



Mesterolone: Historical Perspectives, Clinical Applications, and Emerging Experimental Evidence

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Abstract

Mesterolone (1-alpha-Methyl-5-alpha-androstan-17-beta-ol-3-one) is a synthetic orally active dihydrotestosterone derivative introduced during the 1960s as a comparatively mild androgen with limited antigonadotropic and hepatotoxic effects relative to many contemporary oral anabolic steroids. This paper summarizes the historical development, pharmacological characteristics, clinical applications, and experimental studies related to mesterolone over more than five decades.

Early experimental and clinical investigations demonstrated that mesterolone exerted androgenic activity while producing relatively limited suppression of luteinizing hormone, follicle-stimulating hormone, spermatogenesis, and endogenous testicular function. Unlike many 17 α -alkylated oral androgens, mesterolone was generally associated with a lower incidence of clinically significant hepatotoxicity. These characteristics led to its investigation in a variety of clinical conditions including male hypogonadism, impotence, aging male syndrome, idiopathic oligospermia, renal anemia in chronic hemodialysis patients, depressive symptoms, nocturnal enuresis, and certain hepatic disorders.

The most consistent clinical evidence supports its use in mild to moderate male infertility associated with oligospermia, where several studies demonstrated improvements in sperm concentration, seminal parameters, and pregnancy rates. Additional studies reported beneficial effects on libido, erectile function, psychosomatic symptoms, and quality of life in androgen-deficient males. Long-term studies in renal anemia suggested improvement in hemoglobin levels and reduced transfusion requirements with relatively favorable tolerability.

More recent experimental research demonstrated that mesterolone influences skeletal muscle hypertrophy, satellite-cell activation, nitric oxide signaling, mitochondrial adaptation, tendon remodeling, and connective tissue structure. These findings suggest possible future applications in sarcopenia, rehabilitation medicine, and muscle-wasting disorders, although current evidence remains largely preclinical.

Despite its historically favorable safety reputation, modern studies indicate that mesterolone may adversely affect lipid metabolism and, in rare cases, may induce liver injury. Therefore, careful long-term monitoring remains important during therapy.

Overall, mesterolone represents a distinctive oral androgen with unique pharmacological properties and a broad historical range of therapeutic applications. However, most available evidence predates modern standards of randomized clinical investigation, and contemporary controlled studies are required to better define its efficacy, safety, and optimal clinical role.

Keywords: Mesterolone; Safety; Therapeutic Applications

Mesterolone (1-alpha-Methyl-5-alpha-androstan-17-beta-ol-3-on) is a synthetic dihydrotestosterone with a methyl group at the C1 α position.

In 1966, Neumann et al. reported experimental studies on animal which introduced mesterolone as a new androgen [1]. During the same year, Schirren reported the use of mesterolone in the treatment of postpubertal Leydig cell insufficiency [2], and Hornstein reported its use in the long-term treatment of severe androgen deficiency [3].

The 1966 paper by Ursula Laschet, Leonhard Laschet, and H. F. Paarmann examined how treatment with Mesterolone affected urinary excretion of gonadotropins and steroid hormones in

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men. The authors concluded that mesterolone behaved differently from many other oral androgens available at the time:

It produced androgenic effects while causing little or no suppression of pituitary gonadotropin secretion (especially LH and FSH).

Urinary steroid excretion patterns changed during treatment, showing androgen metabolism, but the hypothalamic–pituitary–gonadal axis appeared to remain comparatively intact.

The investigators interpreted this as evidence that mesterolone might provide androgen replacement without the marked antigonadotropic effects commonly seen with 17 α -alkylated androgens such as methyltestosterone [4].

The 1966 paper by H. D. Pohle evaluated whether the oral androgen mesterolone caused measurable liver toxicity, which was already a major concern with many orally active anabolic/androgenic steroids of that era. The study concluded that:

Mesterolone was well tolerated by the liver under the tested conditions. Standard liver-function parameters showed little or no clinically important impairment during treatment, Mesterolone appeared substantially less hepatotoxic than the commonly used 17 α -alkylated oral androgens available at the time.

In the 1960s, drugs like methyltestosterone and related oral anabolic steroids were increasingly recognized as causing cholestasis, abnormal Bromsulphophthalein (BSP) retention, jaundice, and other liver abnormalities.

