HORMONE THERAPIES: SCIENTIFIC EVIDENCE BASED ON EVIDENCE AND INDISCRIMINATE USE

TERAPIAS HORMONAIS: COMPROVAÇÃO CIENTÍFICA BASEADA EM EVIDÊNCIAS E O USO INDISCRIMINADO

TERAPIAS HORMONALES: EVIDENCIA CIENTÍFICA BASADA EN EVIDENCIA Y USO INDISCRIMINADO

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ABSTRACT

Practices involving the manipulation of sex hormones have persisted for generations, generating positive and negative impacts on both physical and mental health. This study aims to address the latest evidence on the subject from the perspective of different authors, thus consolidating the most up-to-date knowledge on its benefits and disadvantages. This is an integrative review conducted in the SCIELO, LILACS, PUBMED, and BVS databases, including articles from 2020 to 2025. Eighty-five studies that presented significant relevance to the topic were selected. The conclusion is that hormone therapy, when used to treat adverse health conditions, especially those involving loss of muscle and bone mass, and with proper monitoring by a specialized healthcare professional, can significantly contribute to improving quality of life. Similarly, the use of these substances without clinical indications can have serious systemic consequences, particularly in the neurological, cardiac, hepatic, renal, and reproductive systems.

Keywords: Hormone Therapy. Nursing. Indiscriminate Use.

RESUMO

Práticas envolvendo a manipulação de hormônios sexuais perduram durante gerações, gerando impactos positivos e negativos tanto na saúde física quanto na saúde mental. Este estudo tem como objetivo abordar as últimas evidências sobre o assunto na perspectiva de diferentes autores, para assim consolidar o que há de conhecimento mais atualizado em benefícios e o que é desfavorável. Trata-se de uma revisão integrativa realizada nas bases SCIELO, LILACS, PUBMED e BVS, incluindo artigos entre os anos de 2020 à 2025. Foram selecionados 85 estudos que apresentaram importante relevância ao tema. Conclui-se que a terapia hormonal quando utilizada para o tratamento de condições adversas à saúde, principalmente aquelas que envolvam perda de massa muscular e óssea, e com o devido acompanhamento do profissional de saúde especializado pode contribuir significativamente

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para a melhora da qualidade de vida. Da mesma forma, o uso dessas substâncias sem indicações clínicas pode acometer sérias consequências à nível sistêmico, em destaque nos sistemas, neurológico, cardíaco, hepático, renal e reprodutor.

Palavras-chave: Hormonioterapia. Enfermagem. Uso Indiscriminado.

RESUMEN
Las prácticas que implican la manipulación de hormonas sexuales han persistido durante generaciones, generando impactos tanto positivos como negativos en la salud física y mental. Este estudio busca abordar la evidencia más reciente sobre el tema desde la perspectiva de diferentes autores, con el fin de consolidar el conocimiento más actualizado sobre sus beneficios y desventajas. Se trata de una revisión integrativa realizada en las bases de datos SCIELO, LILACS, PUBMED y BVS, que incluye artículos de 2020 a 2025. Se seleccionaron ochenta y cinco estudios con relevancia significativa para el tema. Se concluye que la terapia hormonal, cuando se utiliza para tratar afecciones adversas de salud, especialmente aquellas que implican pérdida muscular y ósea, y con la supervisión adecuada por parte de un profesional de la salud especializado, puede contribuir significativamente a mejorar la calidad de vida. Asimismo, el uso de estas sustancias sin indicación clínica puede tener consecuencias sistémicas graves, especialmente en los sistemas neurológico, cardíaco, hepático, renal y reproductivo.

Palabras clave: Terapia Hormonal. Enfermería. Uso Indiscriminado.

1 INTRODUCTION

Hormone therapy has records dating back about 47 centuries, initially marked by aggressive practices, such as human castration, used in a rudimentary way in the first studies. With scientific evolution, this field has taken on a new meaning, standing out for its therapeutic potential in various health conditions, especially in the preservation of muscle and bone mass.

However, in parallel with medical advances, there is an indiscriminate use of hormonal substances for aesthetic, sports and sexual purposes. This phenomenon is a public health problem, since it entails relevant clinical risks, in addition to reflecting social and scientific barriers to awareness and regulation of the topic. In a scenario marked by the overvaluation of physical appearance, haste and immediacy, discussing the appropriate and inappropriate use of hormone therapy becomes essential.

In view of this, the guiding question arises: "How can hormone therapy be strategically applied to improve quality of life in specific conditions, while addressing the risks associated with indiscriminate use and its potential harms?". The present study aims to analyze the aspects of hormone therapy and the main repercussions associated with the indiscriminate use of these substances.

Therefore, an integrative literature review was adopted, which makes it possible to gather and synthesize the results of different types of research, providing a broader view of the theme. The searches were carried out in virtual databases and relevant physical works.

2 OBJECTIVES

2.1 GENERAL OBJECTIVE

To analyze the main aspects related to hormone therapy and the most relevant consequences of indiscriminate use.

2.2 SPECIFIC OBJECTIVES

Describe the main benefits of hormone therapy in promoting quality of life and treating certain pathologies in men and women;

Measure the possible consequences of inappropriate use of hormones, considering the negative impacts on physical and mental health, both in the short and long term.

3 LITERATURE REVIEW

3.1 WHAT IS HORMONE THERAPY

The concept of hormone therapy as a therapeutic resource is used in the treatment of several diseases. These treatments may involve the direct administration of hormones, the use of hormone blockers, or even drugs that interfere with the hormone production responsible for stimulating the growth of tumor cells [1].

The definition of a hormone as a chemical substance that is released in small quantities and when it arrives in the target tissue, transported by the bloodstream causes some physiological change (response). In addition, the chemical classification of hormones has four sub-divisions: amines, proteins, peptides and steroids [2].

The use of hormonal drugs, however, is not a recent practice. Approximately six decades ago, the commercialization of drugs aimed at the replacement of female hormones began, especially during menopause. This milestone evidences the consolidation of hormone therapy as a relevant clinical tool, especially in women's health H [3].

With regard to male hormone therapy, the initial milestone was the experiment carried out in 1889, in Paris, by the physician Charles Édouard Brown-Séquard. On that occasion, he developed an extract from the testicular glands of guinea pigs and dogs, which he self-administered subcutaneously. As a result, an increase in their strength and physical performance was observed. The substance was later known as "Brown-Séquard's Elixir", in honor of its creator [4].

Although this episode has boosted scientific studies on hormone therapy, historical records indicate that the use of substances with the aim of improving physical performance originates more than 2,700 years B.C., among the Chinese, as well as among Ancient Greek athletes during the Olympic Games [4].

