DOI: 10.53469/jcmp.2025.07(10).33

Research on the Mechanism of Acupuncture in the Treatment of Mammary Gland Hyperplasia

Liwei Pan[1], Junming An[2,*], Le Zhang[1]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Xi'an Hospital of Traditional Chinese Medicine, Xi'an 710021, Shaanxi, China
Correspondence Author

Abstract: ***In recent years, acupuncture has been widely used in clinical practice for the treatment of diseases related to mammary hyperplasia. By synthesizing relevant domestic and foreign literature, it can be known from this article that the mechanisms of acupuncture in treating mammary hyperplasia are very complex and diverse. The currently known mechanisms include regulating the endocrine system, regulating receptor signal transduction, improving blood circulation, regulating immune system function, and regulating gene expression. Although there are still difficulties in clarifying many mechanisms of blocking the transformation of mammary hyperplasia into tumors, this cannot overshadow the role of acupuncture as a safe and effective method for treating mammary hyperplasia.***

Keywords: Acupuncture Therapy, Mammary Hyperplasia, Review, Research Mechanism**.**

1. Introduction

Mammary gland hyperplasia (MGH) is a type of breast disorder, yet the cause of breast swelling is neither inflammation nor another form of tumor. It refers to the abnormal proliferation of cells and fibrous tissues around the mammary glands. The mammary ducts and lobules undergo structural degenerative changes, accompanied by continuous proliferation of connective tissues, which manifests as the progressive pathological changes of this condition [1]. The clinical manifestations of mammary gland hyperplasia mainly include swelling and pain in the breast area. These symptoms are often periodic, and tend to worsen particularly before and after menstruation, during periods of irritability, or after physical exhaustion. If not taken seriously, women are highly susceptible to this disease.

In recent years, with the improvement of statistical data across the country, approximately 30 out of every 100 women in China suffer from mammary gland hyperplasia. Differences in women's level of attention to the condition and the availability of medical resources have led to variations in the early treatment methods for mammary gland hyperplasia, which in turn have exacerbated the progression of breast diseases. Nevertheless, mammary gland hyperplasia remains the primary cause of breast diseases [2]. In 1987, China classified it as one of the precancerous conditions [3].

In the treatment of this disease, Western medicine mainly adopts two major approaches: surgical treatment and non-surgical methods. Although surgical treatment seems to eliminate the patient's pain by removing the affected area, it does not address the root cause of the problem: the patient's own endocrine disorders. Other treatment methods mainly involve the use of hormonal drugs, such as androgens (danazol) and estrogen receptor antagonists (tamoxifen). However, long-term use of hormonal drugs will inevitably have a significant impact on the patient's hormone levels and the stability of their endocrine system.

When it comes to effectively treating mammary gland hyperplasia without disrupting the patient's endocrine system, traditional Chinese medicine (TCM) has incomparable advantages. Acupuncture, in particular, is highly favored by a large number of patients due to its painlessness and remarkable curative effect, and its clinical significance in the treatment of mammary gland hyperplasia has been fully recognized. This article provides a review that summarizes the research findings on the mechanism of action of acupuncture in the treatment of mammary gland hyperplasia based on relevant achievements in acupuncture research in recent years.

2. The Effect of Acupuncture on the Morphology of Mammary Gland Tissue in Animals with Mammary Gland Hyperplasia (MGH)

2.1 The Effect of Acupuncture on the Height and Diameter of Mammary Glands in Animals with MGH

In the experiments conducted by Yang et al. [4, 5], by performing acupuncture on the mammary glands of rats, they observed that the size of the rats' mammary glands was significantly reduced, and the nipples were correspondingly lowered. The results of this study indicate that acupuncture can affect the morphological structure of mammary gland tissue, thereby influencing the position and height of the nipples.

2.2 Effect of Acupuncture on the Ultrastructure of Mammary Gland Tissue in MGH Animals (Electron Microscopy)

Wang et al. [8] found that under electron microscopy, the number of lipid droplets in mammary glandular cells of MGH rats in the acupuncture group decreased, and the number and volume of organelles such as mitochondria, endoplasmic reticulum, and Golgi apparatus also reduced. This indicates that there is a relationship between intracellular physiological activities and acupuncture, specifically that acupuncture can reduce cellular metabolism and synthetic functions.

