International Journal of Pharma Research and Technology

The Dutasteride: Miraculous Drug in Alopecia Treatment A Review

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Abstract

This review paper presents a comprehensive review of Dutasteride, a potent 5-alpha reductase inhibitor. Dutasteride pharmacological properties and therapeutic applications are explored in depth. The paper discusses its mechanism of action, which involves inhibiting 5-alpha reductase enzymes of both types I and II, leading to a reduction in di hydro testosterone (DHT) levels. The impact of Dutasteride on conditions related to androgen excess, such as androgenetic alopecia (AGA) and benign prostatic hyperplasia (BPH), is examined. Clinical efficacy studies of Dutasteride in BPH management are summarized, including its effects on symptom relief, urinary flow rates, and prostate size reduction. The potential synergistic effects of Dutasteride in combination therapy with alpha-blockers are also discussed. Furthermore, the therapeutic applications of Dutasteride in AGA treatment are reviewed, considering its role in hair growth promotion, comparative efficacy, and potential adverse effects. The paper also explores dutasteride's investigational role in prostate cancer prevention and its emerging applications in transgender medicine. By providing a comprehensive understanding of dutasteride's pharmacology and therapeutic uses, this review aims to inform healthcare professionals about its appropriate clinical application.

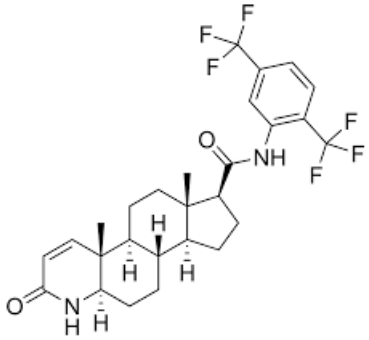
Keywords: Inhibitor, therapy, pharmacology.

Introduction

The intracellular enzyme 5 -reductase creates the potent androgen di hydro testosterone (DHT) from testosterone, DHT is essential. In order for the male external genitalia to develop, Male sexual development, as well as the urethra and prostate as an adolescent.[1] DHT has been identified as the main androgen in accountable for male pattern baldness later in life.[2] In prostatic illnesses such benign prostatic hyperplasia (BPH), DHT also plays a pathogenic role.[3] Steroid 5 -reductase types 1 and 2 enzymes have both been identified.[4] According to reports, type 1 can be discovered in the skin, liver, prostate, and other parts of the body. Type 2 is likewise but is primarily found in extra-prostatic tissues situated in the prostate and male genitalia.[5] each prostate zone has been discovered to contain mRNA for 5-reductase types 1 and 2, according to researchers. When BPH tissue was more abundant than normal prostatic tissue a considerable rise in the expression of 5 -reductase mRNA types 1 and 2. Also

discovered the expression of is greater in prostate cancer specimens. MRNA for type 1 of the 5 -reductase but not type 2 Healthy prostate tissues.[6, 7] It has been discovered that males born lacks the enzyme type 2 5 reductase display a primitive prostate and improper masculinization of the external genitalia. These people don't have prostate cancer or BPH, and as a result of these discoveries, 5 -reductase inhibitors were created and are now used to treat BPH.[8] Dutasteride and finasteride are two 5 -reductase inhibitors that have been given clinical approval to far.

Structure



Mechanism of Action

Type 1 and type 2 5 -reductase isoenzymes are competitively and specifically inhibited by the synthetic 4-azasteroid Dutasteride. The major androgen necessary for the early prostate tissue growth and continuous prostate tissue expansion, 5 -reductase is in charge of converting testosterone to DHT intracellularly. [9] After taking Dutasteride 0.5 mg daily for two weeks, DHT serum levels were 90% lower. The class of Dutasteride is called '5 - alpha reductase inhibitor.[9] Orally is how Dutasteride is given. The time it takes to attain peak serum concentrations (Tmax) after a 0.5 mg dose is two to three hours. The absolute bioavailability in healthy people is 60%, with a range of 40% to 94%. Food does lower the maximum serum concentrations, but it was found that this decrease is not clinically relevant. Dutasteride is broadly dispersed across the periphery and central compartments after it enters the systemic circulatory system and is strongly bonded to albumin (99%) and alpha -1 acid glycoprotein (96.6%).[9]

Dutasteride is substantially metabolised by the Cytochrome P450 (CYP) isoenzymes CYP3A4 and CYP3A5 in the liver. There are four major metabolites (4-hydroxy Dutasteride, 1, 2-dihydro Dutasteride, and 6-hydroxy Dutasteride) and two auxiliary metabolites (6, 4-dihydroxy Dutasteride and 15-hydroxy Dutasteride) discovered in human serum. Only 6-beta-hydroxy Dutasteride of these metabolites keeps up activity close to dutasteride's. The majority of the metabolites and 5% of the unmodified drug Dutasteride are eliminated in the faeces. The amount of Dutasteride that was discovered unchanged in the urine was less than 1% and 55% of a dose was not found. The terminal disposal half-life of Dutasteride is approximately five weeks at steady state. A steady state is reached for serum concentrations at 65% after one month of daily dose, after three months, 90% and lasting anywhere from four to six months before being detected. [9]

