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HORMONAL REPERCUSSIONS OF BREAST SURGERIES: ANALYSIS OF SCIENTIFIC EVIDENCE

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Resume: INTRODUCTION Breast surgeries, including mastectomies, breast reductions, and reconstructions, are increasingly common due to rising breast cancer rates, advancements in surgical techniques, and preventive health measures. These surgeries differ in their objectives and have significant implications for a woman's hormonal balance. Hormonal integrity is crucial for various physiological processes, and disruptions caused by breast surgeries can lead to substantial health impacts. The hypothalamic-pituitary-ovarian (HPO) axis plays a vital role in regulating female sex hormones, and surgical stress can adversely affect this system, leading to hormonal imbalances. Studies have documented various hormonal changes following breast surgeries, necessitating vigilant monitoring and personalized management to mitigate these effects and optimize patient outcomes. **OBJETIVE** To comprehensively review and analyze the impact of various breast surgeries on hormonal changes in women, focusing on the physiological, endocrine, and clinical consequences of these procedures. **METHODS** This is a narrative review which included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases, using as descriptors: "Breast Surgeries" AND "Hormonal Changes" AND "Endocrine Disruption" AND "Postoperative Complications" AND "Hormone Replacement Therapy" in the last years. **RESULTS AND DISCUSSION** Breast surgeries often lead to significant reductions in estrogen and progesterone levels, particularly after mastectomies and oophorectomies, resulting in symptoms similar to menopause. These surgeries disrupt the HPO axis, causing menstrual irregularities and infertility in premenopausal women. Thyroid function can also be affected, with temporary hyperthyroidism or hypothyroidism observed post-operatively. Growth hormone (GH) and prolactin levels may fluctuate, influencing breast tissue regeneration and metabolic health. Elevated cortisol levels due to surgical stress can suppress reproductive hormones and alter glucose metabolism. Insulin resistance and hyperglycemia are common post-surgery, complicating recovery. Changes in androgen levels can impact libido and mood, while alterations in parathyroid hormone levels can lead to hypocalcemia. Long-term hormonal complications, especially after mastectomies, necessitate personalized hormone replacement therapy. The psychosocial impacts of hormonal changes, such as depression and anxiety, are significant and require comprehensive management. Differences in hormonal changes between pre- and post-menopausal women highlight the need for tailored therapeutic approaches. **CONCLUSION** Breast surgeries, including mastectomies, breast reductions, and reconstructions, are increasingly common due to rising breast cancer rates, advancements in surgical techniques, and preventive health measures. These surgeries differ in their objectives and have significant implications for a woman's hormonal balance. Hormonal integrity is crucial for various physiological processes, and disruptions caused by breast surgeries can lead to substantial health impacts. The hypothalamic-pituitary-ovarian (HPO) axis plays a vital role in regulating female sex hormones, and surgical stress can adversely affect this system, leading to hormonal imbalances. Studies have documented various hormonal changes following breast surgeries, necessitating vigilant monitoring and personalized management to mitigate these effects and optimize patient outcomes.

Keywords: Mastectomy**;** Breast Reconstruction**;** Estrogen Levels**;** Hypothalamic-Pituitary-Ovarian Axis**;** Menstrual Disorders

INTRODUCTION

Breast surgeries, including mastectomies, breast reductions, and reconstructions, have become increasingly prevalent due to rising incidences of breast cancer, advancements in surgical techniques, and growing awareness of preventive measures. These surgeries are not only pivotal in the management of breast cancer but also in addressing congenital anomalies, trauma, and aesthetic concerns[1]. As the population ages and screening programs become more widespread, the number of women undergoing these procedures is expected to rise significantly[2]. The primary types of breast surgeries—mastectomies, which involve the removal of one or both breasts, breast reductions, aimed at decreasing breast size, and reconstructions, which restore the breast's appearance post-mastectomy—differ in their approaches and objectives[3]. Mastectomies are often performed as part of breast cancer treatment, while reductions and reconstructions cater to both therapeutic and cosmetic needs. Each type of surgery carries distinct implications for the patient's hormonal milieu, necessitating a nuanced understanding of these effects among medical practitioners[4].

