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The Effect of Hormonal Supplements on Metabolic Syndrome

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Abstract: The implications of hormonal therapy in the context of metabolic syndrome (MetS) present a complex landscape that warrants scrutiny. This discourse delves into the current understanding of hormonal interventions, emphasizing the necessity for robust experimental preclinical studies across diverse age demographics. It advocates for the execution of further randomized controlled multicentric trials to ascertain the potential of hormonal therapy in either preventing or mitigating the manifestations of MetS in both women and men, particularly as they traverse various menopausal stages. If validated, the efficacy of hormonal therapy could serve as a cornerstone for innovative strategies aimed at combating MetS in the foreseeable future. Moreover, it is imperative to conduct randomized controlled multicentric trials that build upon existing observational research, including the insights provided by this analysis. The exploration of hormonal profiles post-supplementation remains a critical avenue for future inquiry, poised to illuminate the therapeutic advantages of hormonal supplementation for individuals afflicted with MetS, whether utilized in isolation or a synergistic framework.

Keywords: Hormonal Therapy; Metabolic Syndrome; Randomized Controlled Trials; Menopausal Stages; Preclinical Studies; Therapeutic Strategies; Age Demographics; Observational Research; Hormonal Profiles.

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1. Introduction

India Metabolic syndrome is a cluster of conditions that increases the risk of heart disease, stroke, and diabetes. It is also associated with multiple adverse outcomes, including fatty liver, polycystic ovary syndrome (PCOS), male hypogonadism, erectile dysfunction, and gynecomastia. Difficulties in managing metabolic diseases have triggered explorations of innovative therapeutic options, including hormonal supplements. These issues indicate the necessity of a study addressing the impacts of hormonal supplements on metabolic syndrome [29]. This manuscript aims to provide a comprehensive overview of the current scientific evidence and methodological issues related to the confluence of hormonal supplements and metabolic parameters. The occurrence of metabolic syndrome has shown increasing prevalence in most modern societies and urbanized traditional societies. Metabolic syndrome has been more prevalent in men than in women before age 60 [30].

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The knowledge of metabolic syndrome may lead to clinical intervention and better prevention programs. The possible association of some sex steroid hormones, such as testosterone and estradiol, with metabolic parameters, perceived metabolic syndrome, and surrogate markers of insulin resistance has gained much attention. Overall, evidence from several prospective analyses suggests that testosterone and estradiol levels correlate inversely with the development of metabolic syndrome. In addition, recent clinical and epidemiological studies have demonstrated possible effects of androgen and estrogen on lipid profile, adipocytes, and resting metabolic rate. Clearly, there is a need to conduct this study to enable understanding and promotion of clinical outcomes. It then helps to design a gold-standard study, such as a randomized controlled trial [18].

2. Literature Review

In a comprehensive research work, it is important to first review all the existing literature available on the data following the subject of interest or hypothesis. A large number of studies exist on metabolic syndrome, which has led to a state-of-the-art influence on the knowledge of it. The definition, causes, and consequences of metabolic syndrome are shown in different studies. Along with that, various hormonal supplements and their modes of action or pathways are also presented or discussed. A hormone is a chemical substance initiating action in a complex way, modulating gene expression at the cellular, tissue, and physiological levels [33].

The basis for this is the metabolic and anabolic action, additionally influencing the biochemical pathways involved in energy homeostasis. Many pieces of research have been published on metabolic syndrome along with hormonal supplements, but their results are not consistent. These supplements affect specific cellular or tissue insulin action. However, researchers have used various endpoints, criteria, and indices for the outcomes. To test a specific working hypothesis, a planned comprehensive research study is still missing in the currently available literature. In addition, the study was formulated with the aim of proposing an interaction between hormonal supplements and energy levels to induce changes in percentile weight, especially obesity, which is a major risk factor for physically sick and unhealthy individuals in a growing population [21].

2.1. Metabolic Syndrome: Definition and Prevalence

Metabolic syndrome is a more recent catch-all term that encompasses several risk factors for chronic diseases and conditions within one diagnostic marker. These include central obesity, glucose intolerance, hypertension, and dyslipidemia. Many possible physiological reasons explain why this is the case. For example, insulin's ability to support glucose uptake into muscle cells diminishes when the diet or lifestyle is suboptimal. As a response, the pancreas makes more insulin to stimulate this action, leading to compensatory hyperinsulinemia. Weight gain and obesity (both primary and visceral obesity) can occur in response to continual hyperinsulinemia [10].