"Half-life" age-related increases were substantial in a one-dose experiment of 36 healthy male volunteers, ages 24-87, who received 0.5 mg of Dutasteride. Males 20 to 49 years old had a half life of 170 hours, males 50 to 69 years old had a half life of 260 hours, and men over 70 years old had a half life of 300 hours. Between the various age groups, there were no differences in safety, and no dose change is currently advised.[9] It has not been investigated how renal and hepatic impairment affect the pharmacokinetics of Dutasteride. Due to the considerable liver metabolization of Dutasteride, patients with hepatic

impairment are more likely to have increased systemic exposure to the medication. No recommended dose modifications have been developed for this group of patients, however.. Due to the fact that the kidneys only discharge a small amount of medicine, individuals who have renal impairment, dosage adjustments are not necessary.[9] Dutasteride is more effective than finasteride which is a particular inhibitor of type 2 5 -reductase, and reduces DHT concentrations more significantly at equivalent doses.[10]

Contraindications / Precaution

Patients who have a history of recognised allergic reaction to Dutasteride (such as angioedema) or any component of the preparation should not take Dutasteride. It's possible for other 5-alpha-reductase inhibitors to cause cross-sensitivity. There hasn't been any review on how renal dysfunction affects the pharmacokinetics of Dutasteride. The amount of Dutasteride recovered in urine from a steady-state dose of 0.5 mg is, however, less than 0.1%, Consequently, no reduction in dosage is predicted for people with kidney dysfunction. Patients who are older (> 65 years old) and other adult patients who are younger than them do not generally differ from one another in terms of safety or efficacy.

Pregnancy in females

Because Dutasteride should not be used by females who are capable of having children, it should not be used during pregnancy. Dutasteride and other 5-alpha-reductase Inhibitors block the conversion of testosterone into DHT, which can result in malformations in a developing male foetus' external genitalia. The fetus may be exposed because Dutasteride gets absorbed through the skin, thus pregnant women or women attempting to get pregnant shouldn't touch the capsules. Wash the affected area using soap and water right away if skin contact with a leaky capsule occurs. Male semen contains Dutasteride that is secreted. It is estimated that the concentration of Dutasteride in semen that can be absorbed vaginally is less than 100 times that which causes defects in the genitalia of male progeny in animals. [11]

Breast feeding

It is not advised for women who are able to have children to use Dutasteride, making it inappropriate to use while nursing a baby. It is uncertain if Dutasteride ends up in human milk. Dutasteride's effects on infants while being breastfed cannot therefore be assessed.

Donating blood

Dutasteride users should wait a minimum of six months after their last dose before giving blood. Dutasteride cannot be given to pregnant women getting blood transfusion during this postponed period. Dutasteride serum levels are detected for 4 to 6 months after the end of treatment.

Hepatic disease

Due to the limited evidence available on the occurrence of side effects or drug accumulation in individuals with hepatic disease, Dutasteride should be administered with caution. The drug's half-life is around 5 weeks at steady state, and the liver significantly metabolises it. Strong hepatic CYP3A4 isoenzyme inhibitors have not been investigated for their impact on Dutasteride metabolism. When giving Dutasteride to individuals who are continuously using strong CYP3A4 inhibitors, caution should be exercised. Children, infants, new born, and teenagers should not use Dutasteride. These age groups have not been proven to be safe or effective.

Obstruction of the urinary tract with prostate cancer

After three months of treatment, around 40% of total serum PSA is decreased by Dutasteride, and after six, twelve, and twenty-four months of treatment, it reduces PSA by 50%. Although this decline is anticipated across the whole range of PSA readings, patient variations are possible. For the purpose of interpreting serial PSAs in men using dutasteride, after three to six months, a fresh starting point PSA percentage should be established. Utilising this updated baseline, evaluate PSA variations that could be indicative of malignancy PSA. A man taking Dutasteride for at least six months should double his isolated PSA value to compare his findings to those of untreated males.[11, 12]

Is It Safe?

Dutasteride medication has been found in clinical trials 12, 28–30 to be both safe and well tolerated. The majority of side effects were not severe and subsided as treatment progressed. Continuing impotence and other negative sexual consequences, reduced libido, gynecomastia, and inability to ejaculate Individuals who received treatment frequently displayed disorders when compared to placebo with dutasteride.[13] At least 1% of patients receiving Dutasteride of 0.5 mg daily for two years experienced sexual adverse effects in three sizable, randomised, clinical trials using a double-blind placebo. [14]

Most of these unfavourable sexual consequences were seen by patients in the first six months of Dutasteride treatment. There were none, with the exception of gynecomastia. After six months, substantial sexual side effects are observed of therapy. Upon completion of a four-year open-label Tolerability was maintained with less in the extension review. Less than 1% of patients discontinuing due to the consequences study because of negative drug-related. [15] The Combat trial examined the effectiveness and safety of mixing Dutasteride and tamsulosin. The combo therapy was shown to be safe and tolerable. Consistent with the individual monotherapy treatments. The adverse medication reactions were greatly increased with the combo therapy compared to the groups receiving monotherapy (P = 0.001) was primarily attributed to the frequency of ejaculatory abnormalities. The percentages of drug-related withdrawal. However, there was no difference in negative impacts between the teams.[16]

