

Effectiveness of acupuncture in reducing pain and improving quality of life of patients with mammary gland hyperplasia: A meta-analysis with systematic review

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Abstract: In recent years, female mammary gland hyperplasia appears in the young age, and many adolescent women will also have symptoms of mammary gland hyperplasia. Acupuncture treatment of mammary gland hyperplasia not only has significant effects, but also has obvious therapeutic advantages with fewer side effects, low pain and no scar. The purpose of this study is to prove that traditional Chinese medicine acupuncture can reduce breast pain in patients with mammary gland hyperplasia, reduce the volume of breast lumps, and improve the quality of life of patients. In this study, we searched China Knowledge Network (CNKI), Wan Fang Database, pubmed, Cochrane Library, Google Scholar, and medicine database for studies published between January 2018 and January 2023. In addition, we also manually searched the Weip Data-base (VIP) database for studies published between January 2018 and January 2023. All randomized controlled trials (RCTs) of acupuncture in the treatment of mammary gland hyperplasia were included. Results: Of the selected 363 records, 57 were eligible and data were available from 16 randomized controlled trials, all of which had a low to moderate risk of overall bias. (16 interventions, 1232 participants) showed that the treatment group had a better effect on mammary gland hyperplasia than the control group (Risk Ratio [M-H, Fixed] 1.22, 95%CI 1.16 to 1.28, I² = 0%). Acupuncture can effectively treat breast pain in patients with mammary gland hyperplasia, reduce the size and hardness of breast lumps, and improve the patient's quality of life. In addition, acupuncture can also regulate patients' emotional changes and menstrual abnormalities. This study was pre-registered on PROSPERO under the registration number CRD42023468786.

Keywords: Mammary gland hyperplasia; Acupuncture; Meta-analysis; Systematic review

1. Introduction

Mammary gland hyperplasia (MGH) is the most common benign breast disease. It is a non-inflammatory, non-tumor benign hyperplasia. MGH has been clinically named as breast dysplasia, breast adenosis, lobular hyperplasia, chronic cystic breast disease, fibrocystic breast disease, etc., according to different stages and pathological changes^[1]. The essence of MGH is that the mammary gland and stroma are hyperplasia to different degrees and incomplete degeneration, leading to the disorder of the normal structure of the mammary gland^[2]. From the point of view of traditional Chinese medicine, MGH is closely related to liver dysfunction. When the mood is bad, the mood is depressed, or the work and life pressure is relatively large, there will be emotional paralysis, liver qi stagnation, Qi machine operation is not smooth, the formation of phlegm turbidites, congestion block meridians, and lead to MGH. Another reason is that long-term spleen deficiency and dampness may cause dampness to suppress the generation of liver Qi, resulting in the formation of liver qi stagnation, phlegm and blood stasis. Therefore, after using acupuncture to clear the liver meridian and stomach meridian, the liver qi condensed in the breast can be evacuated, the smoothness of the liver meridian and stomach meridian can be restored, the movement of qi will return to normal, and the nodules that have formed will gradually dissipate. Ultimately, it serves the purpose of treating MGH.

MGH is more common in women between 30 and 50 years old, and the main reason is endocrine dysfunction^[2]. Due to various reasons, endocrine hormone metabolism imbalance and estrogen level increase, resulting in breast lumps, periodic pain, and other symptoms in patients, Pain causes discomfort to patients and makes some patients very nervous. Generally, the pain caused by MGH can be relieved

by itself or gradually through daily life and drug treatment. The pain is not directly related to breast cancer. Secondly, MGH can cause patients to be emotionally irritable and cause menstrual disorders. In addition, some patients with MGH may develop periodic lumps. With the development of society and the faster pace of society, about 50%~70% of women in China's big cities suffer from MGH to some degree. In recent years, the MGH has appeared adolescently. The MGH in adolescent women is usually thought to be caused by development. Most patients with breast hyperplasia will appear breast enlargement before menstruation. Unexplained breast tenderness, and breast lumps will also make the patient's own mental state changes, and even fear, anxiety, depression, etc.