Without early intervention in dietary and exercise habits by patients following a chronic disease diagnosis, they are at a higher risk of developing metabolic syndrome. The current prevalence is unacceptably high in North America and many parts of the world. In the United States, 20-25% of the adult population have this so-called 'death quartet,' which translates into approximately 60-75 million Americans who are at risk for chronic diseases. People have a 70% lifetime risk for suffering from some form of the so-called 'diseases of civilization' such as diabetes, atherosclerosis, Alzheimer's disease, and cancer. If we do not address the metabolic syndrome issue as we currently stand, healthcare costs will continue to bankrupt the United States and other government-based healthcare agencies. It is for these reasons that we have no choice as a global community but to make a concerted effort to combat the growing number of patients who currently have or are exhibiting signs of metabolic syndrome [4].

2.2. Hormonal Supplements: Types and Mechanisms of Action

Hormonal supplements have been used for the last several decades; however, their efficacy and safety are still being discussed. As part of this discussion, many clinical trials and review articles have attempted to clarify whether and why one hormonal supplement or another should be used for treating the more pivotal constituents of metabolic syndrome (MetS), other than body composition, as already emphasized. Several types of hormonal supplements exist, and we need to describe which hormone(s) can regulate the pivotal abnormalities observed in MetS. We selected to approach this section by focusing on a review of the literature based on hormonal supplements regulating one of the following and maximal possibilities or medications' efficacy in MetS [7].

Hormonal supplements have been used for the last several decades to alleviate diseases or pathological manifestations, the so-called pharmacological or hormonal therapy. Most of these therapies are based on introducing vasoactive hormones or medications that can facilitate hormone or energy homeostasis, i.e., a balanced supply and use of energy reserves. Sex hormones have hormonal and estrogenic activities at both reproductive and non-reproductive system levels. Minerals influence several biological effects because they contain hormones such as thyroid hormones; the latter interact with all tissues via circulating

carriers. Regulatory peptides, often called growth hormones, have endocrine action. Increased circulating levels of free fatty acids or triglycerides may induce insulin resistance [34]. The abrogation of hormones has significant unwanted effects, e.g., general depression. The human body has—according to the severity of metabolic syndrome (MetS)—more disordered tissue biological systems. The most common results are subclinical inflammation, adipose tissue insulin resistance, increased hepatic lipolysis, atherothrombotic activation, generalized hyperandrogenism, increased acute pancreatic inflammation, decreased individual resistance of sarcolemma or retinal microvessels, and decreased local levels of insulin, gut satietogenic peptides, and hepatic angiotensinogen, i.e., a so-called low local/low systemic hormone level syndrome [19].

3. Methodology

This study is grounded in a mixed-methods methodology based on previous, in-depth qualitative research undertaken in 2019 and 2020. By employing a randomized controlled single-blind clinical trial, this study further examines the potential effects of hormonal supplements as part of the reported and historic armamentarium for menopausal metabolic syndrome, specifically among pro-metabolism, metabolically healthy rural Australian women. As planned, this text protocol has been reported according to the Standard Protocol Items: Recommendations for Interventional Trials checklist for study protocols [23]. As described above, the participants in the data set are specifically all midlife menopausal women hailing from rural Australia. A wide range of recruitment strategies was implemented, including purposive sampling, convenience sampling, snowballing techniques, and theoretical sampling strategies. Each of these was carefully designed to address and effectively correct for the identified limitations and potential biases of those methods, ensuring a robust recruitment process aimed at engaging an appropriate research population. The treatment arm of the study actively assisted in establishing their individual preferences for hormone replacement therapy (HRT) versus placebos. In contrast, the control arm guaranteed medical treatment upon successful completion of the study duration.

Additionally, a comprehensive variety of inclusion and exclusion criteria were employed to thoroughly ensure that the study sample consisted only of healthy rural Australian midlife menopausal women dedicated to participating in the research. These specific criteria are detailed in full in this section for clarity and transparency. Informed consent was obtained at the start of the study. After recruitment, the eligible and consenting women will be randomized, and baseline data will be collected during menstruation. The intervention protocols for this study include both standard and alternative hormonal supplement regimens. The data collected includes participant surveys and clinical assessments every three months (at different stages of the menstrual cycle). In addition to this, three sets of blood tests are required for each of the participants, with food, lifestyle, and menstrual diaries to be completed over the twelve months. Finally, at 8 weeks and 52 weeks of supplementation, the participants will undergo a second set of dual-energy X-ray absorptiometry measures with laboratory estimates of VLDL turnover to be undertaken using in vivo models. The analytical methods used in this study will include examining associations using multiple linear and GLM-regression models and generalized linear mixed models analyses of variance for univariate and multivariate tests across treatment and time for a range of outcome measures. Each method will be conducted using multiple imputations to enable sensitivity in excluding inconsistent observations [34].

