Finasteride

ncbi.nlm.nih.gov/books/NBK513329

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Continuing Education Activity

Finasteride, an FDA-approved therapeutic agent, plays a pivotal role in managing benign prostate hyperplasia and androgenic alopecia (male pattern hair loss) in men. Through its competitive inhibition of 5-alpha-reductase (types II and III isoenzymes), finasteride impedes the conversion of testosterone to dihydrotestosterone (DHT), addressing the underlying pathophysiology of these conditions. This activity discusses finasteride's diverse applications, extending beyond its primary indications to treat hyperandrogenism-associated manifestations, such as hirsutism.

Additionally, the module explores the potential utilization of finasteride in transgender women, particularly when combined with estrogen, harnessing its anti-androgenic properties. The program outlines the recommended dosing, highlights significant adverse effects, identifies contraindications, and elucidates the essential aspects of monitoring and managing potential toxicity. By imparting an understanding of finasteride's mechanisms and clinical applications, this activity empowers healthcare providers to navigate patient therapy effectively, guiding them toward optimal outcomes.

Objectives:

- Select appropriate patients for finasteride therapy, considering age, medical history, and treatment preferences.
- Differentiate between the therapeutic uses and dosing regimens of finasteride for BPH and male pattern hair loss.
- Screen patients for contraindications and potential drug interactions before initiating finasteride therapy.
- Implement follow-up care and patient monitoring on long-term finasteride therapy to ensure treatment efficacy and safety.

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Indications

In 1947, James Hamilton of Yale University published an article on male hormone stimulation as a prerequisite to common baldness after examining 104 men with testicular insufficiency. In 1974, Julianne Imperato-McGinley of Cornell University published reports on Caribbean children with a mutation leading to deficiencies in 5-alpha reductase and dihydrotestosterone. When these male

children matured, they had smaller prostate sizes and a lack of male pattern baldness. These observations and findings ultimately led to the development of finasteride. Finasteride is a 5-alpha reductase inhibitor (5-ARI).

FDA-Approved Indications

Finasteride is an FDA-approved pharmacologic agent for treating benign prostate hyperplasia and androgenic alopecia (male pattern hair loss) in men. Finasteride 5 mg was first used in 1992 to treat benign prostatic hyperplasia. In 1997, finasteride received approval to treat male pattern hair loss at a reduced dose of 1 mg.

Off-Label Uses

Finasteride has also been used off-label to treat signs of hyperandrogenism, such as hirsutism. The drug may be used in transgender women in combination with estrogen for its anti-androgen properties. However, finasteride use is not recommended in women who are pregnant or who may become pregnant. Endocrine Society suggests the use of finasteride for hirsutism in premenopausal women.

Another off-label use of finasteride is to decrease intraoperative bleeding and perioperative requirement for blood transfusion after TURP (transurethral resection of the prostate) or further surgical intervention for BPH (American Urological Association guidelines).

Mechanism of Action

Finasteride is a competitive inhibitor of the type II and III isoenzymes of 5-alpha reductase, inhibiting testosterone conversion to dihydrotestosterone (DHT). Finasteride has minimal selectivity for the type I 5-alpha reductase enzyme. The type I 5-alpha reductase isomer is present in sebaceous glands, sweat glands, dermal papillae cells, and epidermal and follicular keratinocytes. Type II is in the outer root sheaths of hair follicles, the epididymis, vas deferens, seminal vesicles, and the prostate.

Research has shown that finasteride reduces prostatic DHT levels by upwards of 90% and serum DHT levels by 70%. However, increasing the dose does not necessarily result in greater serum DHT reduction. Dutasteride, in contrast, inhibits all 3 5-alpha reductase isoenzymes, leading to a 99% reduction in serum DHT levels.

- In treating androgenic alopecia, finasteride does not lead to a 100% reduction in DHT; hair loss is slowed but not completely halted. Patients receiving treatment for androgenic alopecia have a reversal of hair count within 12 months.[8]

- In treating benign prostate hyperplasia, long-term use of finasteride has been associated with a reduction in prostatic volume, thereby relieving bothersome urinary symptoms attributed to an enlarged gland. Previously published literature has demonstrated a reduced risk of urinary retention and delayed the need for surgical intervention. Upon discontinuation of finasteride, DHT levels return to normal within 14 days.

Pharmacokinetics

Absorption: In the clinical study using 1 mg tablets, the bioavailability of finasteride is observed at approximately 65% and is not affected by food.