Testosterone, the main male hormone, has an influence on several organs and systems of the body. Its biological effects—such as the development of secondary sex characteristics—have been known since antiquity, long before its identification as an active agent. Practices such as castration of men were used for social, therapeutic, and even musical purposes (such as the preservation of the high-pitched voice). In addition, testicles were used in organotherapy, therapy based on the removal of tissue fragments, and even transplanted in treatments against symptoms of hypogonadism, although these procedures had only placebo effects (Effects without active ingredient, only psychological) [5].

It was only in the first half of the twentieth century that science, in partnership with the nascent pharmaceutical industry, began to actively seek the identification of the male hormone. In 1935, after several experiments, Ernst Laqueur (Amsterdam) managed to isolate

it. Around the same time, Adolf Butenandt (Gdansk) and Leopold Ruzicka (Zurich) synthesized testosterone. Since then, this hormone has been used clinically. However, its oral administration proved to be ineffective, as the substance was rapidly inactivated by the liver, thus requiring the development of parenteral forms or molecular modifications. Over the decades, the formulations have been improved, making it possible to achieve physiological serum levels with greater efficiency [5].

In the twenty-first century, there has been a substantial growth in hormone supplementation. The trivialized use was driven both by the aesthetic search for better physical shape and by the expansion of clinical use, especially in sports medicine — in postoperative rehabilitation processes, in the treatment of injuries in athletes, and in clinical cases such as hypogonadism [6].

In a scientific context in general, in topics involving hormonal therapies, the terms anabolic and androgenic are frequently used. To better understand these concepts, the term anabolic is the stimulus to the growth and development of non-reproductive tissues, especially muscle and bone tissues, given its relevance in the context [7].

The term androgenic, on the other hand, is conceptualized as the ability to induce the development of secondary male sexual characteristics in the body. The authors also highlight the etymological origin of the word, derived from the Greek: "andro", which means "man", and "gennan", which means "to produce" [6].

The androgen action is divided by four main circulating forms of this hormone in the body: Dihydrotestosterone (DHT), dehydroepiandrosterone (DHEA), Testosterone and dehydroepiandrosterone sulfated (DHEAS) [8].

Hormone production, both in the female and male bodies, has a common origin in the hypothalamus, a structure located in the brain. This organ is responsible for the synthesis of GnRH (Gonadotropin-Releasing Hormone), which stimulates the anterior pituitary gland, or adenohypophysis, to produce two fundamental hormones: LH (Luteinizing Hormone) and FSH (Follicle-Stimulating Hormone) [9].

In the male body, these hormones act directly on the testicles. LH stimulates the production of testosterone, while FSH is involved in spermatogenesis, the process of sperm formation [9].

In women, on the other hand, FSH stimulates the development of ovarian follicles — structures that surround and nourish the egg. LH, in turn, is mainly responsible for promoting ovulation, that is, the release of the egg and the formation of the corpus luteum, a temporary endocrine gland that starts to secrete the hormones progesterone and estrogen, essential for the regulation and maintenance of the menstrual cycle [9].

The human body regulates its hormones through two main mechanisms: negative feedback and positive feedback [10].

In humans, regulation occurs mainly by negative feedback. When there are high levels of testosterone, the testicle sends a feedback signal to the hypothalamus, which reduces the production of GnRH. This decrease prevents excessive production of the hormone in the body [10].

In the female reproductive system, hormonal control is more complex. During the follicular phase (which precedes ovulation), estrogen at moderate levels exerts negative feedback on the hypothalamus and pituitary gland, inhibiting the production of FSH and LH. This prevents multiple follicles from maturing simultaneously. However, in the ovulatory phase, there is an abrupt increase in estrogen levels, which starts to exert a positive feedback, stimulating an LH peak and, consequently, ovulation [10].

After the release of the egg, the corpus luteum forms and begins to secrete high concentrations of progesterone and small amounts of estrogen. This hormonal combination again inhibits the release of LH, FSH and GnRH, preventing new ovulation. If there is no fertilization, the drop in progesterone levels leads to desquamation of the uterine endometrium — a process known as menstruation —, restarting the cycle [10].

3.2 SITUATIONS IN WHICH HORMONE THERAPY CAN BRING HEALTH BENEFITS

The prescription of hormonal drugs is widely studied around the world, being used for therapeutic purposes, especially in the treatment of chronic clinical conditions that cause a reduction in muscle or bone mass. In these cases, hormone therapy aims precisely to reverse these effects, promoting an increase in the mass in these tissues [11].

Below are approaches to diseases in which the use of hormone therapy brings scientifically proven benefits:

3.2.1 Osteoporosis

Osteoporosis is defined as a condition characterized by the progressive loss of bone density and microarchitecture — a process known as osteopenia — which results in greater porosity and fragility of the bones, making them more susceptible to fractures. Among older people, these fractures significantly increase the risk of morbidity and other health complications. The progression of the disease is usually silent, since the loss of bone mass occurs gradually and asymptomatically, unlike a fracture [12].

Osteoporosis (OT) is classified into two main forms. Involutional is subdivided into two types: type 1, more common in women in the postmenopausal period, is triggered by the

reduction and imbalance of estrogen levels; Type 2 (also called senile) occurs in both sexes due to the natural loss of bone minerals associated with cellular aging, also known as senescence, and is often diagnosed after fractures in vertebrae that are the bones of the spine or in the femur, thigh bone, and the origin of the disease may be associated with the prolonged use of corticosteroids or endocrine dysfunctions, that directly compromise bone metabolism [13]. Idiopathic disease, in turn, has no known cause and is known to affect mainly children, young people, and adults [14].

The diagnosis of osteoporosis is mainly made through bone densitometry (MD), an exam that evaluates bone mineral density (BMD) [15], however blood and urine tests can also say a lot about health and indicate clinical conditions that can cause OT [16]. For the diagnosis to be accurate, it is essential to consider the patient's clinical history, including data such as age, ethnicity, onset of menopause (in women), family history of the disease, continuous use of medications, and presence of other clinical conditions [13]. In postmenopausal women, complementary tests such as radiographs and magnetic resonance imaging are recommended, as this phase involves a marked physiological loss of bone mass [17].

Scientific evidence shows that estrogen, calcitonin (the hormone responsible for regulating calcium) and calcium supplementation contributes to the prevention of bone loss. However, treatment must be strictly monitored, through DM — whose score must be maintained above -2.5 standard deviations, as established by the World Health Organization (WHO) — and the blood dosage of the supplements used. The excessive use of these substances can cause an antagonistic effect, causing an increase in bone porosity and structural impairment [12].

The hormones responsible for balancing calcium levels in the human body play a crucial role in bone health. Among them, the parathyroid hormone or parathyroid hormone (PTH), produced by four small glands located in the neck, stands out, which acts by increasing calcium levels in the blood by stimulating the release of the mineral from the bones, renal reabsorption, and the activation of vitamin D [18].