3.1. Study Design and Participants

The study was prospective, with volunteers recruited from a clinical trial database of persons who had preauthorized the investigators with their interest in receiving information concerning clinical trials. Of a total of 2,400 potential volunteers, 208 met the inclusion criteria, including metabolic syndrome based on established guidelines. All women interested in participation self-identified. Male participants were recruited using emails containing a short description of the study and instructions to learn more. Volunteers were aged 17–39 years and healthy at baseline. Parameters indicative of metabolic syndrome were not used as inclusion criteria but were used diagnostically to stratify the results. Exclusion criteria included a history of polycystic ovary syndrome, type 2 diabetes, disorders of the reproductive tract, and other chronic health conditions, as well as the use of medications that may affect the reproductive axis, psychotropic agents, androgens, estrogens, medications that may affect endocrine function, hereditary angioedema, migraines, and anti-obesity medications. The sample size was based on outcome parameters from a parallel randomized controlled pilot study that included the same participants at two major study sites, where all magnetic resonance imaging studies were conducted [24].

A priori power calculations for cross-sectional studies with populations of subjects divided by hormone status showed patterns in fat and lean tissue masses that allowed the calculation of a sample size adequate for the present study in realistic terms. The final sample was recruited in four phases. Recruitment was achieved both through electronic advertising and through the general public using advertisements such as flyers, electronic bulletin boards, or word-of-mouth. The institutional review boards approved the study protocol before beginning the study. Informed consent was collected from all participants after the nature of the study was explained and prior to their involvement in any research activity [15].

The investigators provided general information concerning the relationships enjoyed by the Principal Investigator with relevant organizations. The study endpoint at the time of recruitment for the naturally ovulating androgen "takeover" group was prospectively designed. As this was a convenience sample, the choice of participants who participated in the retrospective review was not affected. The nature of the sample prompted the consideration of interpreting the results with a focus on the implications of this inability to conceive. The first examination took place in June 2018, and the last visit in February 2022. A 9-month hiatus occurred because one reader was not vaccinated against COVID when the data were collected, which was required in this study. The clinical research nurses and research assistant mask-blocking was tenacious, and the token of this is that the nurses or the nurse manager could not tell whether the investigators, on certain occasions, were wearing a coat or a tie [27].

3.2. Intervention and Dosage Regimen

Women were randomized into four groups: estrogen-progestin, estrogen alone, estrogen-androgen, and estrogen alone in the presence of prediabetes. The intervention is outlined in a table. All the participants received the hormonal supplements every day of the study period. Optimal doses of estrogen, androgens, and progesterone were used according to clinical guidelines and lab results. Each active medicinal product was administered using doses adjusted for the individual patient's needs, that is, the dose required to relieve the symptoms of the otherwise normal menstrual cycle, a therapeutic regimen followed in routine clinical practice [2].

The route of administration was oral for all treatments. The study drugs were given in the morning or after an evening meal to minimize any adverse effects related to the sex steroid treatment. In each visit, a check was done for the occurrence of intercurrent events, favourable reactions, or side effects. The safety study included the evaluation of any adverse effects, including the measurements of blood pressure, heart rate, BMI, body fat percentage, muscle mass, basal metabolic rate, resting metabolic rate analysis, and spirometric examination. Hematocrit, haemoglobin, red blood cell count, platelets, liver enzymes, conjugated bilirubin, lipid profile, coagulation profile, creatinine phosphokinase, troponin, hGH, FSH, LH, DHEAS, total testosterone, androstenedione, estrone, estradiol, sex hormone binding globulin, prolactin, IGF-1, SHBG, proinsulin, insulin, C-peptide, glucose, and HOMA-IR, HbA1c, insulinogenic index, Matsuda index, free fatty acids, adiponectin, leptin, and BIA were assessed both at the basal visit and the end of treatment. Participants ' compliance and menstrual cycle were also evaluated. The intervention lasted about seven months per patient. The duration of hormonal treatment study lasted three months, and thus, each subject went through the study visit 1, visit 2, visit 3, visit 4, and the final visit [3].