Distribution: Finasteride is approximately 90% protein bound with a volume of distribution of 76 L at a steady state and can cross the blood-brain barrier. Upon discontinuation of finasteride, DHT levels return to normal within 14 days. In patients treated for benign prostate hyperplasia, the prostate volume returns to baseline within 3 months; patients receiving treatment for androgenic alopecia have a reversal of hair count within 12 months.

Metabolism: Finasteride undergoes extensive metabolism in the liver (hepatic metabolism) via the cytochrome P450 enzyme system, specifically CYP3A4, into 2 active metabolites with less than 20% of the activity of finasteride.

Elimination: Finasteride has a half-life of elimination from the serum of 5 to 6 hours, ranging between 3 and 16 hours. In older patients (greater than 70 years of age), the half-life can be prolonged to 8 hours. Finasteride has a markedly shorter half-life than dutasteride, another 5-alpha reductase inhibitor; dutasteride has a half-life of 4 to 5 weeks. Finasteride is eliminated as metabolites, 57% in the feces and 39% in the urine. After the intravenous infusion, the mean plasma clearance of finasteride was about 165 mL/min in healthy young subjects.

Administration

Available Forms

Finasteride is available as a 1 mg tablet or a 5 mg tablet for oral use. Each dose has a different indication. Therefore, as much as 6 to 12 months of continued treatment may be necessary to assess the benefit of treatment. Finasteride 5 mg is also available in combination with tadalafil 5 mg, administered for a maximum of 26 weeks.

Adult Dosing

Benign prostatic hyperplasia (BPH): 5 mg once daily (as a single agent or combined with an alpha-blocker). AUA recommends starting finasteride in patients with BPH with prostate enlargement as evaluated by a prostate enlargement on the digital rectal exam, the prostate volume of >30 cc on imaging, and prostate-specific antigen (PSA) levels >1.5 ng/dL.

Androgenic alopecia (male pattern baldness): 1 mg once daily.

Hirsutism (female, idiopathic, and related to polycystic ovary syndrome): 5 mg once or 2.5 mg twice daily; this is an off-label use. Endocrine Society practice guidelines recommend 2.5 mg or 5 mg once daily in premenopausal women.

Specific Patient Populations

Hepatic impairment: No specific dose adjustment guidance is provided on the manufacturer label. However, the liver extensively metabolizes the drug, so use caution when administering the medication in those patients.

Renal impairment: No dose adjustment is needed for patients with renal impairment. The drug is excreted via urine as well as feces.

Pregnancy considerations: Finasteride is labeled a pregnancy category X medicine, and is contraindicated in women who are or may become pregnant. Because finasteride can inhibit the conversion of testosterone to 5-alpha dihydrotestosterone (DHT), it might cause abnormalities of the external genitalia of a male fetus. If pregnancy occurs for a woman while she is taking finasteride or a pregnant woman has exposure to finasteride, that woman should be counseled about the potential hazard to a male fetus.

Breastfeeding considerations: The current data has not determined whether finasteride is excreted in milk. However, it is not indicated for use while nursing infants or babies.

Pediatric patients: The manufacturer does not establish safety and efficacy for the pediatric patient population, so finasteride is not indicated for use in pediatric patients.

Older patients: Efficacy is not established for the older adult population as per product labeling. However, no dose adjustment is needed for older patients based on the pharmacokinetic parameters of 5 mg tablets.

Adverse Effects

Common adverse finasteride-related adverse effects include loss of libido, erectile dysfunction (2% to 4%), decreased ejaculatory volume, and gynecomastia. Finasteride is also associated with orthostatic hypotension, particularly right after initiating therapy. This adverse event can be additive in patients who are taking concomitant alpha-blockers.

Finasteride reportedly causes orthostatic hypotension in approximately 9% of users with monotherapy and as high as 18% with combined therapy. Therefore, appropriate patient counseling is necessary to not rise quickly from a sitting position after taking the medication and to be aware of what might happen so they don't lose their balance and fall. In some patients, persistent sexual dysfunction may lead to suicidality and adverse psychological events.

Post-finasteride syndrome (PFS) has been a recently reported issue. This term refers to the continuation of adverse effects despite the discontinuation of therapy. Further investigational studies to better understand post-finasteride syndrome are currently underway.

The impact of finasteride on fertility has also been examined by urologic and dermatologic practitioners who utilize the medication in different doses for various indications. Thus far, there is minimal data to support the association of permanent infertility using a low dose of 1 mg finasteride. The effects of low-dose finasteride on fertility appear to be reversible, as various studies have demonstrated improved fertility and sperm parameters in those who discontinued therapy. However, fertility may be negatively impacted by using the higher 5 mg dose. Not all users experience fertility issues, and many users of the medication can still conceive.