Vitamin D, which can be obtained through diet and skin synthesis after sun exposure, is associated with innate immunity and bone metabolism, especially when interacting with sex hormones in both sexes [19]. This nutrient, in turn, contributes to the efficient absorption of calcium in the intestine, promoting its availability to the bones. Calcitonin, a hormone produced by the thyroid gland, exerts the opposite effect to that of PTH: it inhibits the release of calcium from the bones into the blood, favoring the maintenance of bone mass [20].

These three components — PTH, vitamin D, and calcitonin — act in an integrated manner in the regulation of bone metabolism, being essential to prevent diseases such as

osteoporosis, which weakens bone structure, and osteomalacia, a condition characterized by the softening of bones due to a deficiency of minerals, especially calcium [21].

From an epidemiological point of view, the causes of osteoporosis can be classified as reversible or irreversible. Among the non-modifiable factors are female gender, natural aging, white ethnicity and genetic predisposition. Modifiable factors include prolonged use of anti-inflammatory drugs, hormonal changes, excessive alcohol consumption, smoking, sedentary lifestyle, calcium and vitamin D deficiency, and unbalanced diet [22].

Sex hormones — both male and female — play a key role in bone formation and regeneration, as they stimulate the production of cytokines, proteins that activate the cells responsible for the synthesis of bone matrix and the immune system [23].

Some warning signs that may indicate the presence of the disease include recurrent or spontaneous fractures, loss of height, acute or chronic bone pain, especially in the lower back, postural changes, and difficulty walking, which considerably increases the risk of falls [24]. The continuous use of analgesics for prolonged periods without effective pain improvement may also be an indication of the need for diagnostic investigation [12].

Osteoporosis prevention is strongly associated with the adoption of a healthy lifestyle, including smoking cessation, reduction of alcohol consumption, regular load-bearing exercise, and a balanced diet rich in essential nutrients [25] [17].

With regard to treatment, the drug approach should be started early, with a limited duration, in order to maximize its efficacy and reduce the risk of disease progression or generate an antagonistic effect [12]. The available drugs act through different mechanisms: some inhibit the resorption of bone tissue bisphosphonate and denosumab [26], while others regulate the processes of formation and degradation, which are vitamin supplements - calcium and vitamin D [27] and drugs with hormonal load - estrogen, testosterone and similar to parathyroid hormone, among others - contributing to the gradual restoration of balance in skeletal metabolism [17]element.

With an emphasis on female hormonal approaches, osteoporosis therapy can be conducted mainly through two groups of drugs: selective estrogen receptor modulators (SERMs) and hormone replacement therapy (HRT) [28].

SERMs are substances that partially mimic the effects of estrogen on bones, promoting the maintenance of bone mineral density and reducing the risk of fractures, without stimulating breast and endometrial tissues, which reduces the risk of side effects in these organs [29]. HRT, on the other hand, consists of the administration of estrogen, alone or combined with progesterone, and is indicated especially for women in the postmenopausal period, with the aim of compensating for hormone deficiency and preserving bone health.

However, its use requires individualized evaluation, considering cardiovascular and oncological risks [30].

Comparisons were made between a collection of studies in mice that correlate vitamin D and sex hormones in the development and progression of osteoporosis [31]. In an in vitro experiment, it was observed that androgens can affect, directly and indirectly, the action of osteoclasts — cells responsible for the resorption of bone tissue [32]. Another study reports that estrogen, a female sex hormone, has an effective action to stimulate the programmed death (apoptosis) of osteoclasts, that is, by the degradation of bones. This mechanism contributes to the preservation of bone mass, reducing the loss of important minerals such as calcium and phosphorus [33].

In an experiment with a significant sample of human subjects, of both sexes, aged between 40 and 60 years, with a diagnosis of osteoporosis, evaluating the action of circulating vitamin D (25-hydroxyvitamnios D/ 25(OH)D) in association with four sex hormones: total testosterone (TT), androstenedione (A4), estradiol (E2) and testosterone/17b-estradiol. The investigation was conducted with magnetic resonance imaging exams, as well as analysis of blood samples in order to monitor the amount of components, the focus of the research, in the bloodstream [31].

The results showed that only total testosterone had a causal effect, i.e., a high risk for OP, so TST was the only one considered as a potential mediator and played a relevant role in mediating the risk of osteoporosis, since it showed a positive correlation with 25(OH)D. This hormone was shown to act on osteoblasts — cells responsible for the formation and regeneration of bone tissue — and on osteoclasts, modulating the activity of these cells through the so-called androgen receptors, which are cellular structures sensitive to male sex hormones [31].

However, when total testosterone is in dysregulated concentrations, it can have the opposite effect, inducing apoptosis not only of osteoblasts but also of chondrocytes — cells that produce the cartilage that covers the ends of bones. In addition, under certain conditions, testosterone can be converted by the aromatase enzyme into estradiol, a hormone from the estrogen family, which has a protective effect against bone loss [34].

Despite the promising results, the authors reinforce that more research is needed to confirm the therapeutic efficacy of this approach, especially due to the complexity of hormone regulation in bone metabolism. It is essential to emphasize that this experiment obtained a favorable outcome in analyzing the interaction between 25(OH)D and TT, however the action of other sex hormones may be effective through other mechanisms in the prevention of OP [31].

3.2.2 Menopause

The transition from the reproductive to the non-reproductive phase of women, marked by the decline in ovarian function and permanent cessation of menstrual cycles, is a physiological process associated with chronological aging [35]. This transition, known as climacteric, is made up of three phases: perimenopause, menopause, and postmenopause.

Perimenopause represents the beginning of the transition, usually lasting an average of four years, and is characterized by menstrual irregularity and progressive failure of ovarian function. At this stage, the most common symptoms include hot flashes, mood swings, depression, insomnia, vaginal dryness, and decreased libido [36].

Menopause, in turn, is diagnosed retrospectively after 12 consecutive months of the last menstrual period without a pathological cause, usually occurring between 45 and 55 years of age, with individual variations [37].

Postmenopause is the last stage, which lasts until the end of life, in which climacteric symptoms can be maintained, intensified or decreased, depending on factors such as smoking, diet, consumption of alcohol and other substances, regular practice of physical activity and use of hormone therapy [38]. With the decrease in estrogen levels and the relative androgen predominance, susceptibility to chronic diseases, such as cardiovascular, osteoarticular, and metabolic diseases, increases [37].

Studies indicate that hormonal changes in the climacteric are related to the development of conditions such as sleep disorders, anxiety, migraines, type 2 diabetes, hypertension, weight gain, redistribution of body fat (especially abdominal), increase in fatty plaques inside blood vessels, sexual dysfunctions, as well as musculoskeletal, cognitive, cardiovascular, genitourinary, dermatological, and capillary changes [39].

Early menopause, defined as ovarian failure before the age of 40, is a rare condition that can occur without a defined cause or be induced by genetic, autoimmune, infectious issues, chemotherapy, enzyme deficiencies or surgical removal of the ovaries (oophorectomy). This condition is associated with increased risk of cardiovascular disease, nonalcoholic liver involvement, stroke, and early mortality [40].