Hormonal integrity is crucial for maintaining various physiological processes in women, including reproductive health, metabolic balance, and emotional well-being[5]. The ovaries, adrenal glands, and adipose tissue are central to hormone production and regulation, particularly of estrogen and progesterone[5]. These hormones play vital roles in the menstrual cycle, pregnancy, and overall homeostasis. Disruptions in hormonal levels can lead to significant clinical manifestations, impacting a woman's quality of life and long-term health outcomes[6]. The impact of breast surgeries on hormonal health is multifaceted and can lead to both immediate and long-term changes. Surgical stress, tissue removal, and subsequent healing processes can alter hormone production and regulation. For instance, mastectomies and oophorectomies (if performed concomitantly) can drastically reduce estrogen levels, precipitating menopausal symptoms in premenopausal women[7]. Even less invasive surgeries, such as breast reductions, can influence hormone levels through stress-related mechanisms and altered fat distribution[8].

The physiology of female sex hormones, primarily estrogen and progesterone, is tightly regulated by the hypothalamic-pituitary-ovarian (HPO) axis[9]. This complex feedback system ensures balanced hormone levels, crucial for reproductive health and overall well-being. Estrogen, produced mainly by the ovaries, affects various tissues, including the breasts, bones, and cardiovascular system[10]. Progesterone, also ovarian in origin, is essential for regulating the menstrual cycle and supporting pregnancy[10]. Disruptions to the HPO axis, such as those caused by breast surgeries, can therefore have wide-reaching implications. Surgical stress is a well-documented factor that can significantly impact the endocrine system[11]. The body's response to surgery involves the activation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased cortisol production. Cortisol, the primary stress hormone, can inhibit reproductive hormones, alter insulin sensitivity, and affect thyroid function[11]. Prolonged elevation of cortisol post-surgery can thus contribute to persistent hormonal imbalances, compounding the effects of direct surgical interventions on hormone levels[12].

The relationship between breast surgeries and the HPO axis is particularly pertinent. Surgical interventions can disrupt the ovarian blood supply, affect nerve pathways, and alter the signaling mechanisms within the HPO axis[13]. These disruptions can lead to anovulation, menstrual irregularities, and premature ovarian insufficiency[13].

Studies have shown that women undergoing mastectomies, especially with concurrent oophorectomies, experience significant reductions in estrogen and progesterone levels, necessitating careful management of these hormonal changes Clinical studies have documented a range of hormonal changes following breast surgeries[14]. For example, reductions in estrogen and progesterone levels are commonly observed post-mastectomy and breast reduction surgeries[14]. These changes can lead to symptoms reminiscent of menopause, such as hot flashes, mood swings, and vaginal dryness[15]. Additionally, altered levels of other hormones, including prolactin, growth hormone, and androgens, have been reported, further complicating the endocrine landscape of post-surgical patients[16].

The literature on hormonal complications in patients undergoing breast surgeries underscores the need for vigilant monitoring and management[17]. Hormonal dysregulation can manifest as metabolic disturbances, cardiovascular issues, and osteoporosis, among other complications[17]. Thus, a thorough understanding of the potential endocrine repercussions is essential for optimizing patient outcomes[18]. Studies highlight the importance of personalized care plans, incorporating hormone replacement therapy (HRT) and other interventions to mitigate these risks. Monitoring hormonal changes in post-breast surgery patients is imperative to address the myriad complications that may arise. Regular assessment of hormone levels, coupled with symptom evaluation, can guide therapeutic interventions[19]. Hormone replacement therapy, tailored to individual needs, can alleviate symptoms and improve quality of life. Additionally, non-hormonal strategies, including lifestyle modifications and pharmacologic agents, play a critical role in managing the complex hormonal milieu of these patients[19,20].

OBJETIVES

To comprehensively review and analyze the impact of various breast surgeries on hormonal changes in women, focusing on the physiological, endocrine, and clinical consequences of these procedures.

SECUNDARY OBJETIVES

1. To evaluate the incidence and types of hormonal changes, particularly in estrogen and progesterone levels, following different breast surgeries.
2. To investigate the effects of breast surgeries on the hypothalamic-pituitary-ovarian axis and related menstrual disorders.
3. To analyze the impact of surgical stress and trauma on thyroid function, cortisol levels, and insulin production.
4. To assess the long-term hormonal complications and the need for hormone replacement therapies in post-surgical patients.
5. To explore the psychosocial effects of hormonal changes and their influence on the quality of life in patients undergoing breast surgeries.

METHODS

This is a narrative review, in which the main of various breast surgeries on hormonal changes in women, focusing on the physiological, endocrine, and clinical consequences of these procedures. in recent years were analyzed. The beginning of the study was carried out with theoretical training using the following databases: PubMed, sciELO and Medline, using as descriptors: "Breast Surgeries" AND "Hormonal Changes" AND "Endocrine Disruption" AND "Postoperative Complications" AND "Hormone Replacement Therapy" in the last years. As it is a narrative review, this study does not have any risks.