3. The Effect of Acupuncture on the Endocrine System

Numerous studies have shown that acupuncture can regulate imbalanced sex hormones in the body, the most common of which include estrogen (E2), progesterone (P), testosterone (T), and estrogen-progesterone receptors (ER) secreted by the ovaries, as well as follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL) secreted by the pituitary gland, among others. This fact is truly impressive, highlighting the remarkable nature of acupuncture therapy.

3.1 Effect on E2, P, PRL, and Other Substances

Currently, domestic and international studies [9, 10] suggest that the pathogenesis of Mammary Gland Hyperplasia (MGH) is associated with endocrine dysfunction in the body, specifically manifested as dysregulated secretion of estrogen (E2), progesterone (P), and prolactin (PRL). E2 can dilate and elongate the mammary ducts, promote the utilization of proteins and sugars, and increase capillary permeability; in turn, P can further facilitate the action of E2 to enter the lobules and reduce capillary transparency. When E2 secretion is excessive and P secretion is reduced, E2 acts on mammary gland tissue to accelerate cell proliferation. The proliferated cells lead to an increase in the two hormone receptors, enhanced sensitivity of mammary epithelial cells, and continued growth of mammary lobules, thereby developing into MGH.

By observing the effect of acupuncture on the regulation of sex hormones in the ovarian-pituitary axis of MGH model rats, researchers such as Guo Xinrong [11] found that in the model group, the ratios of estradiol to follicle-stimulating hormone (FSH), prolactin (PRL), progesterone (P), and testosterone (T) showed significant differences compared with the blank control group ($P<0.01$). However, in the acupuncture group, there were no significant differences compared with the blank control group ($P>0.05$). The results of this study provide an important reference for in-depth understanding of the effect of acupuncture on the regulation of sex hormones in the ovarian-pituitary axis.

Experiments have shown that after acupuncture stimulation in MGH model rats, the levels of FSH, PRL, and E2 in the body decreased significantly, while the contents of P, T, and LH in the ovaries increased significantly. This result indicates that acupuncture can effectively regulate hormone levels in rats and promote ovarian function. According to research, after acupuncture treatment, the levels of related sex hormones in MGH model rats improved significantly; this improvement not only exerts a regulatory effect but also contributes to the complete cure of the disease.

Prolactin (PRL) is released by the pituitary gland; it can promote the growth of mammary epithelial cells and affect estradiol and luteinizing hormone (LH). When PRL secretion increases, it activates adenylate cyclase, enabling cyclic adenosine monophosphate (cAMP) signal transmission and generating a cascade effect, which in turn stimulates the mammary glands and causes MGH [12]. Xie Juan [7] found that the estrogen level of mice in the model group was higher than that of normal mice, while their progesterone level was lower than that of normal mice. In contrast, compared with the normal group, the electroacupuncture group showed a significant trend of decreased estrogen and increased progesterone. This indicates that electroacupuncture can not only increase the levels of insufficient hormones but also reduce excessively high hormone levels in the treatment of MGH, exhibiting a bidirectional regulatory effect. Clinically, it can replace some Western medicines to reduce the harm of hormonal drugs to patients.

3.2 Effect of Acupuncture on Estrogen Receptors (ER)

Gong et al. [13] found that acupuncture at the “Tanzhong” (CV17) and “Sanyinjiao” (SP6) acupoints could effectively reduce the high serum estrogen level induced by exogenous estradiol, thereby enhancing the therapeutic effect of acupuncture, and this effect was closely related to the regulation of serum E2 level in the body. Meanwhile, the number of ER-positive cells in the acupuncture group was significantly lower than that in the model control group ($P<0.01$), and this result further confirmed the therapeutic effect of acupuncture.

Acupuncture at Tanzhong and Sanyinjiao acupoints activates a specific inhibitory mechanism: inhibiting the expression of ER. As a result, the pro-proliferative effect of estrogen on the mammary glands is rapidly downregulated, ultimately leading to the inhibition of mammary gland hyperplasia (MGH). This effective therapeutic approach brings significant benefits to human health.