The paper's overall interpretation was that mesterolone represented a potentially safer oral androgen because its chemical structure differed from the classic C17- α -alkylated steroids strongly associated with cholestatic liver injury [5].

In 1968, paper Petry et al. investigated whether the oral mesterolone could provide androgenic effects in men without suppressing pituitary gonadotropins or damaging testicular function, a major problem with many oral anabolic/androgenic steroids available at the time.

The study reported that:

- No major suppression of gonadotropin secretion was observed.
- Sperm counts were not significantly reduced.
- Testicular tissue showed no clear pathological changes even after several months of treatment and relatively high cumulative doses.
- Mesterolone produced a measurable androgenic effect.
- Liver function appeared largely unaffected in their subjects.

The authors concluded that mesterolone appeared to produce androgenic effects without significantly suppressing the Hypothalamic–Pituitary–Gonadal (HPG) axis or impairing spermatogenesis during the treatment periods they studied.

The authors proposed a mechanistic explanation: because mesterolone is a non-aromatizable androgen, it cannot readily convert into estrogen, it may avoid the estrogen-mediated negative feedback that suppresses pituitary gonadotropin release.

The paper emphasized that mesterolone behaved differently from classic 17 α -alkylated oral anabolic steroids. It contributed to the later

reputation of mesterolone as a comparatively “mild” androgen with less suppression of endogenous testosterone production than many other anabolic steroids [6].

In 1969, Komatsu and colleagues reported the treatment of 13 male patients with hypogonadism with oral mesterolone. Treatment was considered satisfactory and was not associated with impairment of liver function [7].

In 1970, Petry et al. reported a study which showed that:

Mesterolone produced little or no significant suppression of pituitary gonadotropin secretion or testicular function, especially compared with conventional oral anabolic/androgenic steroids.

Metenolone acetate showed greater inhibitory effects on the hypothalamic–pituitary–gonadal axis than mesterolone.

Mesterolone therefore appeared unusual among oral androgens because it preserved LH/FSH activity, sperm production, and testicular morphology/function.

The authors suggested that mesterolone which is non-aromatizable (unable to convert to estrogen) and therefore less capable of exerting strong negative feedback on the pituitary.

Mesterolone behaved more like a weak peripheral androgen than a strongly suppressive anabolic steroid.

They specifically suggested that the saturated A-ring structure of mesterolone reduced suppression of gonadotropin secretion.

Compared with many oral anabolic steroids available at the time, mesterolone appeared to exert relatively weak inhibitory effects on the pituitary–testicular axis, particularly regarding LH/FSH secretion and spermatogenesis [8].

In 1972, Cooper and Ismail reported a pilot study of the use of mesterolone in impotence. One of the paper's most important observations was that mesterolone produced androgenic effects without major suppression of pituitary–testicular function.

This was considered unusual for an oral androgen at the time and aligned with earlier studies from the same era suggesting relatively weak suppression of LH/FSH and spermatogenesis compared with other anabolic steroids.

This pilot study suggested that mesterolone may provide modest clinical benefit in selected men with suspected androgen-related impotence, while exerting comparatively little suppression of the pituitary–gonadal axis. The authors viewed this as potentially advantageous because many androgen treatments could worsen endogenous gonadal function during chronic use [9].

Ton M.C.M. Schellen and Joseph M.J.H.A. Beek Schellen and Beek emphasized that mesterolone does not negatively affect pituitary activity and the hormonal homeostasis, and therefore, it does not suppress spermatogenesis and testicular testosterone production. They also emphasized that mesterolone has no hepatic adverse effect on liver function.

They reported a study which included 80 infertile male patients who had oligospermic or azoospermia (9 patients). 70 patients had an elevated gonadotropic excretion. The patients were treated with mesterolone 75 mg daily for 2 months and then 50 mg. daily for one month.