Hormone therapy (HT) for menopausal symptoms began to be widely used in the 1960s, gaining notoriety in the 1990s after studies suggested benefits in the prevention of osteoporosis, cardiovascular disease and dementia. Until 2002, its use was widespread, often without critical assessment of the risks, such as breast cancer and thromboembolism. With the advancement of science, there was a significant reduction in the number of users [41].

Administration of estradiol and progestogens by non-oral routes, such as transdermal (patch) or vaginal, prevents first-pass hepatic metabolism, reducing the risk of side effects such as thromboembolism and cardiovascular events. Transdermal estradiol has a lower risk of clot formation compared with the oral form, although more studies are needed. On the other hand, the oral route favors the reduction of LDL cholesterol (bad cholesterol), and is indicated for women with high cholesterol. The combination of non-oral estradiol with intrauterine progestin represents an effective and safe strategy. Vaginal estradiol, on the other hand, is the best option for the treatment of genitourinary symptoms, such as vaginal dryness and pain when urinating [42].

Female sexual dysfunctions affect more than one-third of women at some point in their lives, characterized by complaints such as decreased desire, arousal, and sexual responsiveness [43].

Androgens, such as testosterone and its precursors, play a key role in regulating female sexual desire. Androgen deficiency can occur at any stage of life, and is more common in the postmenopausal period or after treatments that compromise ovarian function, such as oophorectomy, chemotherapy, or pelvic radiotherapy [44].

In the female body, these hormones are produced in the adrenal glands, ovaries, and peripheral tissues (adipose, muscle, and cutaneous). The main substances involved are: testosterone, androstenedione, dehydroepiandrosterone (DHEA), its sulfate (S-DHEA) and dihydrotestosterone. Testosterone is considered the main marker of androgenic activity [45].

In women, small amounts of testosterone are naturally produced by the ovaries and adrenal glands—which are located above the kidneys. This hormone, although present in lower concentrations in the female body, plays an important role in the regulation of libido. Part of testosterone is converted into estradiol, an estrogen that acts directly in the modulation of sexual desire, in addition to exerting influence on neurological functions related to pleasure and sexual motivation [46].

Receptors for sex hormones are widely distributed, especially in the central nervous system and genital region, explaining the effects on both central (desire and arousal) and peripheral (such as lubrication) aspects of sexual function [47].

Studies suggest an association between reduced S-DHEA levels and hypoactive sexual desire (DSH), especially in women over the age of 45. In young women, this relationship is also observed, although without significant correlation with total or free testosterone levels [48].

Androgen deficiency syndrome was clinically recognized in 2002 and includes symptoms such as decreased libido, fatigue, loss of bone and muscle mass, decreased body hair, and cognitive changes, even with normal estrogen levels [49].

The diagnosis is clinical, complemented by laboratory tests. The dosage of free testosterone can be useful, although limited by the low sensitivity of the available methods. Levels below 25 % of the reference values may suggest deficiency [43].

Testosterone therapy is indicated in cases such as premature ovarian failure, oophorectomy, adrenal or pituitary insufficiency, or levels below 20 ng/dL. Women of childbearing potential with normal levels should not undergo therapy [48].

A 2014 international consensus recommends testing testosterone therapy in postmenopausal women with DSH for three to six months, monitoring hormone levels and withholding treatment in the absence of response [50].

The main forms of presentation include:

- **Injectable (testosterone decanoate):** prolonged effect, increased risk of adverse effects, use limited to six times a year [51].
- **Oral (methyltestosterone):** rapid hepatic metabolization, higher incidence of side effects [52].
- **Transdermal patch:** continuous release, not yet approved in Brazil [53].
- **Vaginal topical:** effective for desire and body recognition [45].

Tibolone, a synthetic steroid with estrogenic, progestogen, and androgenic action, is effective in improving libido and well-being in climacteric women [48].

Despite the advances, the long-term effects of testosterone on women remain uncertain. As most products were developed for men, female use is considered off-label (with no indication provided for in the package insert), requiring caution. Orally, testosterone can alter the lipid profile, raising LDL (bad cholesterol) and reducing HDL (good cholesterol) and triglycerides. Non-oral forms (topical and injectable) present a lower risk in this regard [54].

Testosterone therapy is contraindicated in cases of hormone-dependent neoplasms, liver or cardiovascular diseases, pregnancy, lactation, androgenic alopecia, severe acne, and when the origin of the low libido is psychosocial or the increase in desire represents a risk to the patient. Individualized evaluation, especially of holistic aspects, is essential before prescribing [47].

3.2.3 Endometriosis

The endometrium, the tissue that lines the inside of the uterus, undergoes cyclical transformations throughout a woman's reproductive life, in response to variations in sex hormones, especially estrogen and progesterone. During each menstrual cycle, it thickens in order to enable the implantation of the embryo; In the absence of fertilization, this tissue is eliminated through menstruation [55].

This lining is made up of two distinct layers: a functional, outermost layer, which undergoes desquamation during the menstrual period; and a basal layer, innermost, which remains intact and has the main function of regenerating the functional layer with each new cycle. The drop in progesterone levels is the main trigger for the onset of the endometrial desquamation process, a process known as menstruation [56].

Endometriosis is a benign gynecological condition characterized by the presence of endometrium-like tissue — the layer that lines the inside of the uterus — implanted in places outside the uterine cavity, such as the ovaries, bladder, intestines, and the peritoneum (lining of the abdominal cavity). This cellular ectopy can cause severe pelvic pain, especially during menstrual periods and during sexual intercourse, as well as changes in menstrual flow and reproductive difficulties [57]. These symptoms are related to chronic inflammatory responses, hormonal changes, or the presence of systemic comorbidities, such as allergies, arthritis, and autoimmune diseases, such as thyroiditis [58].

Epidemiological studies indicate that the prevalence of endometriosis varies from 2% to 10% among women of childbearing age, and in about 30% to 50% of confirmed cases, there is a direct association with infertility [59].

During the menstrual cycle, it is common for a small amount of blood, containing cells from the endometrium (tissue that lines the inside of the uterus), to flow back through the fallopian tubes towards the abdominal cavity — a phenomenon known as retrograde menstruation. Under normal circumstances, these displaced cells are recognized and eliminated by the immune system through apoptosis, which is a natural process of programmed cell death [60].

However, in women with endometriosis, this defense mechanism is flawed. Endometrial cells end up surviving, attaching themselves to organs of the pelvis and forming lesions that behave in a similar way to uterine tissue, responding to the hormones of the menstrual cycle. This persistence is associated with cellular and immunological changes, such as reduced immune system activity, increased local inflammation, and failure in the apoptosis process. In addition, these cells start to produce estrogen autonomously, become

more sensitive to this hormone and develop resistance to progesterone — which impairs the natural control over tissue growth and favors the progression of the disease [60] [58].