At present, the treatment of MGH is mainly based on traditional Chinese medicine. When a lump appears in the breast, most doctors will give the patient oral Chinese medicine and hormone western medicine, and certainly, there is also surgery to treat the breast swelling lump. The surgery is mainly minimally invasive, but the sequelae of surgery also bring troubles to patients, such as surgical site pain before and after menstruation, breast surgical site pain in rainy days, and surgical scars will also affect the appearance of the breast and affect the future life. According to relevant studies, acupuncture in the treatment of MGH has significant therapeutic effect and few side effects, low pain, and no scars and adolescent patients can avoid surgical scars. Many studies have shown that acupuncture has a significant effect on treating the pain caused by MGH in patients with MGH and improving the quality of life of patients with MGH, such as reducing the breast pain of patients, reducing the distribution range and size of breast lumps, and reducing the hardness of lumps. Lu et al. (2022) conducted acupuncture therapy has obvious advantages in improving clinical efficiency, alleviating breast pain, reducing the distribution range and size of breast lump, and improving lump hardness^[3]. Zhang (2019) concluded that the treatment method of deep-acupuncture perineal point group could effectively improve and relieve the clinical symptoms and signs of patients with breast cystic hyperplasia, and had certain influence on the changes of estrogen and progesterone levels and the structural changes of color ultrasound display^[4]. This study mainly through meta-analysis and systematic review, studies on the treatment of MGH by acupuncture are collected, and the methods of acupuncture for the treatment of MGH are synthesized, to evaluate the curative effect of acupuncture on MGH and determine the curative effect of acupuncture on MGH.

2. Study Objectives

(1) What are the existing randomized controlled trials that determined the effectiveness of acupuncture in reducing pain and improving quality of life of patients with mammary gland hyperplasia? (2) How to evaluate the effect of acupuncture in treating mammary gland hyperplasia? (3) Is acupuncture effective in reducing pain and improving the quality of life of patients with mammary gland hyperplasia based from the estimated pool of evidence?

3. Methods

Search China Knowledge Network (CNKI), Wan Fang Database, pubmed, Cochrane Library, Google Academic, medicine database for studies published between January 2018 and January 2023, in addition to this, we will manually search the Weip Data-base (VIP) database for studies published between January 2018 and January 2023.

3.1 Eligibility criteria

Inclusion Criteria:

(1) Research published between January 2018 and January 2023. (2) All randomized controlled trials marked with the word "randomization" are included, regardless of allocation concealment or blinding, and the language is limited to Chinese or English. (3) Participants were 18 years and older female patients with MGH (diagnosed according to any authoritative diagnostic criteria), regardless of race, disease duration, weight or education. (4) The intervention type is acupuncture therapy (regardless of acupuncture and stimulation methods) or acupuncture based on the intervention measures in the control group. The control group can use oral Chinese medicine, external application of Chinese medicine, acupoint massage, placebo and other therapies. (5) Results include: ① Breast mass size score: compare the size of the target mass before and after treatment. ② The effectiveness of treatment. ③ Breast pain before and after treatment. ④ MGH cure rate. ⑤ Adverse reactions, etc.

Exclusion Criteria:

(1)Patients with other breast diseases. (2)The patient did not have a definite diagnosis of MGH.(3)There are no clear outcome indicators.(4)Patients with acute illness or pregnancy.

3.2 Search strategy

The search method is to combine free words and related subject words to search step by step. Mainly use MeSH (Medical subject heading) terms and related free words, and use truncation and Boolean logic operations to conduct literature searches, including "hyperplasia of mammary glands", "mammary glands hyperplasia", "mammary hyperplasia", and "acupuncture", "acupuncture treatment", "acupuncture method", "acupuncture therapy", the details of the PubMed search strategy are as follows, and other electronic databases also use similar search strategies:

((((Hyperplasia[MeSH Terms]) AND (Mammary Glands[MeSH Terms])) AND (Human[MeSH Terms])) OR (((Hyperplasia of mammary glands) OR (mammary glands hyperplasia)) OR (Mammary hyperplasia))) AND ((Acupuncture[MeSH Terms]) OR (((Acupuncture) OR (Acupuncture treatment)) OR (acupuncture method)) OR (acupuncture therapy))) AND (2018:2023[pdat])

3.3 Data extraction and quality assessment

According to the Cochrane Handbook for Systematic Reviews of Interventions, Two researchers were responsible for data extraction of the authors of the included literature, publication year, sample population, patient age, intervention measures, treatment duration, outcome indicators, and diagnostic criteria. And populate the extracted data into the form. For articles with missing data, we will contact the author to obtain the original data. If the missing data is not available, we will exclude the study.

We used the Cochrane randomized Trials Bias Risk tool to assess the risk of bias in the included studies. The figure below (Figure 1) shows the risk of bias for each of the areas of bias in each of the included studies. The methods and treatments that are superior to most of the included studies did not fully adopt the blinding principle, and there is a low to moderate risk of bias.

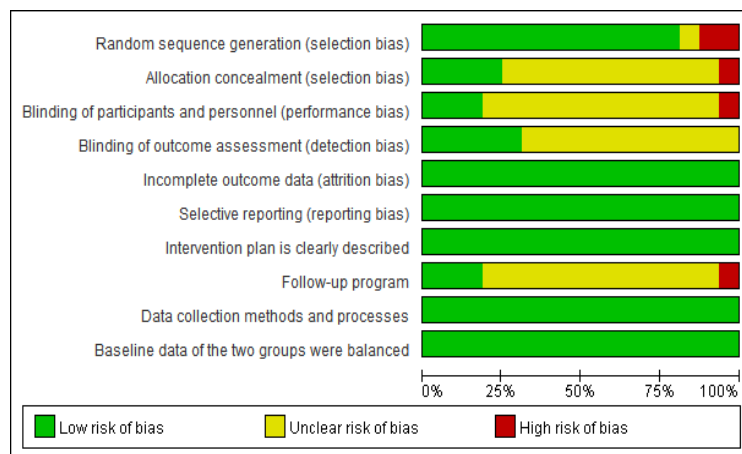


Figure 1: Percentage of items included in the study for each risk of bias.

4. Results

4.1 Study selection

We found 363 records in the database search. After removing 138 duplicates, we screened 225 records and excluded 163 references (mainly animal studies or not randomized controlled trials or not relevant to the purpose of this study). There were 62 articles, and we read the title and abstract, excluding 1 case report, 3 research advances, and 1 meta-analysis. Fifty-seven full texts were reviewed, and 16^[5-20] papers were finally included. The flow chart (Figure 2) is as follows:

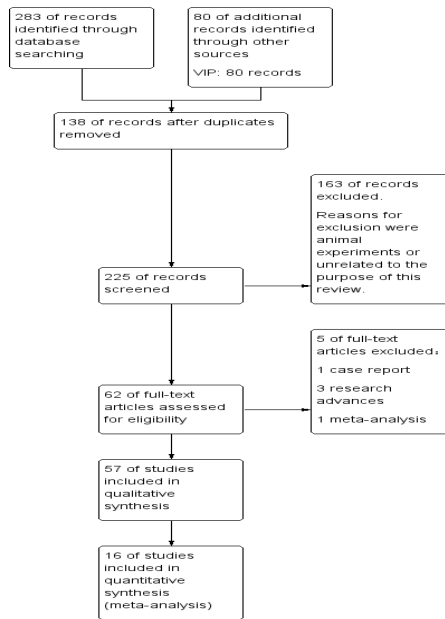


Figure 2: Study selection flow chart

4.2 Study characteristics

The data we extracted from the study are shown in the table (table 1):