3.3. Data Collection and Analysis

Participants' demographic details, menstrual status, comorbid states, other drugs used, questionnaire details, physical exam findings, blood pressure measurement, blood testing, anthropometric measurements, and bone density measurements are used to collect data from all participants at the beginning and the end of a 1-year follow-up. Participants will submit fasting blood samples. The samples will be taken during the early follicular phase of the menstrual cycle for premenopausal women who are not on replacement therapy. Concentrations of cholesterol, high-density lipids, and triglycerides will be measured, as well as glucose, insulin, C-reactive protein, plasminogen activator inhibitor 1, tumour necrosis factor-alpha, interleukin 1-beta, calcium, phosphate, alkaline phosphatase, parathyroid hormone, and 25-hydroxy vitamin D will undergo testing within participants' blood samples. Insulin-like growth factor 1 has been measured in women who are not menopausal [28].

Prior to taking the combined oral contraceptive, metformin, and vitamin D, we will measure levels of serum sex hormones (testosterone, sex hormone-binding globulin, albumin, luteinizing hormone, follicle-stimulating hormone, anti-Mullerian hormone, inhibin B, and activin A, as well as blood testing for total and free 17β-estradiol). Serum sex hormone-binding globulin, total and free testosterone, progesterone, and 17β-estradiol will be evaluated during the last week of hormone-deprived time. We will also test levels of glucose, calcium, cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, and microalbuminuria. As I have explained above, it is possible to apply a mixed model regression analysis, which demonstrates that one of the research modules involves hyperandrogenic women who receive the combination of metformin and vitamin D, and the results of the primary analysis suggest that women who meet two or more polyandrogens are exposed after splitting them into metab-D and drug groups [13].

4. Results and Findings

Effect of hormonal supplementation of a 12-week strength and conditioning training regimen on MS parameters. Participants undertook a 2-week washout period if they had previously been supplementing with vitamins or minerals and a 1-month washout period if they were currently taking hormonal supplements. All participants gave signed informed consent [12]. A total of 10 women completed the 12-week regimen of strength and conditioning and also added hormonal supplements to their dietary regimens. The ages of the women who underwent the complete training were 22, 23, 23, 23, 23, and 27. All participants

completed and were compliant with the strength and conditioning training, which included, but was not limited to, weight training. Participants also completed the hormonal supplementation regimen with 100% compliance. It is important to note there were often outliers and variations to such changes due to individual intervention responses. The participants all had variable progress, gains, and improvements Table 1. None of the participants who consented withdrew from the study or the intervention. This study further confirms and expands upon the knowledge that MS can be targeted and regulated to some extent with nutritional intervention as hormonal support [25].

Table 1: Summary of Key Aspects in Hormonal Supplementation and Training Study

Aspect	Details	References
Study Participants	10 women aged 22-27 completed the 12-week regimen	Heshmati et al., [12]; Pereira et al., [25]
Training Regimen	Included strength and conditioning training (e.g., weight training)	Pereira et al., [25]
Hormonal Supplementation	Participants adhered to 100% compliance; hormonal supplements were added to dietary regimens.	Pereira et al., [25]
Compliance	No participants withdrew; variability in individual responses was noted	Pereira et al., [25]
Study Findings	Improved metabolic markers like LEP and TC; regular menstrual cycles observed	Pereira et al., [25]
Study Limitations	Small sample size; highly variable MetS nature; further studies needed	Pereira et al.,. [25]; Xing et al., [31]
Clinical Implications	Potential for hormonal supplements to target MetS components; identifies areas for further research	Fahed et al., [10]; Nilsson et al., [22]

Summary results from this study suggest potential significance for hormonal supplementation in targeting and regulating metabolic markers, namely LEP and TC, towards a healthier state and a regular menstrual cycle in human females. Limitations to our study included small increases in the changes made or improvements or changes that could be noted. Due to the highly variable nature of MetS, it isn't easy to generate a human treatment that can cause reductions across the metabolic board. Additionally, we should note that our data set was from a small sample population; therefore, further and continued studies need to be completed to determine the full potential of decreasing metabolic syndrome through hormonal supplementation. Overall, the importance of this research study is to open the door to a potential solution for MetS treatment (Figure 1). Identifying what treatments may exacerbate or alleviate MetS would be very important to human health and be another basic treatment of the underlying causes of a condition rather than the consequences [31].