This condition can affect several systems of the body, depending on the classification and impairment caused by the disease. Although there is still no definitive cure, the treatment aims to control pain and improve fertility. In more severe cases, surgical intervention may be indicated, usually followed by continuous drug treatment, in order to avoid recurrence of the lesions and the need for new surgeries [61].

Endometriosis can be classified according to the anatomical location of the lesions, presenting itself in three main forms. The most common form is superficial peritoneal endometriosis, characterized by small lesions that settle on the surface of the membrane that lines the abdominal cavity internally, called the peritoneum. Another form is ovarian endometriosis, in which there is the formation of cysts in the ovaries, known as endometriomas, composed of endometrial tissue and blood. The most severe form is deep infiltrative endometriosis, defined by the presence of lesions that penetrate more than five millimeters below the peritoneal surface and can affect organs located in the pelvis, such as the intestine, bladder, and adjacent muscles [62].

In addition to anatomical classification, different systems have been developed to describe the extent of the disease and guide clinical management. One of the most widely used is the American Society for Reproductive Medicine (ASRM) Classification, which divides endometriosis into four progressive stages, numbered from I to IV. This classification considers criteria such as the number, size, and depth of lesions, as well as the presence of adhesions – which are bands of fibrous tissue that connect organs to each other – and the involvement of the ovaries. In stage I, considered minimal, few superficial lesions are observed. Stage II is classified as mild, with a higher number of lesions, still predominantly superficial. In stage III, considered moderate, there is the presence of ovarian cysts and some adhesions. Finally, stage IV, classified as severe, involves large endometriomas and extensive adhesions that compromise the pelvic anatomy. Although widely adopted, this classification does not always reflect the intensity of clinical symptoms, such as chronic pelvic pain or infertility, which limits its prognostic utility [63] [55].

In order to complement these limitations, especially with regard to the evaluation of deep infiltrating endometriosis, the ENZIAN Classification was developed. This system proposes a more detailed anatomical division of the pelvis, segmenting it into different compartments (called A, B and C) and including specific structures such as the intestine, ureters and vagina. The depth and extent of lesions are numerically graded, allowing a more

accurate description of deep organ involvement and contributing to more appropriate surgical planning [64].

Another possible approach is the so-called functional clinical classification, which, although less used in the scientific literature, has relevant practical application. This proposal categorizes endometriosis according to its predominant clinical manifestations and its functional impact on the body. Thus, the disease can be described as asymptomatic, when it does not cause noticeable symptoms; painful, when there is pelvic pain or during sexual intercourse; associated with infertility; or with involvement of visceral organs, such as the bladder and intestine. This perspective allows for a more patient-centered approach, favoring individualized therapeutic conducts based on the clinical picture presented [65].

The choice of therapeutic strategy should consider the patient's clinical condition, age, reproductive desire, symptom intensity, and impact on quality of life, and an individualized approach is essential [66].

Hormone therapy is widely used in the treatment of endometriosis, aiming to relieve symptoms and improve the quality of life of patients. Several therapeutic options are available, each with specific characteristics regarding efficacy, benefits, and limitations. The following is an analysis of the main hormonal approaches, based on recent studies.

Combined estrogen and progestogen-based oral contraceptives are often used as the first line of treatment for endometriosis. They work by suppressing ovulation and reducing estrogen levels, which can slow the growth of ectopic endometrial tissue. In addition, they help regulate the menstrual cycle and can relieve pain associated with the condition. However, its effectiveness may be limited in more severe cases, and symptoms may return after stopping use. Studies indicate that while effective for many patients, about one-third may not get significant symptom relief from this therapy [67].

Progestogens, such as dienogest and norethisterone acetate, are used alone to treat endometriosis. They work by suppressing ovulation and promoting atrophy of endometrial tissue, which can reduce pain and bleeding. These medications are considered effective and have a more favorable side-effect profile compared to other hormonal therapies. However, adverse effects such as mood swings and irregular bleeding may occur. Recent literature highlights the efficacy of progestogens in controlling endometriosis symptoms, with good long-term tolerability [68].

GnRH analogues, such as leuprolide, are used to induce a state of hypoestrogenism by suppressing ovarian hormone production. This approach may be effective in reducing the symptoms of endometriosis, especially in cases refractory to other therapies. However, the associated side effects, such as menopause-like symptoms and loss of bone density, limit its

long-term use. Studies recommend the use of these agents for limited periods, with careful monitoring of adverse effects [69].

GnRH antagonists, such as elagolix and linzagolix, represent a newer class of hormonal therapies for endometriosis. They work by directly blocking GnRH receptors, resulting in a rapid and reversible suppression of hormone production. These medications have been shown to be effective in reducing pain associated with endometriosis, with a more manageable side-effect profile. Linzagolix, for example, was recently approved for use in the treatment of endometriosis, showing significant benefits in clinical trials [70].

Intrauterine devices (IUDs) that release progestogens, such as levonorgestrel, are used as a therapeutic option for endometriosis. They act locally, reducing the growth of endometrial tissue and relieving pelvic pain. This approach has the advantage of minimal systemic effects and long duration of action. However, adverse effects such as irregular bleeding and initial discomfort after insertion may occur. Recent studies have highlighted the efficacy of hormonal IUDs in the management of endometriosis symptoms, with good acceptance by patients [71].

The choice of hormone therapy for endometriosis should be individualized, considering the severity of symptoms, reproductive desire, and the side-effect profile of each option. Although none of the available hormonal therapies offer a definitive cure, they play a crucial role in controlling symptoms and improving patients' quality of life. The therapeutic decision should be made together with the health professional, considering the latest scientific evidence and the patient's preferences.

3.2.4 Aplastic anemia and bone marrow failure

Aplastic anemia is a rare and serious hematological condition, characterized by the failure of the bone marrow — the tissue responsible for the production of blood cells. This failure compromises all hematopoietic lineages, that is, the three main types of blood cells: red blood cells (which carry oxygen), white blood cells (which fight infections) and platelets (which participate in coagulation). The disease occurs in the absence of tumor infiltrations or bone marrow fibrosis, distinguishing it from other bone marrow pathologies [72].

The causes of aplastic anemia can be acquired or hereditary. Acquired forms are often associated with exposure to toxic substances, such as benzene and certain pesticides, long-term use of medications, including chemotherapy and anticonvulsants, viral infections (such as hepatitis, HIV, and herpesviruses), autoimmune diseases, hematological malignancies, or even pregnancy [73]. Hereditary cases, although rarer, usually appear as late manifestations of genetic syndromes that compromise the function of the bone marrow. Among these

syndromes, the following stand out: dyskeratosis congenita, a disease characterized by changes in the skin, nails and mucous membranes, as well as progressive bone marrow failure; Shwachman-Diamond syndrome, which combines pancreatic insufficiency, skeletal alterations, and hematological (blood) dysfunction; and Fanconi anemia, a genetic disorder that leads to multiple congenital malformations, chromosomal hypersensitivity (changes in the structures or number of chromosomes), and increased risk of cancer [74].