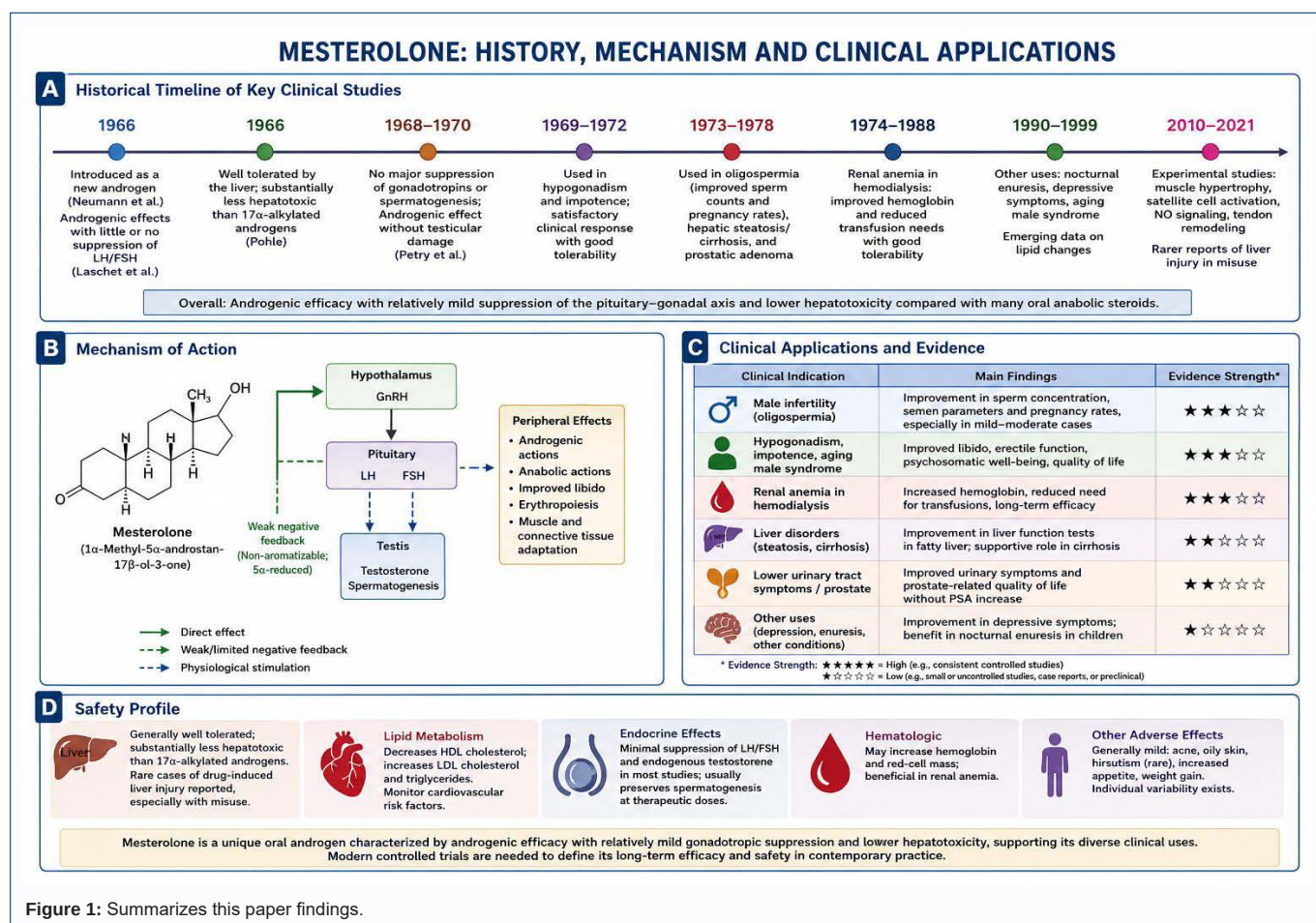


Figure 1: Summarizes this paper findings.

More 50% of the patients experienced an increase of the sperm count; 25 patients experienced a good, and 14 patients experienced a moderate, increase. Nine patients achieved pregnancy. The study showed beyond doubt that mesterolone treatment was associated with impressive improvement of oligospermia, but not azoospermia. Mesterolone was more effective when the oligospermia was associated with high-normal or elevated urinary gonadotropin levels [10].

In 1973, Figueroa reported a study on the use of mesterolone in patients with hepatic steatosis and cirrhosis. Treatment was generally well tolerated with no serious liver-related adverse effects. In fatty liver, mesterolone showed some improvement in liver function tests. In cirrhosis, benefits were modest, mainly supportive rather than curative [11].

In 1974, Carl reported a study which reported a beneficial effect of mesterolone prostatic adenoma [12].