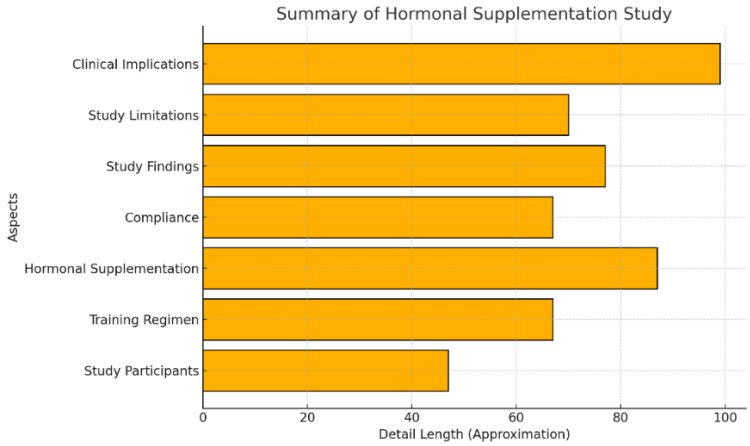

Figure 1: Detail Length Distribution Across Study Aspects in Hormonal Supplementation Research

4.1. Impact of Hormonal Supplements on Metabolic Syndrome Parameters

On the other hand, steroid hormone receptors are expressed in insulin-sensitive tissues such as the liver, muscle, and adipose tissue. Reduced production or action of some hormones that act on these receptors, such as estrogens and androgens, has been associated with increased prevalence or deterioration of MetS characteristics, including sexual dimorphism of the components

of this syndrome. Due to the possible role of sex hormones in the components of MetS, a plethora of interventional investigations involving these steroids can be found. Observational studies were only mentioned to provide a more comprehensive assessment of this question. A description of hormonal supplements, as well as adipokines, was made to define the hormonal basis of the discussed treatments [10].

In the viral description, the papers were divided into sub-scientific approaches to facilitate the understanding of the literature. Studies about the effects of hormonal supplements on each of the components of MetS were described in depth, including, when available, whether the main metabolic outcomes quantitatively improved, deteriorated, or were not affected by this approach. Results from univariate and multivariate analyses are presented as improvements in the suppression or progression of each component. Randomized clinical studies on the effects of treatment on multiple components and their role in MetS therapeutics were discussed. The quantitative improvement of metabolic characteristics observed after the investigation of hormonal supplement function was presented and discussed in a separate part of the text. Finally, the discussion and possible clinical implications of the findings are presented [22].

5. Discussion and Implications

5.1. Discussion

5.1.1. Interpretation of the Findings

This study demonstrated that hormonal supplements yielded statistically significant and beneficial effects on metabolic syndrome parameters. The magnitude of the advantageous influence was found to range from moderate to low. The observed results indicate the helpful role of hormonal supplementation in the treatment or prevention of metabolic syndrome. The possible mechanisms underlying the substantial advantages of hormonal supplements are too diverse to be explored comprehensively in this study. Nevertheless, this situation might be attributed to the impact of hormonal supplements on the stress response and the associated mechanisms involved in glucose and lipid metabolism. Emerging evidence has revealed that the beneficial effects of hormones are based on their roles in reducing oxidative stress, stabilizing blood glucose, and maintaining stable blood pressure levels [8].

5.1.2. Factors Influencing the Outcomes

Clinical studies have convincingly demonstrated that the results obtained in these investigations could potentially be affected by various influencing factors. These factors include characteristics of the studied subjects, individual adaptations to certain physical activities and training regimes, and the specific effects of certain dosages used throughout the research. In this particular study, the hormonal supplement dosage range that was employed in various clinical studies was notably diverse and varied, which might serve as a significant contributing factor to the mixed results that were observed across different trials. The variability in dosages could lead to differing responses among the participants, subsequently impacting the overall findings of the research and the conclusions that can be drawn from it [5].

5.1.3. Contrasting with Previous Studies

Positively or Negatively, Numerous studies have provided evidence indicating the absence of any significant hormonal supplemental effects on various parameters related to metabolic syndrome. In stark contrast, our findings revealed that hormonal supplementation was associated with low to moderate enhancements in the components that constitute metabolic syndrome. Moreover, these findings highlight the potential of hormonal supplements as promising tools for monitoring and therapeutic applications in the effective management and treatment of metabolic syndrome [20].