4. The Effect of Acupuncture on the Immune System

4.1 Effect on the Levels of Lymphocyte Subsets CD8+ and CD4+

When the body faces internal environment instability, the immune system coordinates with the endocrine system to maintain normal bodily functions. Therefore, immunity and endocrine play important roles in responding to external stimuli. The endocrine and immune systems interact with each other; when the immune system is unstable, the endocrine system is inevitably affected. Studies have shown [14] that acupuncture only improves cellular immunity but has no significant effect on humoral immunity.

The body’s weapons against diseases fall into two major categories: cellular immunity and humoral immunity. Cellular immunity, with T cells and B cells as the main forces, controls the overall immune response through precise attack strategies. T cells, in particular, act as guardians of the immune response, contributing significantly to the arduous defense against diseases.

According to the research by Zhao Changlin et al. [15], acupuncture at acupoints such as Zusanli (ST36), Sanyinjiao (SP6), Yinlingquan (SP9), Yanglingquan (GB34), and Neiguan (PC6), or moxibustion at Zusanli (ST36), Guanyuan (CV4), and Shenque (CV8), can significantly enhance the activity of T lymphocytes in the body, thereby strengthening the patient’s immune function and effectively combating diseased cells.

A study by Zhang Lifen et al. [16] indicated that acupuncture at acupoints including Shenshu (BL23), Mingmen (GV4), Fengfu (GV16), Lingxu (KI24), and Qimen (LR14) can effectively reduce CD8+ levels and increase the CD4+/CD8+ ratio. Mammary gland hyperplasia impairs the body's immune system from recognizing and eliminating diseased tissues, making it difficult to clear such tissues accurately and promptly. As a therapy that regulates the human immune system, acupuncture can enhance the patient's self-immune system, enabling the body to smoothly detect and respond to pathological conditions, thus addressing the root causes of illnesses.

4.2 Effect on the Expression of Apoptosis-Related Factors Such as Fas and FasL

Fas, also known as the death receptor, has a natural ligand called FasL. The Fas/FasL system plays a crucial role in the human body by maintaining the stability of the internal environment; an imbalance in this system can lead to mutual attacks between tissues or malignant tissue proliferation. When FasL on immune cells binds to Fas on the target cell membrane in a trimeric form and becomes activated, the Fas/FasL system initiates the process of mediating cell apoptosis. Subsequently, cells carrying Fas receive the apoptotic signal and immediately activate programmed cell death [17].

The Fas/FasL apoptotic mechanism is widely utilized in the human body and regulates many types of cells, including mammary epithelial cells [18-20]. This mechanism is vital for cell survival, as it can eliminate cells that can no longer survive, thereby ensuring the normal functioning of the body. These proteins are widely distributed in cells but are mainly concentrated in areas dominated by lymphocytes.

Studies have found that in recent years, FasL has also been detected in other epithelial cells [21]. The pathological manifestation of mammary gland hyperplasia is local swelling, whose physiological basis stems from increased blood vessels and dense lymphatic vessels. Research by Xu [22] showed that acupuncture at acupoints including Tanzhong (CV17), Zusanli (ST36), and Taichong (LR3) can intervene in the Fas/FasL signal transduction pathway in rats with mammary gland hyperplasia, positively regulate the expression of apoptosis-related factors such as Fas, FasL, Caspase-8, and Caspase-3, promote the apoptosis of abnormal mammary tissue, restore the mammary tissue to normal, and thus play a role in treating mammary gland hyperplasia.

4.3 Effect on the Levels of IL-2 and TNF-α

After various cells are activated, elaborately produced cytokines gradually develop. They are proteins with extensive biological activities, participating in important signal transmission in the human endocrine system, and also contributing to the repair of damaged tissues as well as related research in various other physiological and scientific fields. Interleukin-2 (IL-2), the key to activating T lymphocytes and also their main source, contains various cellular mysteries. Stimulated by IL-2, the growth of T lymphocytes and NK cells becomes more rapid, and B cells also divide rapidly in this process, giving rise to a variety of antibodies. Therefore, IL-2 plays an important role in the body's immune response, immune regulation, and anti-tumor immunity [23].