Kraft and colleagues (1974) reported a study which included 12 chronic hemodialysis patients of treated with oral mesterolone (150 mg daily) for 6 months. The need of blood transfusions markedly reduced, but increased again during the 6 months after stopping treatment. In seven untreated control patients with comparable hemodialysis program, there was no significant change in need for blood transfusions and hemoglobin. Mesterolone treatment was not associated with changes in neither iron kinetics nor the bone marrow composition. Treatment was not associated with significant side effects neither in males nor in females [13].

During the same year, Christina Wang and her research group reported a study in which two groups of five healthy males were treated with oral mesterolone at doses of 100 mg or 200 mg daily for one week. Treatment was associated with slight reductions in FSH, LH, and testosterone levels in both groups. However, the reductions were greater in the group receiving 100 mg of mesterolone, with decreases of 19% in LH, 21% in FSH, and 9% in testosterone. In the 200 mg group, treatment decreased FSH by 18%, LH by 15% and testosterone by 8% [14].

In 1975, Guillon reported a study which included 141 male patients who had primary and secondary male sterility (oligospermia, asthenospermia, limited sperm survival time, abnormal sperm viscosity) treated with mesterolone (30–75 mg daily for 2 months). Treatment was associated with improvement in at least one parameter in 44 patients, and pregnancy was achieved in 19 patients. Lower dose was associated with rather higher improvement rate. Treatment was well tolerated and side effects were seen in 2 patients [15].

In 1977, Jackaman *et al.*, reported a study which included 23 subfertile males with oligospermia treated with mesterolone for 6–9 months. Treatment resulted significant decrease in serum testosterone, marked increase in serum luteinizing hormone. However, there was no significant change in serum follicle stimulating hormone before and after treatment [16].

In 1978, Szöllösi and colleagues reported a study which included 42 patients who had pathospermia, treated with mesterolone (25 mg/daily) was examined for 100 days. Improvement was seen in

patients with hypozoospermia and oligozoospermia with low initial ejaculate fructose content. Fructose content was normalized after the treatment. Eleven patients achieved pregnancy. Mesterolone didn't affect plasma FSH, LH and testosterone levels [17].

Nikkanen (1978) reported a study which included 42 males with sub-fertility attributed to moderate oligoastheno-teratozoospermia. The patients were treated with mesterolone. Treatment was not associated with change in plasma FSH, testosterone or prostate phosphatase. Semen acid phosphatase and citric acid activity was increased. A decreased in semen fructose was attributed to an increase in the number of spermatozoa, which need more fructose. 30% of the treated patients achieved normozoospermia, and 6 patients achieved pregnancy [18].

Nikkanen (1979) reported a study which included 24 healthy infertile males treated with mesterolone (75 daily mg) for six months. Treatment was not associated with side-effects or with changes in plasma FSH, testosterone, cholesterol, and triglycerides levels [19].

Lowe *et al.*, (1979) reported a study which included 9 healthy men (Volunteers) who received mesterolone (100 mg daily) for 3 weeks. There was no significant in platelet count, hematocrit, clotting times, fibrinogen, Factor VIII related antigen, antithrombin III activity, factor VIII coagulant activity, fibrinogen-fibrin degradation products, plasminogen, urokinase sensitivity, euglobulin lysis time, whole blood viscosity and plasma viscosity. The authors concluded that in this dose taken for 3 weeks, mesterolone was not associated with a measurable prothrombotic state or an increased fibrinolysis [20].

In 1980, Lunglmayr and colleagues reported a controlled study which included 17 male patients (Age: 45 -60 years) who had impotentia coeundi and were treated with either mesterolone (75 mg daily) or placebo for 2 months. Treatment was not associated with changes in serum LH and testosterone. Treatment resulted in improvement in potency and psychosomatic parameters [21].

During the same year, Kraft reported a study which included 26 patients (10 males, 16 females) with renal anemia (Iron deficiency was excluded or treated) on chronic hemodialysis (3 times for 5 hours) for at least 6 months. Treatment with oral mesterolone (150 mg per day) resulted in progressive improvement in anemia. After 39 months the hemoglobin increased from 74 ± 4 g/l to 95 ± 5 g/l, hematocrit increased from 0.22 ± 0.01 to 0.28 ± 0.02 , and the red-cell count increased from $2.44 \pm 0.12 \times 10^{12}/l$ to $3.09 \pm 0.2 \times 10^{12}/l$. Side effects were rarely seen. Some patients experienced increased appetite with increased body weight. Some female developed acne or hirsutism. Mesterolone didn't affect liver function tests [22].