The clinical manifestations of aplastic anemia reflect the deficiency of different cell types in the blood. The shortage of red blood cells causes symptoms such as fatigue, pallor, headache, shortness of breath on exertion and dizziness. Low platelet count leads to the occurrence of spontaneous bleeding in the gums and mucous membranes, easy appearance of bruises, red dots on the skin (petechiae) and prolonged bleeding even after mild trauma. Neutropenia, on the other hand, which is the reduction of neutrophils — a specific type of white blood cell responsible for defending against infections — significantly increases the risk of serious bacterial and fungal infections, which can manifest themselves as persistent fever, chills and lesions in the oral cavity [75].

Although the diagnosis of aplastic anemia is relatively straightforward, it is essential to exclude other causes of pancytopenia, a term that designates the simultaneous reduction of all blood cells (red blood cells, leukocytes, and platelets). The investigation begins with the complete blood count, an exam that quantifies blood cells; the reticulocyte count, which evaluates the ability of the marrow to produce young red blood cells; bone marrow aspirate, which provides cellular material for microscopic analysis; and bone marrow biopsy, which allows the evaluation of the structure and degree of cellularity of hematopoietic tissue. These tests are essential to confirm the diagnosis and exclude other pathologies, such as leukemia or myelodysplastic syndromes – disorders in the production and maturation of blood cells [76] [77].

Complementary tests are also used to deepen the diagnostic investigation. Flow cytometry allows the identification and precise quantification of the presence of specific types of proteins present in some cells through molecular markers, helping to exclude malignant hematological diseases. Genetic analysis and chromosomal tests are used to detect mutations or structural alterations in chromosomes, enabling the recognition of rare hereditary syndromes that affect blood formation, such as the aforementioned genetic dysfunctions [74] [76] [77].

The treatment of aplastic anemia and bone marrow failure varies according to the severity of the clinical condition and the characteristics of the patient. Initially, supportive measures, such as blood and platelet transfusions, are necessary in order to prevent bleeding

and infections, avoiding iron overload and the development of immunological reactions against transfused components as much as possible [78]. In severe cases, bone marrow transplantation (also called allogeneic hematopoietic stem cell transplantation) is considered the therapy of choice, especially for young patients who have a fully compatible family donor. This strategy offers curative potential by replacing the compromised marrow with healthy cells [79].

When transplantation is not possible, either due to the absence of a donor or due to clinical contraindications, immunosuppressive treatment is used. This approach aims to reduce the autoimmune response which, in many cases, is implicated in the destruction of marrow stem cells. The main drugs used are antithymocyte globulin (ATG), cyclosporine, both of which act on T lymphocytes in the regression of action of this cell directly or indirectly, and eltrombopague, the latter being a stimulator of platelet production. This therapeutic regimen requires close follow-up due to possible side effects, especially in elderly patients or those with concomitant autoimmune diseases [80].

Another therapeutic alternative is the use of hematopoietic growth factors, which stimulate the proliferation of progenitor cells in the bone marrow. While this approach does not promote healing, it may temporarily improve cell levels in debilitated patients. Agents such as G-CSF and GM-CSF (which stimulate the production of white blood cells) and erythropoietin (which stimulate red blood cells) are used, always with caution regarding adverse effects such as thrombosis and elevations in blood pressure [81].

In specific cases, androgens such as danazol, oxymetholone, metonolone, norethrolone, enanthate, oxandrolone, fluoxymesterone and stanozolol may be considered. These hormones have a stimulating effect on the production of red blood cells and modulating the immune response. However, their use requires caution, as they can cause important adverse effects, such as liver changes, virilization in women, changes in the lipid profile, and overdevelopment of breast tissue in men. They are usually indicated only when other therapeutic options are not feasible, and are contraindicated in pregnant women and in people with liver or kidney diseases or malignant neoplasms. To make this therapy viable, both physical-clinical and psychological aspects of the patient should be evaluated as a result of possible side effects [82].

3.2.5 The indiscriminate use of hormone therapy

The trivialization of anabolic androgenic steroids (AAS) is one of the factors that is associated with the increase in epidemiological indicators of morbidity and mortality. Neuropathological alterations such as changes in neuroendocrine functioning, apoptosis of

neurons, were evidenced in individuals in abusive use of anabolic steroids. Therefore, some symptoms may be common to the conditions mentioned, such as neurological disorders, such as difficulty regulating sleep, anxiety, depression, increased aggressiveness, appetite variations, hallucinations, failure in memory, attention and reasoning. In addition, in the long term, it can accompany consequences such as chemical dependence accompanied by withdrawal crises (83).

The use of anabolic androgenic steroids has become common among young people and athletes in several countries. The search for quick benefits, such as increased strength and physical endurance, as well as muscle toning and increased sexual desire, stands out among the main reasons identified by researchers in the field. Thus, the indiscriminate use of such substances, especially with serious consequences, especially on heart health(84).

However, the randomized study introduces the use of AAS in young men over 18 years of age, in the first cycle of use, in individuals with satisfactory cardiovascular health. The risk of ventricular hypertrophy was monitored by means of echocardiography. The results found left ventricular hypertrophy, in addition to systolic and diastolic impairment, associated with the use of androgens in the short term, with verification of total recovery observed after the end of use (84).

On the other hand, the analysis performed only during a short cycle expresses a limitation for the identification of consequences to large-scale use, either due to prolonged cycle time or short pause between cycles. In addition, the study presented obstacles in proving a causal relationship due to differences in the physical training routines of the research participants (84).

Artificial hormone-based compounds for non-therapeutic purposes induce a reduction in liver metabolism, this occurs mainly to increase the results in time and effectiveness in the body. However, the action of testosterone on the liver is evident in a ramified form, from dyslipidemia caused by electrolyte imbalances in the bloodstream, to lesions in the liver and hepatic pathways (85).

The infiltration of inflammatory cells is the main cause of hepatotoxicity, organ damage and a disproportionate increase in collagen synthesis. In addition to causing a significant increase in the risks of developing tumors and liver cancer, the use of steroids can also affect the functionality of the bile ducts, causing excessive production of bilirubin, which in increased quantities becomes toxic to the body, especially to the neurological system. The article mentions other serious conditions in patients who use supraphysiological hormonal substances, such as cholestasis, peliosis, hepatic steatosis, and benign and malignant tumors (85).

At the nephrological level, the consumption of anabolic steroids increases renal toxicity and involves glomerular and interstitial damage, which can range from acute to chronic kidney injury, depending on the time of use and clinical history of the user. In addition, the conditions mentioned are a consequence, in a majority, of hyperfiltration in the glomeruli and hypercalcemia. In summary, the elimination of protein through the urine, the formation of kidney stones due to the increase in calcium and changes in creatinine levels in the blood are some of the indicators of the damage caused (86).