Databases: This review included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases.

The inclusion criteria applied in the analytical review were human intervention studies, experimental studies, cohort studies, case-control studies, cross-sectional studies and literature reviews, editorials, case reports, and poster presentations. Also, only studies writing in English and Portuguese were included.

RESULTS AND DISCUSSION

The incidence of changes in estrogen and progesterone levels post-breast surgeries is well-documented, with significant reductions noted particularly after mastectomies and oophorectomies[21]. Studies indicate that these surgeries can lead to hypoestrogenism, manifesting as vasomotor symptoms, osteoporosis, and urogenital atrophy[21]. Hormone replacement therapy has been shown to mitigate these effects, although the benefits must be weighed against potential risks, such as the increased incidence of breast cancer in certain populations[22]. The effects of breast surgeries on the HPO axis are profound, with disruptions leading to menstrual irregularities and anovulation[22]. Research demonstrates that surgical trauma and subsequent stress responses can impair the normal functioning of the HPO axis, resulting in reduced gonadotropin secretion[22]. This can cause secondary amenorrhea and infertility in premenopausal women[22]. Long-term studies suggest that these effects may persist, necessitating ongoing hormonal monitoring and management[23].

Menstrual disorders are a common consequence of breast surgeries, particularly in younger women[23]. The disruption of the HPO axis and direct ovarian damage can lead to oligomenorrhea, amenorrhea, and irregular menstrual cycles[23]. Clinical data support the use of cyclic hormone replacement therapy to restore regular menstruation and alleviate symptoms[24]. However, the risk of thromboembolic events and breast cancer recurrence must be carefully considered when prescribing HRT[25]. Thyroid function can also be impacted by breast surgeries, with studies showing alterations in thyroid hormone levels post-operatively. [25] The stress response associated with surgery can lead to transient hyperthyroidism or hypothyroidism[25]. These changes are often temporary but can exacerbate underlying thyroid disorders. Regular thyroid function tests are recommended to identify and manage these imbalances promptly[26].

Growth hormone (GH) and prolactin levels may also be affected by breast surgeries. Surgical stress and trauma can alter the secretion of these hormones, with implications for breast tissue regeneration and overall metabolic health[27]. Elevated prolactin levels, in particular, have been associated with galactorrhea and amenorrhea, complicating the post-surgical recovery process[27]. Monitoring and managing these hormonal changes are crucial for optimal patient outcomes[27]. Cortisol levels and the body's stress response play a significant role in the endocrine changes observed post-breast surgeries[28]. Elevated cortisol can suppress reproductive hormone secretion, alter glucose metabolism, and affect immune function. Studies emphasize the importance of stress management techniques and supportive therapies to mitigate the adverse effects of elevated cortisol on recovery and overall health[29,30].

Insulin production and glycemic control can be adversely affected by breast surgeries, with surgical stress inducing insulin resistance[31]. This can lead to hyperglycemia, complicating the recovery process and increasing the risk of

postoperative infections[32]. Research supports the use of insulin sensitizers and strict glycemic control protocols to manage these changes effectively. Androgen hormone levels may also fluctuate following breast surgeries, with both increases and decreases reported in different studies[33]. These changes can impact libido, mood, and overall well-being. The use of androgen replacement therapy remains controversial, with potential benefits weighed against the risk of adverse effects[34].

Changes in parathyroid hormone levels and calcium metabolism are less commonly reported but can occur following extensive breast surgeries, particularly those involving the chest wall[35]. These changes can lead to hypocalcemia, with symptoms such as muscle cramps and tetany. Monitoring calcium levels and administering calcium supplements as needed can prevent and manage these complications[36]. The impact of breast surgeries on reproductive function and fertility is a critical concern, particularly for younger women[37]. Surgical interventions can lead to premature ovarian insufficiency and infertility, necessitating the use of fertility preservation techniques and assisted reproductive technologies[38]. Hormonal support and counseling are essential components of the management strategy for these patients[38].

Hormonal changes in patients undergoing breast reconstructions with implants are complex, with both local and systemic effects observed[39]. Studies indicate that the presence of implants can influence hormone levels, potentially affecting the overall endocrine balance[40]. Ongoing research is needed to fully understand these interactions and their clinical implications. Long-term hormonal complications in patients undergoing mastectomies include persistent hypoestrogenism and its associated sequelae[41]. The use of long-term HRT remains controversial, with ongoing debates about the balance between symptom relief and the risk of cancer recurrence[41]. Personalized treatment plans and regular monitoring are crucial in managing these patients effectively[42].

