 1 week before the test, which for sure was not an easy task to perform. On the wash day, patients would cover the drain with a gauze to collect hair as they rinsed. Because the count of vellus hair on the wash test does not effectively reflect the number found on a biopsy. Study investigators did not define a bar for the test to diagnose AGA. Rather, the means of the two groups were plotted against each other across the whole duration of the study.

**Patient’s perception**

Suchonwanit et al. [23,24] in his two studies of topical FNS included patients’ perception of their progression over the course of intervention. Participants’ inputs were subjective; however, they were still valuable if collected properly with validated and standardized tools. Mazzarella et al. [20] used a basic four-point scale to register participants’ self-evaluations. Later, another group of investigators developed a survey for men diagnosed with AGA [27]. The questionnaire consists of four items that record participants’ general appreciation of their hair status. A similar validated one was also created for female cases [28]. Despite the availability of previous validated questionnaires, Ateeq Ahmad measured patients’ subjective evaluations with a new tailored survey for the purpose of his study [29].

**Conclusion**

This review highlighted the available tools of hair evaluation in the reviewed literature. Objective tools represent the majority. These assessment methods were inconsistently applied across the reviewed studies, which as discussed earlier led to results that are hard to combine statistically. Considering these observations, future investigators are encouraged to make use of validated and standardized methods. Despite their growing significance subjective measures of hair growth on the other hand were not included in all the investigations. Participant’s input is valuable in accomplishing a patient-centered approach. For that reason, investigator should seek input from participants whenever feasible and appropriate.

**List of Abbreviation**

AGA Androgenetic alopecia
DHT dihydrotestosterone.
FNS Finasteride

**Conflict of interest**

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