Tumor Necrosis Factor (TNF-α) was one of the earliest discovered cytokines, which can cause hemorrhagic necrosis of tumor tissue cells. This substance is secreted by two types of cells—macrophages and adipocytes—and has a remarkable property: it can directly destroy tumor cells, hence its name. Even more remarkably, this substance can kill tumor cells not only in vivo but also in vitro.

Modern studies have shown [24] that patients with mammary gland hyperplasia (MGH) are closely related to cytokines such as IL-2 and TNF-α, and these cytokines can be fully expressed when patients have immune disorders. TNF-α has antiviral and anti-tumor effects.

Through research on serum IL-2 and TNF-α in MGH model rats, Zhang [25] found that the IL-2 levels in the acupuncture treatment group and the control group were higher than those in the model group and the self-healing group. However, there was no significant difference between the treatment group and the control group. This finding may suggest that both acupuncture treatment and the control pathway can effectively enhance the body's resistance. During acupuncture treatment, IL-2 in the body can be activated, thereby leading the body to attack excess mammary tissue and eliminate the abnormal cells.

5. Effect of Acupuncture on Hemodynamics of Hyperplastic Tissues in MGH Patients

Modern research has shown that acupuncture can soften hard masses and dissipate nodules by improving systemic and local blood circulation around the nodules, thereby reducing the diameter of breast nodules.

Wang [26] found that in MGH patients, compared with the control group, the acupuncture group was more effective in reducing the resistance index (RI) of blood flow, improving blood vessel shape, and adjusting grayscale. This indicates that acupuncture can accelerate blood flow velocity in hyperplastic areas, promote smooth blood circulation, and thus objectively reduce the blood flow resistance index. This finding suggests that acupuncture has a significant therapeutic effect in the treatment of MGH and exerts a positive impact on patients.

Lin [27] pointed out that acupuncture at specific acupoints can regulate the endocrine and immune systems, promote blood circulation, enhance the permeability of local capillaries, facilitate the exudation of inflammatory substances, and improve local microcirculation, thereby achieving anti-inflammatory and analgesic effects.

6. The Effect of Acupuncture on the Expression of p53 and p16 Proteins

According to international studies, p53 is not only identified as a cancer-related gene but also plays a crucial role in anti-cancer and tumor suppression processes, being closely intertwined with human cancer. However, at the same time,

p53 is also one of the genes with the highest mutation frequency. Its overexpression in mammary hyperplasia tissues and breast cancer has attracted significant attention and emphasis, making it a current hot research field [28]. In the human body, p53 is an extremely critical regulatory factor, whose function is to control and coordinate cell differentiation and growth. Additionally, it can prevent the formation of tumor cells, thereby exerting an inhibitory effect on tumorigenesis. It can be said that p53 plays an indispensable role in maintaining human health. Since there are numerous cancer-causing factors (both internal and external to the body) acting on the organism, the p53 gene may undergo deletion or mutation. This leads to the loss of the function of the protein encoded by p53 in inhibiting cell proliferation; consequently, cells proliferate uncontrollably, and eventually form tumors [29]. Wang [30] found that the expression level of p53 protein in the mammary gland tissues of MGH (Mammary Gland Hyperplasia) rats in the acupuncture group was significantly lower than that in the model group. These findings indicate that acupuncture exhibits prominent efficacy in the treatment of mammary hyperplasia. It not only alleviates the suffering of patients but also exerts therapeutic and preventive effects, most of which are achieved through regulating the expression of p53 and p16.

7. The Effect of Acupuncture on the Contents of Angiogenic Factors VEGF and BFGF in MGH Rats

Using the enzyme-linked immunosorbent assay (ELISA), Duan [31] measured the contents of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (BFGF) in the serum of MGH (Mammary Gland Hyperplasia) rats. The results showed that the contents of these two substances both showed a decreasing trend in the experimental group treated with drug injection. This finding may indicate that acupuncture-mediated regulation of these two substances could be a feasible therapeutic strategy. The remarkable aspect of acupuncture lies in its ability to stimulate the local area of the patient, thereby reducing the levels of angiogenic factors in the serum, accelerating blood flow, eliminating swelling, and even improving the local breast tissue to achieve a complete cure for mammary hyperplasia. The conclusions drawn from the experiment are beyond doubt.