Uses

Prostate cancer and benign prostatic hyperplasia. [17]

Dutasteride is used to treat BPH, also referred to as "enlarged prostate" informally.[18]

It has been authorised for this use by the Food and Drug Administration, or FDA, in the United States.[19]

5-reductase inhibitor chemoprevention decreased the incidence of prostate cancer by 25–26%, according to a 2010 Cochrane study.[20]

Excessive hair growth and scalp hair loss.[21]

Dutasteride is approved for the therapy of male androgenetic alopecia in South Korea and Japan at a dose of 0.5 mg per day.[22]

Due to dutasteride's more thorough inhibition of 5-reductase with subsequent decrease in dihydro testosterone (DHT) generation within the hair follicles, it is more effective than finasteride for this indication. Female pattern hair loss is treated with Dutasteride off-label as well.[23, 24]

Finasteride, a type 2 inhibitor, and other 5-reductase inhibitors have been utilised off-label to treat people with hirsutism that has excessive hair growth.[25]

Dutasteride has the potential to be a more successful treatment for hirsutism since it inhibits type 1 and type 2 5'-reductases.Dutasteride is not recommended for this application due to a lack of solid clinical data and a considerable risk of birth defects in women who accidentally become pregnant.[26]

Gender-neutral hormone treatment

In hormone therapy for transgender women, Dutasteride is occasionally combined with an oestrogen and/or another antiandrogen, such as spironolactone. It might be helpful for people who have trouble tolerating spironolactone or for addressing scalp hair loss.[27]

Accessible formats

Soft, oil-filled gelatin capsules containing 0.5 mg of Dutasteride are used to administer the drug.[11]

Adverse Effects

Overall, review on both men and women have revealed that Dutasteride is well tolerated and has few side effects. Headache and stomach pain are two negative consequences. There are also isolated accounts of changes in menstruation, acne, and lightheadedness.[28]

Men taking the medication during the first few months of therapy have shown a slight risk of sexual adverse effects.[29]

Dutasteride now has a black-box warning from the FDA that details an elevated risk of high-grade prostate cancer in men who use the medication.[30]

It has not been proven that 5-reductase inhibitors cause prostate cancer directly or indirectly.[31] This isn't because there's a direct correlation between Dutasteride or other 5'-reductase inhibitors and cancer per se, but rather because those who take them may have lower prostate-specific antigen (PSA) levels, which could make increases in PSA (a marker for potential cancer) harder to detect in them.[32]

The size and prevalence of benign prostate tumours have been shown to be reduced by dutasteride.[33]

With 5-reductase inhibitors, a 2018 meta-analysis indicated no increased risk of breast cancer.[34]

Side effects related to sexuality and mood, such as erectile dysfunction. [35]

As many as 4.8% of patients on 5-reductase inhibitors [36], such as Dutasteride, experience loss of libido, depression [37], and decreased semen volume.[38]

Semen volume decreases by an average of 30% in affected men.[39]

A smaller minority of patients additionally experienced a 6-12% reduction in sperm motility.[40, 41] Male fertility is not impaired, and sperm shape and function are unaltered. 3–4 months after stopping the medicine, these side effects go away.[42]

Conclusion

In conclusion, this review paper on Dutasteride has shed light on various important aspects of the drug, including its mechanism of action, contraindications, safety profile, and adverse effects. The mechanism of action of Dutasteride involves the inhibition of both type I and type II 5-alpha reductase enzymes, resulting in a decrease in dihydro testosterone (DHT) levels. This mechanism has proven effective in the treatment of conditions such as benign prostatic hyperplasia (BPH) and

androgenetic alopecia (AGA).When considering contraindications, Dutasteride is generally not recommended for use in women, especially those who are pregnant or planning to become pregnant, due to the potential risk of fetal abnormalities. Additionally, caution should be exercised in patients with known hypersensitivity to Dutasteride or any of its components. Regarding safety; Dutasteride has been generally well-tolerated in clinical studies. However, it is essential for healthcare professionals to consider individual patient characteristics and potential drug interactions before prescribing it. Routine monitoring and appropriate dosage adjustments may be necessary, particularly in patients with hepatic impairment. Like any medication, Dutasteride does have potential adverse effects. Some commonly reported adverse effects include sexual dysfunction, breast disorders, and gastrointestinal disturbances. It is crucial for healthcare providers to inform patients about these potential risks and monitor them closely during treatment. In summary, Dutasteride has demonstrated efficacy in the management of BPH and AGA, primarily through its mechanism of action. While it has a generally favourable safety profile, healthcare professionals should be aware of contraindications, individual patient factors, and potential adverse effects. This review paper contributes to the existing knowledge about Dutasteride, aiding healthcare professionals in making informed decisions regarding its use in clinical practice.

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