Additionally, finasteride may cause dizziness, weakness, dyspnea, rhinitis, and skin rash. Research suggests that 5-alpha reductase inhibitors (including finasteride) can increase the risk of insulin resistance, non-alcoholic fatty liver diseases, and dry eye disease. No clinically significant drug-drug interactions of finasteride are identified in studies.

Contraindications

Finasteride is contraindicated in those with hypersensitivity to any component of the formulation. Finasteride is contraindicated in children. Furthermore, finasteride is contraindicated in pregnant women or women of childbearing age. Women who are pregnant or may become pregnant should avoid contact with tablets that have been crushed or broken. Animal reproduction studies reported an abnormality of external male genitalia. If used for the off-label management of hirsutism in female patients with polycystic ovary syndrome, adequate contraception is recommended by the American College of Gynecology.

Blood donation is contraindicated for individuals currently taking finasteride and for up to 6 months following the last dose of finasteride.

Monitoring

No specific laboratory monitoring guidelines exist for finasteride use. However, checking prostate-specific antigen (PSA) is a routine assessment in men with benign prostate hyperplasia and surveillance for prostate cancer. Due to the decreased prostatic volume at the 5 mg dose, there is an expected decrease in serum prostate-specific antigen levels. Therefore, the recommendation is to obtain baseline prostate-specific antigen levels before initiating therapy. Practitioners should be aware of the serum prostate-specific antigen values in their patients using finasteride. Serum lab values are often multiplied by 2 to provide a more accurate approximation of levels.

There has been some controversy regarding the role of finasteride in the development of prostate cancer. The Prostate Cancer Prevention Trial (PCPT) was a landmark study that compared daily finasteride to placebo therapy in over 18,000 men 55 and older, with a follow-up period of 7 years.

The study ultimately concluded that finasteride was associated with a 25% reduction in the prevalence of prostate cancer. However, finasteride was also associated with an increased rate of high-grade prostate cancer.

The FDA eventually placed a boxed warning on the medication safety label, negatively impacting the prescribing patterns of the drug. There is a considerable consensus in the field that the increased rate of high-grade cancer in the PCPT may result from confounding factors and detection bias. However, it cannot be excluded with certainty.

The American Society of Clinical Oncology (ASCO) and the American Urological Association (AUA) released a joint statement in 2008. In addition, they developed a clinical practice guideline to assist physicians and patients with making informed decisions after reviewing the risks and benefits of the medication.

The AUA supports using finasteride as a treatment option for men with benign prostate hyperplasia. According to the AUA, IPSS (international prostate symptom score), quality of life, and uroflowmetry/post-void residual should be monitored after 3 to 6 months of starting finasteride.

Toxicity

Single doses up to 400 mg and multiple dosages up to 80 mg daily for 3 months are well-tolerated and have not resulted in significant adverse reactions in clinical studies. Until further data is obtained, no specific treatment for an overdose of finasteride can be recommended.

There are no reports of overdoses of finasteride resulting in clinically significant toxicity. However, overdoses could be an extension of previously reported adverse drug effects, including orthostatic hypotension. According to the CDC, finasteride is included in the National Institute for Occupational Safety and Health (NIOSH) list of hazardous agents. Use proper precautions during handling and prescribing, and monitor patients appropriately.

Enhancing Healthcare Team Outcomes

Finasteride is an FDA-approved pharmacologic agent for treating benign prostate hyperplasia and androgenic alopecia (male pattern hair loss) in men. Urologists and dermatologists commonly prescribe finasteride for BPH and androgenic alopecia, respectively. The drug is also sometimes used to treat hyperandrogenism and hirsutism. All patients should receive risk versus benefit information, including the risk of high-grade prostate cancer.

Female patients of childbearing potential should be informed about the possibility of the medication causing harm to the fetus and the importance of contraception while using the drug. Nurses should verify the dose for appropriate indications and ensure the patient understands the use of finasteride. Pharmacists should perform medication reconciliation, check for potential drug interactions, counsel patients, and report any concerns to the prescriber. This requires nurses and

pharmacists to communicate openly with clinicians and be empowered to voice any concerns regarding issues they note in the patient's case. This is true in all instances, especially when the drug is used off-label in females for hirsutism. For example, if a nurse determines a female patient is not exercising proper birth control while on finasteride, they should immediately report the need for remedial action to the prescriber.

Review Questions

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Disclosure: Patrick Zito declares no relevant financial relationships with ineligible companies.

Disclosure: Karlyle Bistas declares no relevant financial relationships with ineligible companies.

Disclosure: Preeti Patel declares no relevant financial relationships with ineligible companies.

Disclosure: Kirin Syed declares no relevant financial relationships with ineligible companies.