In the male reproductive system, androgenic substances cause a reduction in pituitary hormones in the testicle, this drives the inhibition of natural testosterone production and impairs sperm production. In addition, the reduction of LH and FSH in the testicles increases the levels of estradiol in the body, which generates complications such as increased acne, hair loss and gynecomastia. The abusive use of anabolic steroids can cause low libido and erectile dysfunction, especially in diabetic men or those with other adverse health conditions (87).

In the female body, the effects of improper hormonal supplementation can have temporary and permanent consequences that can affect everything from physical health to mental health and self-esteem. Among the most common consequences, temporary infertility, absence of menstruation, significant clitoral enlargement can be highlighted. There is also the virilization of female characteristics such as dilation of the waist and shoulders, breast atrophy, deepening of the voice and excessive hair growth. The factors listed negatively influence social relationships and sex life, in addition to several reports, women confirmed a negative impact on libido, self-esteem and reported regret after using anabolic steroids (88).

4 METHOD

4.1 TYPE OF STUDY

The present study is a Final Paper of an undergraduate course in Nursing from the Faculty of Military Principles and addresses an integrative systematic bibliographic review of scientific articles that address the use of hormone therapy as the main subject.

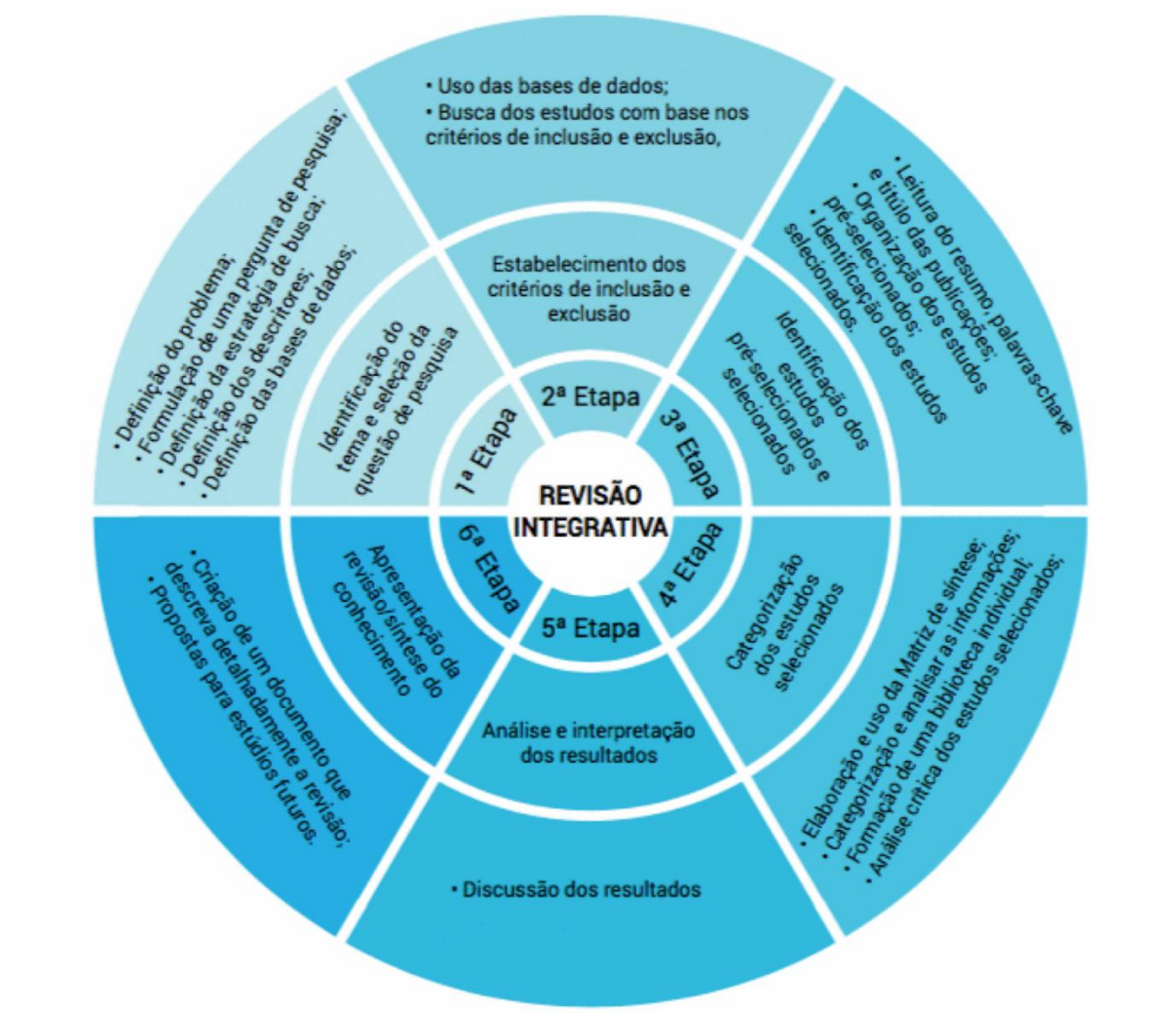
Integrative review is a type of research method that seeks to summarize the existing literature on a particular subject, both empirical and theoretical, with the goal of providing a more complete understanding of the phenomenon in question. The main objective of this approach is to analyze the existing knowledge in previous research on the subject, allowing the synthesis of multiple studies and the generation of new knowledge based on the results presented by previous studies.

The concept of "integrative" comes from the combination of opinions, concepts or ideas originating from the research used in the method. Whitemore and Knafl (2005) believe that it is at this moment that the potential to build science becomes evident. The authors state that a well-done integrative review should present the state of the art on a topic, contributing to the development of theories. The integrative review method is an approach that allows the inclusion of studies that use different methodologies, including experimental and non-experimental approaches.

The literature review study is an integrative evaluation analysis that is carried out in six stages, namely: identification of the theme and selection of the research question; establishment of inclusion and exclusion criteria; definition of pre-selected and selected studies; categorization of the selected studies; analysis and interpretation of results; presentation of the review/synthesis of knowledge (BOTELHO, CUNHA, MACEDO, 2011).

Figure 1

Stages of the integrative review



Source: BOTELHO; WEDGE; MACEDO, 2011.

The integrative review gets its name because it provides details about certain problems that are held in the literature by various scientific opinions and formalized studies, so the research that does the integrative review can offer a wide variety of useful views that improve the idea, evaluate the concept or evaluate the research method in a specific article (ERCOLE *et al.,* 2014).

To define the research question that will guide the entire following study, we used the PICO strategy, which consists of an acronym for Patient, Intervention, Comparison and "Outcomes", thinking about these four strands we formulated our guiding question: "How can hormone therapy be strategically applied to improve quality of life in specific conditions, while addressing the risks associated with indiscriminate use and its potential harms."

From the formulation of the guiding question, the writing of the objectives of this study began, in which it was defined: To analyze the main aspects related to hormone therapy and the most relevant consequences of indiscriminate use.