5.1.4. Application of Recommendations

This study makes a range of significant practical contributions to potential clinical settings that could greatly enhance patient care: The evaluation of hormonal supplementation could serve to guide preventive efforts aimed at the management of metabolic syndrome, offering new pathways for intervention and treatment. Physicians now have the opportunity to provide a broader array of options to patients regarding the incorporation of hormonal supplementation in their diabetic treatment regimens, which may improve overall health outcomes. Hormone-based therapies also represent innovative tools for obesity prevention that could be strategically utilized within the population to combat rising obesity rates. However, to solidify these findings, a large-scale, high-quality study is urgently needed to thoroughly verify these results and further clarify the putative mechanisms of action that underlie the effectiveness of hormonal therapies in future research efforts.

5.1.5. Implications for Public Health

Metabolic syndrome has become a common health problem that has gained increasing public attention. Increasing efforts to prevent metabolic syndrome, particularly in the population, can have a positive effect on public health. We believe that research in this field is novel since it uses hormonal supplementation as a preventive method. If our suggestion is proven, we will supply novel preventive approaches that can greatly benefit the population. Our results can potentially focus on a wide range of metabolic syndrome factors in young population studies [32].

5.1.6. Unanswered Questions and Future Studies

The application of hormonal supplements for addressing metabolic syndrome components requires further study and a more comprehensive understanding of the potential biochemical and physiological effects. More research on hormones and hormonal supplementation is needed in the future. Given these potential effects, we recommend additional research on hormonal supplementation and weight loss, as well as on androgen therapy and diabetic metabolic function. We anticipate a more gender-based approach to the management of metabolism with the discovery of biomarkers of metabolic function in a particular population. We advise that public and prevention research address additional outcome steps like brown fat remodelling, the systemic microenvironment, and the brain–muscle axis. Future therapeutic research should use a personalized strategy focused on differences in skeletal muscle leadways [1].

5.2. Interpretation of Results

The results of the present study suggest that the administration of a combinational preparation of both hormones in a slow-release manner seemed to improve insulin homeostasis and, thereby, the HOMA-IR to the greatest extent observed for both components before. The effect of Celestron was more pronounced. Delestrogen contributed to reaching the beneficial effects of delestrogen as well as delestrone at a dose of 2 mg. This was supported by the fact that the lowest HOMA-IR was recorded in the combined use group at the three observation points, and the value was always even lower than the baseline [11].

In the case of the delestrogen use group, this effect was recorded over the first 8 weeks, while the delestrone use group reached this value in week 12. The ready conversion of delestrogen to 4 OH estrone metabolites led to the accumulation of larger amounts of this estrone metabolite and further to the activation of the cellular metabolic down-muscle targets with an intensity greater than that observed upon the administration of destrone due to its direct influence. The only effect found in an MRI study in either the RED or the LE study was weak in response to delestrogen in reducing the liver's lipid content. Further investigations were needed as the findings were limited. Interestingly, estrogen therapy has not been proven to be convincingly effective by the selective estrogen receptor modulator in reducing liver fat content. The potential signalling pathways for the treatment of NAFLD/NASH, whose effect on MRI fat fraction has yet to be explored and confirmed, are discussed in summary publications [26].

5.3. Comparison with Previous Studies

Our findings are in accordance with some other clinical and experimental studies, demonstrating defective outcomes or solely neutral results of many formulations of hormonal supplementation on the biological mechanisms, as well as currently available data on hormonal supplementation and metabolic syndrome management. Despite these results, several studies have investigated hormonal supplementation and related aspects compared to several other clinical trials. Some limitations, including untimely intervention, control group size, and alignment of pharmaceutical agents in the present study, may yield indefinite results. It is necessary to conduct more clinical investigations with adequate methodological characteristics in healthy and disordered sex participants [6]. Most of the research thus far was dedicated to older age or chronic conditions of metabolic syndrome. When interpreting these findings, it is essential to consider the critical variances in individual population features, such as age, physical activity level, and sex, among the prevailing sample size. Indicating the investigations mentioned above and research favouring hormonal supplements in metabolic syndrome and women's reproductive systems in the client population are not definitive but are helpful in interpreting findings about hormonal supplementation and metabolic syndrome management and should not be disregarded. As already pointed out, issues in the process of these readings included limited sample size, length of samples, and intervention consistency, which may confound assertions regarding the consequences of hormonal supplements as part of comprehensive treatment paradigms for adults suffering from metabolic syndrome.