Hormonal recovery in patients post-breast reduction is generally more favorable, with most patients experiencing a return to normal hormone levels over time[43]. However, some patients may require short-term hormonal support to manage perioperative symptoms[44]. The role of HRT in this context is less controversial but still requires careful consideration. The need for hormone replacement therapies in patients post-breast surgery varies based on individual risk factors and clinical presentations[44]. While HRT can provide significant symptom relief and improve quality of life, it must be tailored to the patient's specific needs and monitored for potential adverse effects. The decision to initiate HRT should be based on a comprehensive risk-benefit analysis[45].

The relationship between breast surgeries and the risk of developing endocrine diseases is an area of active research[46]. Studies suggest that surgical interventions can predispose patients to conditions such as hypothyroidism, diabetes, and adrenal insufficiency[46]. Early identification and management of these conditions are essential to prevent long-term complications[47]. The psychosocial effects of hormonal changes post-breast surgery are significant, impacting mental health, self -esteem, and overall quality of life. Depression, anxiety, and body image issues are common among patients who experience significant hormonal fluctuations post-surgery[47]. Psychological support, counseling, and hormonal management strategies are critical in addressing these issues and improving patient outcomes[47,48].

The influence of breast surgeries on the quality of life related to hormonal changes cannot be overstated[49]. Hormonal imbalances

can lead to a range of symptoms that significantly impair daily functioning and well-being[49]. Addressing these imbalances through comprehensive care plans that include medical, psychological, and social support is essential for optimizing recovery and long-term health[50]. Evaluating the effectiveness of different surgical approaches in minimizing hormonal changes is crucial for improving patient outcomes[51]. Comparative studies have shown that less invasive techniques, such as nipple-sparing mastectomies and minimally invasive breast reductions, may lead to fewer hormonal disruptions. Ongoing research and advancements in surgical techniques hold promise for reducing the endocrine impact of breast surgeries[52].

Clinical management strategies for hormonal changes post-breast surgeries include the use of hormone replacement therapy, non-hormonal medications, and lifestyle modifications[53]. Tailoring these strategies to individual patient needs, considering factors such as age, menopausal status, and comorbidities, is essential for effective management[54]. Multidisciplinary care teams, including endocrinologists, gynecologists, and mental health professionals, play a vital role in this process[55]. Investigating differences in hormonal changes between pre- and post-menopausal patients undergoing breast surgeries is essential for developing targeted management strategies[56]. Studies have shown that pre-menopausal women are more likely to experience significant hormonal disruptions, necessitating different therapeutic approaches compared to post-menopausal women[57]. Understanding these differences can inform personalized care plans and improve patient outcomes[56,59,60].

CONCLUSION

Breast surgeries, including mastectomies, breast reductions, and reconstructions, significantly impact the hormonal milieu of patients, necessitating comprehensive management strategies to address these changes. The interplay between surgical stress, direct tissue removal, and the body's endocrine response creates a complex landscape of hormonal alterations that can affect various aspects of health and well-being. This review highlights the need for vigilant monitoring, personalized therapeutic approaches, and multidisciplinary care to mitigate the adverse effects of these hormonal changes and optimize patient outcomes.

Hormonal changes post-breast surgery include reductions in estrogen and progesterone levels, disruptions in the hypothalamic-pituitary-ovarian axis, and alterations in cortisol, thyroid hormones, and androgens. These changes can lead to a range of symptoms and complications, from menopausal symptoms and menstrual irregularities to metabolic disturbances and psychosocial impacts. Understanding these effects and developing effective management strategies is crucial for improving the quality of life and long-term health of patients undergoing breast surgeries.

The use of hormone replacement therapy and other hormonal management strategies must be carefully tailored to individual patient needs, considering the risks and benefits in the context of each patient's unique clinical situation. Multidisciplinary care teams are essential for providing comprehensive care that addresses both the physical and psychological aspects of recovery. Ongoing research and advancements in surgical techniques and hormonal therapies hold promise for reducing the endocrine impact of breast surgeries and improving patient outcomes.

In conclusion, the hormonal changes

induced by breast surgeries are complex, requiring a nuanced and individualized approach to management. By integrating medical, psychological, and social support, healthcare providers can help patients navigate these changes and achieve optimal recovery and long-term health. Further research is needed to continue advancing our understanding of these hormonal changes and to develop more effective strategies for their management.

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