Thus, the inclusion and exclusion criteria emerged, as an inclusion criterion we use articles ≥ 2020; integrative reviews; systematic reviews; studies in the area of nursing; articles written in English, Spanish and Portuguese; As exclusion criteria, we used a study in which there was no relationship between the diseases or conditions in focus, nursing and hormone therapy. We used the studies available between January 2020 and August 2025.

A search was carried out in the online databases of international and national literature. The results of the present study were based on the following databases: LILACS (Latin American and Caribbean Literature on Health Sciences); PUBMED (National Libery of Medicine); SCIELO (Scientific Electronic Library Online); and VHL (Virtual Health Library).

In all four databases, the following descriptors were used: "nurse", "Anabolic Androgenic Steroids", "Hormone Replacement Therapy", "Hormone Replacement Therapy", "Hormone Deficiency".

The search returned the following results: 10 SCIELO (Scientific Electronic Library Online), after applying the inclusion, exclusion and evaluation criteria according to the guiding question, the result of this database was given by 8 studies. On the LILACS platform (Latin American and Caribbean Literature on Health Sciences) we obtained the results of 159 studies, in which they met the same criteria, resulting in 9 studies. In the PUBMED (National Libery of Medicine) database, 1524 were located, which in the sequence, after using the criteria of inclusion, exclusion and fit our objective given through the guiding research, resulted in 200 studies, finally in the VHL (Virtual Health Library) we obtained 7039 results and after applying the criteria, the result was 68 studies.

In all, we obtained 8,732 studies as bibliographic return, and only 285 of them were used, for the next phase, in which the titles, abstracts and full studies were carefully read, and only 88 articles were selected for this study.

5 INCLUSION AND EXCLUSION CRITERIA

5.1 INCLUSION CRITERIA

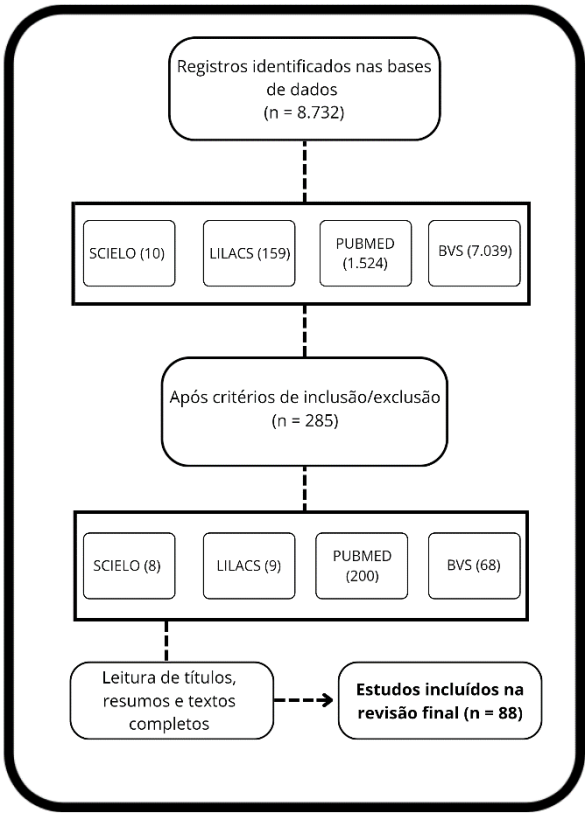
The inclusion criteria were: all types of articles that addressed the topic, articles ≥ 2020 studies in the field of nursing were used; articles written in English, Spanish, and Portuguese. Studies available between January 2019 and August 2025 were used. We selected 398 articles for reading in full, in which 88 articles were used to compose this work.

5.2 EXCLUSION CRITERIA

The exclusion criteria were defined articles that did not address the topic in full, studies where there was no relationship between hormone therapy and applicability in humans

The following is a flowchart in which the search for the articles that were part of this integrative systematic review is carried out:

Figure 2



Source: Authors.

6 VENUE AND PARTICIPANTS

The study was carried out in Goiânia, Goiás, Brazil, by students of the 9th period of the nursing course of the Faculty of Military Principles: Geovanna Fernandes Lacerda Sousa and Josué Batista Maciel under the guidance of Professor Katiulcy Carvalho Oliveira.

7 ETHICAL ASPECTS

All ethical and legal aspects that guide integrative systematic review research will be followed. Attesting to the elaboration of the articles studied in this work, having citations and references of the authors following the standards of the Brazilian Association of Technical Standards (ABNT).

8 DATA ANALYSIS

All types of articles that addressed the topic of Hormone therapy were analyzed and articles referring to the years 2020 to 2025 were selected.

A total of 285 articles were selected for reading, in which 88 articles were used to compose this work.

Articles that did not address the topic in full were not analyzed, studies where there was no relationship with the use of hormones, except for 200 articles, according to exclusion criteria.

9 FINAL CONSIDERATIONS

Hormone therapy is an important therapeutic strategy in clinical practice, with established applications in various conditions, such as menopause, endometriosis, osteoporosis and aplastic anemia. The rational and individualized use of these therapies, combined with multidisciplinary follow-up, allows not only the control of symptoms and the improvement of quality of life, but also the reduction of systemic complications associated with hormonal dysfunctions.

Among the drugs used, tibolone stands out for its multifunctional profile, exerting estrogenic, androgenic and progestogenic effects. Although it has recognized benefits in the management of climacteric symptoms and in the prevention of osteoporosis, its off-label use by women, outside of formal indications, remains a controversial topic. Studies point to positive effects on female well-being and libido; However, there are still significant gaps regarding cardiovascular safety, metabolic impact, and potential long-term repercussions on hormone-sensitive tissues. Thus, indiscriminate use without clinical-scientific support should be strongly discouraged.

In general, the present review reinforces the importance of delimiting ethical and scientific boundaries between the therapeutic use and the aesthetic or sports use of hormonal substances. The use of anabolic steroids and other hormonal agents for the purpose of body modification or physical performance has serious health consequences, including neurological, cardiovascular, hepatic, renal, and reproductive impairments, as well as significant psychological effects resulting from female virilization. Such changes may be irreversible and require continuous clinical and psychological follow-up.

Despite advances in understanding the mechanisms of action and clinical effects of hormonal therapies, there is still a need for longitudinal and multicenter studies that elucidate the cumulative risks of prolonged use, as well as the relationship between dose, exposure time, and individual vulnerabilities. Future research should also include the analysis of

psychosocial and quality of life aspects, especially in specific populations, such as young women of reproductive age and elderly women in long-term use of hormone therapy.

Finally, the essential role of the nursing professional in health education, in monitoring therapeutic and adverse effects, and in promoting the safe and conscious use of hormonal therapies is highlighted. Scientific and ethical deepening on the subject is essential for evidence-based practice, ensuring comprehensive, humanized care free of unnecessary risks to women's health.

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