Luisi and Franchi (1980) reported a study which included 26 male patients with hypogonadism. 14 patients were treated with mesterolone and 12 patients were treated with testosterone undecanoate. After 4 weeks, mesterolone was associated with significantly better improvement in libido, erections, ejaculations and mental state [23].

In 1985, Vogel and colleagues a study which showed that amitriptyline and mesterolone, were equally effective in reducing depressive symptoms. However, mesterolone was associated with significantly fewer adverse side effects than amitriptyline [24].

In 1987, Bhathena and colleagues reported a controlled study which included 40 subfertile male patients with idiopathic

oligospermia. They were treated with either mesterolone or placebo for more than 4 months. Mesterolone treatment was associated a marked increase of semen volume, mean sperm concentration, and mean total sperm count per ejaculate. Sperm morphological and motility characteristics were not affected by mesterolone therapy. The authors concluded that mesterolone was effective in improving sperm concentration in mild and moderate idiopathic oligospermia [25].

In 1988, Varma and Patel reported a controlled study which included 250 subfertile male patients with idiopathic oligospermia (Count less than 20 million/ml) treated with mesterolone (100-150 mg daily) for one year.

75 patients who had moderate oligospermia experienced marked improvement in total sperm count and motility and sperm density mesterolone with treatment. Only 12% of the patients who had severe oligospermic showed improvement. Mesterolone treatment was not associated with a suppressive effect on low or normal serum follicle stimulating hormone and luteinizing hormone levels but was associated with suppressive effect on 25% if the levels were elevated. There was no important adverse effect on testosterone levels or on liver function tests. 115 (46%) pregnancies were achieved. However, 9 (7.8%) aborted and two (1.7%) had ectopic pregnancy. Mesterolone was more effective in patients with a sperm count of 5 to 20 million/ml. Treatment was not associated with obvious benefit in patients having severe oligospermia (count less than 5 million) [26].

In 1990, el-Sadr *et al.*, From Egypt reported a controlled study which included 30 boys, (Age: 6-10 years) who had primary nocturnal enuresis. Twenty patients were treated with mesterolone (20 mg per day for 2 weeks) and patients 10 received placebo. 14 patients (70%) became dry during treatment, and 5 (25%) continued to be dry for 4 months. Improvement was associated in most patients with increased cystometric bladder capacity and disappearance of uninhibited detrusor contractions. Treatment was not associated with side effects. The authors suggested corrected the defective neural mechanism contributing to the pathogenesis of nocturnal enuresis [27].

In 1992, Sadullah *et al.*, reported a 65-year-old man with severe transfusion-dependent anemia from myelofibrosis. He was initially treated with the anabolic steroid oxymetholone, which improved his hemoglobin but quickly caused significant hepatotoxicity (jaundice, enlarged liver, and markedly abnormal liver enzymes). After stopping oxymetholone, liver function normalized. The patient was then switched to mesterolone at 100 mg/day. Mesterolone was associated with a comparable improvement in hemoglobin/erythropoiesis. Unlike oxymetholone, it did not cause liver toxicity in this patient.

In 1999, Jockenhövel *et al.*, from Germany reported a study showing that oral mesterolone (100 mg daily) in hypogonadal male patients increased serum dihydrotestosterone levels without significantly increasing serum testosterone concentrations. Despite the limited elevation in testosterone, mesterolone produced marked adverse lipid changes similar to those observed with other androgen replacement modalities.

Total cholesterol increased by approximately 18.8%, while LDL cholesterol rose by 46.4% during therapy. HDL cholesterol decreased significantly by nearly 35%, suggesting a potentially unfavorable cardiovascular lipid profile. Triglyceride levels also increased substantially (46.4%), indicating broader metabolic effects of androgen therapy.

These lipid alterations appeared independent of achieved serum testosterone concentrations, implying that androgenic activity itself may influence lipid metabolism.

Clinically, mesterolone may provide symptomatic androgenic benefits in hypogonadal patients; however, careful monitoring of serum lipids and cardiovascular risk factors is recommended during long-term therapy.