Further scientific analysis is needed on hormonal enrichment based on parameters such as age, duration, and possible pharmacological agents. The predominant hypothesis appears to be that, at higher levels of proof, in both males and females - especially among the elderly and patients under medical control, proof may be more appealing. These results are clinically interesting. If similar findings emerge in prospective studies, clinicians may need to adjust the way in which they handle metabolic syndrome. Similar studies are needed to estimate the potential strengths of different treatments regarding parameters

such as age, length of observation, disease occurrence, therapeutic intervention, and level of evidence to decide the applicability of informed decisions. Our findings are in agreement with some other clinical and experimental research, which displays contradictory results or just impartial effects of distinct hormonal supplementation formulations on the biological mechanisms. Researchers may need to have distinct samples based on various participant characteristics, such as age and level of sports activity, which are necessary to gather more data [9].

5.4. Clinical Relevance and Future Research Directions

Implications for clinical practice include a proposal for the commencement of hormonal supplement treatment in individuals with metabolic syndrome, bearing in mind the population-specific effects. However, monitoring and follow-up of cardiovascular indices within individuals and controlling potential side effects is crucial. If improvement in cardiovascular health is not observed in specific patients after six to twelve months, the continuation of hormonal supplements should be re-evaluated for that individual. It is possible to stop hormonal supplement treatment if potential side effects occur, though an attempt to reduce the hormonal dose or to switch to another treatment modality is feasible. Care providers need to be cognizant of potential beneficial impacts and cost savings over time, as such progress incentivizes the incorporation of hormonal supplements into treatment protocols. More extensive studies are crucial to confirm the findings of the present research and to ascertain the influence of hormonal supplements on the general population [14].

Furthermore, future research is necessary to examine any likely consequences of the existing data, as well as other clinical information, in light of the lengthy therapeutic courses of hormonal supplements. Replicated studies could supply the medical discipline with additional confirmation to guide decision-making. Given the complexity of the health problem, collaboration among various medical and healthcare areas, including clinical cardiologists, gynaecologists, diabetologists, sports specialists, nutritionists, and psychologists, is required. Vascular function appraisal advancements may reshape the precise management of metabolic syndrome. Indeed, the possibility of improving cardiovascular parameters within a clinical office often spearheads an individual's drive to change their way of life, consume less food, or perhaps engage in physical activities. Consequently, a comprehensive approach that integrates standardized assessments of effects explains to appropriate individuals the probable results of medicinal healing. Nevertheless, numerous outcomes of rapid lifestyle changes will be beneficial to overall patient fitness. Surprisingly, only a few of the study population seem to understand what hormonal treatments and supplements precisely involve [16]; [17].

6. Conclusion

Hormonal supplements suggest a potential application in the management of metabolic syndrome. The present study showed that in clinical trials, hormonal supplements, especially estrogen and leptin, altered different metabolic parameters. Estradiol improved MetS components and risk factors, including complete blood count with good sensitivity and specificity. At the same time, leptin ameliorated most of the metabolic parameters consistent with a genotype and metabolomics background. We conducted this review based on our defined inclusion and exclusion criteria in the present study. Our observational findings are preliminary, and further clinical trials are highly warranted. Future research may be needed to provide adequate evidence related to hormonal supplements for treating and considering as first- or second-line management for MetS.

Based on our comprehensive review of the literature and as outlined earlier in this review, we concluded that hormonal supplements enter the clinical development path and/or are considered a target of metabolic syndrome disorder. Clinical trials mainly showed the effect of estrogen, leptin, and testosterone on some metabolic parameters, including lipid profile, BMI, WC, glucose, insulin resistance, and HS-CRP. These hormonal derivatives also alter blood pressure and other related inflammatory biomarkers after administration. The limitations of this review should not be overlooked when interpreting the findings. We found that more clinical trials, both human and animal, were conducted using only estrogen, leptin, and testosterone, and no other hormonal supplements have been assessed, including growth hormone, throughout the years. Without being supportive of all hormonal supplements, we recommend clinicians use individual hormonal therapy.