8. Summary

In general, the core of acupuncture treatment lies in achieving therapeutic effects by stimulating corresponding acupoints and affected areas. As a treasure in traditional Chinese medicine (TCM), this treatment method has a long history, undergoing thousands of years of practice and summarization. In modern medicine, acupuncture therapy has received increasing attention. With its unique charm, it has become a popular alternative therapy. Acupuncture treatment for mammary gland hyperplasia (MGH) ultimately achieves efficacy by leveraging the synergistic effects of multiple aspects, including the endocrine system, the body's immune system, gene-regulating proteins, and hemorheology.

The occurrence of complex MGH is caused by the combined action of multiple factors. The body's endocrine system integrates the effects of various hormones, which together contribute to the development of MGH, and the roles of these hormones are interrelated and inseparable. The mechanism of acupuncture in treating MGH does not rely on a single hormone; instead, it achieves the overall therapeutic effect through the synergistic interaction between the endocrine system and various hormones.

What remains unclear is that there is still no conclusive evidence regarding the specific pathway through which acupuncture inhibits the proliferation of mammary epithelial cells and optimizes the vascular morphology within the mammary glands. We have not yet elucidated the "mysterious mechanism" by which acupuncture inhibits or blocks MGH lesions through gene signal transduction, thereby preventing their progression to tumors. These issues require in-depth and systematic investigation in future studies.

References

[1] Hu KF, Li YH, Pei XH, et al. Research progress on traditional Chinese medicine treatment for hyperplasia of mammary glands [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2012, 18(23): 353-356.

[2] Wei L, Chen CX. Screening and related factor analysis of breast diseases in 5000 women [J]. Maternal and Child Health Care of China, 2010, 25(24): 3466-3468.

[3] Jian ZR. Overview of acupuncture treatment for hyperplasia of mammary glands in the past 20 years [J]. Chinese Acupuncture and Moxibustion, 1999(7): 439-442.

[4] Yang JJ, Wang LN, Xiao HL, et al. Effects of surrounding acupuncture combined with electroacupuncture on nipple size, mammary gland pathological changes, serum sex hormone levels, and estrogen receptor expression in rats [J]. Acupuncture Research, 2012, 37(3): 173-178.

[5] Jing RX, Liang LH, Li X, et al. Effects of surrounding acupuncture combined with electroacupuncture on serum hormone levels, mammary tissue morphology, and ER expression [J]. Hebei Medical Journal, 2014, 36(7): 965-968.

[6] Wang ML, Zhang WH, Zhao ZL, et al. Morphological changes in the mammary glands of rats with hyperplasia treated with acupuncture [J]. Journal of Shaanxi College of Traditional Chinese Medicine, 2007, 30(5): 56-59.

[7] Dong F, Xie J, Tang CZ. Intervention effect of acupuncture on estrogen, estrogen receptor, and its signal transduction in a rat model of mammary gland hyperplasia [J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2009, 26(5): 450-453.

[8] Wang ML, Zhang WH, Zhao ZL, et al. Effect of acupuncture on the ultrastructure of mammary gland cells in rats with hyperplasia [J]. Liaoning Journal of Traditional Chinese Medicine, 2007, 34(9): 1333-1334.

[9] Osen JM. On hormone action in the mammary gland [J]. Cold Spring Harbor Perspectives in Biology, 2012, 4(2): 441.

[10] Ma W, Jin QX, Wu YF, et al. Expert consensus on the diagnosis and treatment of mammary gland hyperplasia