In 2010, Karina Fontana from Brazil reported and her research team reported a mouse soleus muscle study which showed that both exercise and the androgenic mesterolone caused significant muscle fiber hypertrophy, especially in slow-twitch (Type I) fibers.

The study found no true muscle hyperplasia; muscle growth mainly occurred through enlargement of existing fibers rather than formation of entirely new fibers.

Mesterolone increased mitochondrial number and size, suggesting enhanced oxidative and endurance-related muscle adaptations. Capillary density also increased, which may improve oxygen delivery and muscular endurance capacity.

Animals receiving mesterolone showed more activated satellite cells than exercise alone, indicating a potential role in muscle repair and remodeling. The combination of exercise plus mesterolone produced the greatest overall muscular adaptations, including larger muscle mass, greater hypertrophy, and higher satellite-cell activation.

The findings suggest that mesterolone may potentiate training-induced skeletal muscle adaptation, particularly in endurance-oriented muscle characteristics rather than explosive fast-twitch growth [30].

In 2010, Karina Fontana from Brazil reported and her research team reported another animal study examined how intensive treadmill exercise and Mesterolone affect Achilles tendon remodeling and collagen structure in mice. The study showed that mesterolone alone increased collagen-related protein content and stimulated tendon-cell (tenocyte) activity compared with sedentary controls. Exercise combined with mesterolone produced larger collagen fibrils with greater diameter and area, suggesting stronger tendon structural adaptation. Both exercise and mesterolone appeared to stimulate protein synthesis within tendons, including collagenous and non-collagenous proteins important for tissue remodeling.

Activated tenocytes and altered fibril organization indicate enhanced tendon turnover and repair processes under androgen exposure.

From a clinical perspective, the findings suggest mesterolone may influence connective-tissue healing or adaptation, potentially relevant in rehabilitation or sports medicine research.

As a performance enhancer, mesterolone may contribute indirectly to athletic performance by improving tendon resilience and adaptation to training stress rather than dramatically increasing muscle size [31].

Allouh and Aldirawi (2012) conducted an experimental study on the pectoralis muscle of chickens to investigate the effects of mesterolone on satellite cells, which are muscle stem cells essential for postnatal muscle repair and hypertrophy. Mesterolone administration significantly increased muscle mass, muscle fiber size, and the number of myonuclei in treated birds. Immuno-cytochemical and

molecular analyses revealed marked increases in satellite cells indices, DNA concentration, and Pax7 protein expression. These findings suggest that mesterolone promotes skeletal muscle hypertrophy by stimulating satellite cell proliferation and differentiation. Overall, the study supports the role of satellite cells as key cellular mediators of mesterolone's anabolic and performance-enhancing effects [32].

Fontana and colleagues (2012) reported an experimental study on mice showing that mesterolone administration significantly altered the expression of Nitric Oxide Synthase (NOS) isoforms in different skeletal muscles of mice. Specifically, mesterolone upregulated NOS I and NOS III expression in a muscle phenotype-specific manner, particularly in the tibialis anterior, soleus, and gastrocnemius muscles. These findings indicate that Nitric Oxide (NO) signaling may play a key role in mediating the anabolic effects of mesterolone on skeletal muscle. Moreover, the interaction between exercise and mesterolone produced variable responses depending on muscle type and metabolic characteristics. The results support the concept that mesterolone can enhance muscle adaptation and performance through modulation of NO/NOS pathways. Overall, the study highlights the complex molecular mechanisms underlying the anabolic and performance-enhancing effects of mesterolone in skeletal muscle [33].

In 2014, Dugeroglu *et al.*, from Turkey reported a study which included 34 patients with aging male syndrome and/or low testosterone. 22(64.70%) of the patients had increased prostate volume, and 12(35.29%) had decreased prostate volume.

Mesterolone markedly improved aging male syndrome symptoms and prostate symptom. Treatment decreased total testosterone, estradiol, and sex-hormone binding globulin. However, free testosterone was not affected, and the fraction of free testosterone increased. Prostate-specific antigen showed no change. The authors concluded that mesterolone was safe and improved lower urinary tract symptoms and prostate-related quality of life [34].