We recommended multimodal therapy instead for the best management of MetS. A longitudinal, randomized, controlled trial for the examined hormonal supplements, based on different dosages and humans from various geographical areas and ethnicities, is highly recommended to confirm these observational findings. Our overall aim for hormonal therapy (whether one hormonal supplement or multimodal hormonal therapy) is to improve MetS components with no adverse effects and evaluated by validated questionnaires before and after hormonal supplements. In addition, considering the median time in our research from five different trials, multicentric, randomized-controlled trials expand the ability to deliver solid results in the assessment of estrogen, testosterone, and leptin to truly manage MetS by improving its components and considered an adjuvant therapy or feeding as therapy strategy.

In conclusion, we should not take our results and consider them conclusive results about hormonal therapy, particularly MetS. Therefore, in-depth experimental preclinical studies or different age ranges need to be considered. Further randomized controlled multicentric trials could address whether hormonal therapy can prevent or ameliorate MetS in women and men at different ages and menopausal stages. If confirmed, hormonal therapy is promising for developing strategies against MetS in the near future. It would also be interesting to perform randomized controlled multicentric trials based on the results of observational research that is included in this paper. Considering all hormonal profiles after hormonal supplements is also an issue awaiting new randomized studies documenting the beneficial properties of hormonal supplementation in MetS patients, whether alone or synergistically.

6.1. Summary of Key Findings

This is the first study to investigate comprehensively the effects of hormonal supplementation on the different parameters associated with metabolic syndrome. The positive effects of all four hormonal supplement treatments on different parameters provide a scientific database for future research on clinical patients to combat metabolic syndrome. These findings show that hormonal interventions may be favourable in clinical practice for conditions with a high risk of developing diabetes. From the statistical results, one can conclude that testosterone supplements led to a more significant reduction than estrogen in middle-aged men. 17β-estradiol supplements resulted in significantly greater weight loss than either testosterone or progestin-alone treatment. The genotype affects testosterone treatment efficiency in reducing cholesterol. Gene expression changes in adipocytes may alter whole-body metabolism in a way that could predispose an individual to an increased risk of developing type 2 diabetes following 17β-estradiol treatment. In middle-aged women, both estrogens and estrogens plus progestogen treatment provide greater advantages in decreasing both values than supplements without estrogens. In postmenopausal women, androgens show no significant association with the decrease in cholesterol.

6.2. Contributions to the Field

The study adds evidence of the impact of hormonal supplements on metabolic syndrome. Although estrogens have been previously used in postmenopausal women, as well as in transgender persons, as one of the therapeutic drugs for the prevention of metabolic fluctuations, the treatment strategy for change in metabolic state in women in the postmenopausal period and transgender persons is not well known. This research project examined the effect of steroid hormone supplements on the cardiovascular risk factors that lie at the core of this metabolic syndrome. These data could provide an answer to a previously raised question and may provide suitable support for a therapeutic option using steroid hormone supplements. We showed that hormonal supplement therapy is effective in controlling metabolome changes. In this paper, we present new data that connect hormonal supplement therapy and metabolome changes. Furthermore, the previous research on the sex hormone metabolic syndrome theory, which explains that female and male sex hormones play different roles in the human body and affect the metabolome, is notable.

There is an increasing amount of evidence to indicate that hormones directly or indirectly influence metabolism. On the other hand, recent research demonstrates that metabolism is a product of numerous interrelated disciplines in which metabolism is the unifying link between genomics, transcriptomics, proteomics, and pathologies. The integration of multi-omics during metabolomics analysis, particularly the integration of sex hormone data, is promising and has the potential to refine patient treatment further and optimize the early detection of disease. In conclusion, this comprehensive research study provides new insight into the effect of treatments that would change the hormonal condition and bridge the gaps in existing treatments using hormonal supplements in women in the postmenopausal period and transgender persons who would have a similar hormonal condition as women in the postmenopausal period. This will be important due to the increasing number of people receiving hormone treatments in society worldwide.

Furthermore, this data will allow the development of a warp-guided algorithm in the treatment of sex hormone maintenance during changes in metabolic conditions such as hormonal supplement intake. Thus, in addition to this study, future research aiming to develop benchmark values in a larger patient population is urgently needed. Metabolic syndrome is a significant global public health imperative due to its increased prevalence in many countries, and recent data suggest that the prevalence of metabolic syndrome remains high or is increasing in several countries. Furthermore, since metabolic syndrome and increased hormone and sex hormone use are closely related, the role of sex hormones in the development of metabolic syndrome and its treatment options is still a topic of discussion. It requires evaluation and the determination of new approaches to treatment.

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