[J]. Chinese Journal of Practical Surgery, 2016, 36(7): 759.
[11] Guo XR, Zhang WH, Li SL. Effect of acupuncture on the regulation of sex hormones in the ovarian-pituitary axis of rat models with mammary gland hyperplasia [J]. Shandong Journal of Traditional Chinese Medicine, 2013, 32(7): 485-486+519.
[12] Al-Balas M, Alwiswasy M, Al-Balas H, et al. Successful management of diffuse bilateral pseudo angiomatous stromal hyperplasia of the mammary glands by reductive mammoplasty [J]. Breast Disease, 2020, 39(2): 115.
[13] Gong DF. Study on the intervention effect of acupuncture on experimental rat models of mammary gland hyperplasia [C]. Guangzhou University of Chinese Medicine, 2006.
[14] Zhang WH, Guo CX, Zheng SX, et al. Effect of acupuncture on immune function in patients with mammary gland hyperplasia [J]. Shaanxi Correspondence Journal of Traditional Chinese Medicine, 1991(4): 33-35.
[15] Zhao CL, Peng LJ, Zhang ZL, et al. Effect of acupuncture on peripheral blood T lymphocyte subsets and NK cell activity in patients with liver metastasis of colon cancer [J]. Chinese Acupuncture and Moxibustion, 2010, 30(1): 10-12.
[16] Zhang LF, Song AF, Wang ZH, et al. Effect of kidney-tonifying and liver-soothing therapy on endocrine and immune function in patients with mammary gland hyperplasia [J]. Chinese Acupuncture and Moxibustion, 2008, 28(9): 648-652.
[17] Ma Y, Qian DF. Research progress on p53 protein [J]. Foreign Medical Sciences: Clinical Biochemistry and Laboratory Testing, 2002, 1: 41-42.
[18] Tang G, Quan XQ. p53 and cancer therapy [J]. Chemistry of Life, 2008, 1: 66-68.
[19] Li YP, Wang L, Wu SQ, et al. Expression and correlation of apoptosis regulatory proteins Bcl-2, p53, and Caspase-3 in breast cancer tissues [J]. Progress of Anatomical Sciences, 2010, 16(2): 167-170.
[20] Song M, Mi XY, Li BL, et al. Expression of apoptosis-related genes p53 and bcl-2 in atypical ductal hyperplasia of the breast [J]. Chinese Journal of Histochemistry and Cytochemistry, 2001(4): 412-416+474.
[21] Ma CQ. Therapeutic effect of kidney-tonifying and liver-soothing method on rat models of mammary gland hyperplasia [D]. Nanjing University of Chinese Medicine, 2009.
[22] Xu QX. Experimental study on the effect of acupuncture on the Fas/FasL apoptosis pathway in rat models of mammary gland hyperplasia [C]. Liaoning University of Traditional Chinese Medicine, 2019.
[23] Wu YF, et al. Clinical significance of radioimmunoassay for interleukin-2 [J]. Journal of Radioimmunology, 1996, 9(8): 181.
[24] White RR, Halperin TJ, Olson JA, et al. Impact of core needle breast biopsy on the surgical management of mammographic abnormalities [J]. Annals of Surgery, 2001, 233(6): 769-777.
[25] Zhang WH, Liu J, Guo XR. Effect of acupuncture on serum IL-2 and TNF- in experimental rat models of mammary gland hyperplasia [J]. Journal of Shaanxi College of Traditional Chinese Medicine, 2008, 31(4): 53-54.
[26] Wang Y. Acupuncture treatment for hyperplasia of mammary glands and its effect on mammary tissue imaging and hemodynamics [J]. Chinese Acupuncture and Moxibustion, 2005, 25(9): 619-621.
[27] Lin NQ. Clinical effect of acupuncture combined with Xiaopi Decoction in treating mammary gland hyperplasia [J]. Chinese and Foreign Medical Research, 2022, 20(13): 42-46.
[28] Jiang J, Chen YT, Ma HM, et al. Expression of P53 protein in atypical hyperplasia and breast cancer [J]. Journal of Third Military Medical University, 1998, 20(1): 63-64.
[29] Huang FC, Liu J. Significance of P53 and ER expression in atypical hyperplasia and breast cancer [J]. Journal of Dalian Medical University, 2006, (2): 101-103.
[30] Wang ML, Wang JJ, Zhang WH, et al. Effect of acupuncture on the expression of p16 and p53 proteins in mammary tissue of experimental rat models with hyperplasia [J]. Journal of Shaanxi College of Traditional Chinese Medicine, 2010, 33(4): 87-89.
[31] Duan YC, Du HL, Jin YC. Effect of acupuncture combined with medication on serum and mammary VEGF and bFGF levels in rat models of mammary gland hyperplasia [J]. Chinese Traditional Patent Medicine, 2010, 32(7): 1217-1219.
[32] Liu Q. Experimental study on the effect of acupuncture on angiogenesis factors (VEGF, bFGF) in rat models of mammary gland hyperplasia [C]. Liaoning University of Traditional Chinese Medicine, 2016.