In 2019, David Pérez Palacios and colleagues described a patient who developed drug-induced liver injury after short-term use of mesterolone for bodybuilding purposes. The patient presented with jaundice and abnormal liver function tests approximately three weeks after exposure. Other causes of liver disease, including viral, autoimmune, and biliary disorders, were excluded through clinical evaluation. The liver injury pattern was predominantly hepatocellular, which is less typical for anabolic steroid toxicity. After discontinuation of mesterolone, the patient gradually recovered without progression to liver failure. Using the CIOMS/RUCAM scale, the authors classified the association between mesterolone and liver injury as probable [35].

In 2021, Asfour *et al.*, reported an experimental study on adult female White Leghorn chickens which showed that mesterolone demonstrated differential effects on oxidative and glycolytic skeletal muscle fibers, with significant hypertrophy observed primarily in glycolytic pectoralis major fibers. The study showed that mesterolone increased overall body and muscle weight while stimulating satellite cell proliferation in both muscle types. Enhanced myonuclear accretion was evident mainly in glycolytic fibers, suggesting improved muscle regeneration and adaptation.

These findings indicate that muscle fiber composition influences the anabolic response to androgen therapy. Clinically, mesterolone may have potential benefits in preserving or restoring muscle mass in conditions associated with muscle wasting. The observed anabolic

effects support its possible therapeutic role in age-related sarcopenia and other catabolic muscle disorders [36] (Figure 1).

Conclusion

The accumulated literature over more than five decades suggests that mesterolone occupies a distinctive position among orally active androgenic agents. Unlike many classic 17 α -alkylated anabolic steroids, early experimental and clinical studies repeatedly indicated that mesterolone exerts androgenic effects with comparatively limited suppression of the hypothalamic-pituitary-gonadal axis, relatively preserved spermatogenesis, and generally lower hepatotoxic potential. These pharmacologic characteristics formed the basis for its wide historical investigation in male hypogonadism, infertility, sexual dysfunction, renal anemia, and other androgen-responsive conditions.

The strongest and most consistent clinical evidence concerns male infertility associated with mild to moderate oligospermia. Multiple uncontrolled and controlled studies reported improvement in sperm concentration, seminal parameters, and pregnancy rates, particularly in patients with moderate oligospermia and elevated or high-normal gonadotropin levels. In contrast, mesterolone showed little or no benefit in severe oligospermia or azoospermia. Several studies also suggested beneficial effects on libido, erectile function, psychosomatic symptoms, and aging male syndrome, often without major suppression of gonadotropins or endogenous testosterone production.

Another important historical application was the treatment of renal anemia in chronic hemodialysis patients. Long-term administration was associated with improvement in hemoglobin levels and reduced transfusion requirements, while appearing substantially less hepatotoxic than anabolic steroids such as oxymetholone. Additional exploratory studies suggested possible benefit in hepatic steatosis, cirrhosis, depressive symptoms, nocturnal enuresis, and benign prostatic symptoms, although these indications remain insufficiently validated by modern standards.

Experimental studies published after 2010 expanded interest in mesterolone beyond classical endocrinology. Animal investigations demonstrated significant effects on skeletal muscle hypertrophy, satellite-cell activation, nitric oxide signaling, mitochondrial adaptation, collagen remodeling, and tendon structure. These findings suggest potential roles in muscle preservation, rehabilitation, connective tissue adaptation, and sarcopenia-related research. However, these observations remain largely preclinical and require confirmation in well-designed human studies.

Despite its historically favorable reputation regarding hepatic safety, later evidence indicates that mesterolone is not completely free of adverse effects. Rare cases of drug-induced liver injury have been reported, particularly with non-medical or bodybuilding use. Furthermore, modern investigations demonstrated potentially unfavorable lipid effects, including reductions in HDL cholesterol and increases in LDL cholesterol and triglycerides, raising concerns regarding long-term cardiovascular risk during chronic androgen therapy.

Overall, the historical and experimental literature portrays mesterolone as a unique oral androgen characterized by relatively mild gonadotropic suppression, generally low hepatotoxicity compared with older oral anabolic steroids, and clinically useful androgenic

activity. Nevertheless, much of the evidence originates from small studies conducted before modern standards of randomized controlled trial methodology. Contemporary large-scale, evidence-based clinical trials are still needed to clearly define its long-term efficacy, safety profile, cardiovascular risks, and potential therapeutic role in modern andrology, reproductive medicine, anemia management, and muscle-wasting disorders.

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