Table 1: Basic features of the included literature

Research ID	Sample size		Age		Control group measures	Experimental group measures	Treatment course	Outcome indicators	Diagnostic criteria
	T	C	T	C					
Su Peixuan 2018	33	34	32.18±7.32	31.39±7.41	Ruhe Sanjie tablet, 4 capsules/time, 3 times/day	Acupuncture, once a day, 5 consecutive treatment for two days rest	1 month	①②③④⑤⑥	《Criteria for the Diagnosis and Curative Effect of TCM Diseases》
Wang Yayi 2022	50	50	33.24±2.51	32.16±2.48	Xiaojin capsule, 5 capsules/time, 2 times/day	Acupuncture once /d + Xiaojin capsule, 5 capsules/time, 2 times/day	1 month	①②③⑤⑥	NR
Lu Xianqiu 2018	31	33	35.16±5.10	35.87±4.78	Rupixiao capsule, 2 capsules/time, 3 times/day	Acupuncture, 3 times /w, once every other day	8 weeks	①②③⑤⑥	《Diagnostic criteria for hyperplasia of milk glands》
Jiang Xiaowei 2021	50	50	21 to 50 years old	22 to 52 years old	RuPi number 1, twice a day	RuPi number 1, twice a day+ Acupuncture once/day	20 days	①②③	《Clinical treatment guide》
Li Ting 2020	21	30	37.53 years old	33.67 years old	Tamoxifen 10mg twice a day	Acupuncture once a day	3 days	①②③⑥	《Diagnosis, differentiation of symptoms and evaluation criteria of curative effect of breast hyperplasia》、 《Experience of TCM diagnosis and treatment of mammary hyperplasia》
Si Haijun 2020	32	31	46.7±12.41	45.3±12.1	Chai Xiangning Shen Decoction 2 times/day, 400ml/time	Chai Xiangning Shen Decoction 2 times/day, 400ml/ times + acupuncture 3 times /w	2 months	①⑤	NR
Zhao Dong 2020	34	35	33.82±7.20	33.49±7.23	Hongjin Xiaojie capsule, 4 capsules/time, every 3 times/day	Acupuncture, 3 times /w + Hongjin Xiaojie capsule 4 capsules/times, every 3 times/day	3 months	①②③⑤⑥	《Science of acupuncture and moxibustion》 《Chirurgery》
Zhong Yue 2021	30	30	36.63±7.26	33.97±6.66	Xiao jie an capsule 3 times/day, 2	Acupuncture ,3 times /w+ Xiao jie an capsule 3	8 weeks	①②③⑤⑥	《Expert consensus on diagnosis and treatment of breast

					capsules/time	times/day, 2 capsules/times			hyperplasia》 《Science of acupuncture and moxibustion》
Lu Xianqiu 2021	31	33	35.16±5.10	35.87±4.78	Rupixiao capsule 2 capsules/time, 3 times/day	Acupuncture, 3 times/week, 1 treatment interval 1 ~ 2 days.	8 weeks	①②③⑥	《Chirurgery》、 《TCM disease diagnosis and curative effect criteria》
Li Yunping 2023	50	50	34.63 ±5.94	35.87 ± 6.43	Xiaotong Sanjie Decoction, 2 times/day	Xiaotong Sanjie Decoction, 2 times/day + acupuncture 3 times /w	8 weeks	①②③④⑥	《Surgery of Chinese medicine》
Wang Li 2018	49	49	35.72±3.19	36.05±3.26	Xiaojin capsule, 4 ~ 10 capsules/time, 2 times/day	Xiaojin capsule, 4 ~ 10 capsules/time + acupuncture once /d	4 weeks	①②③⑥	NR
Wen Qingfen 2021	60	60	35.36±4.79	35.36±4.79	Xiaopi Ruan Decoction, 2 times/day	Xiaopi Ruan Decoction, 2 times/day + acupuncture 3 times/w	3 months	①②③	《Mammary pathology》 《Modern traditional Chinese medicine breast science》
Ji Senbiao 2020	34	32	43.15± 8.85	43.15± 8.85	Rupixiao tablets, 5 tablets/time, 3 times/day	Rupixiao tablets, 5 tablets/time, 3 times/day + Acupuncture once/day	30 days	①②③⑥	《Surgery of Chinese medicine》
Feng Chun 2021	50	50	44.40±5.76	44.26±5.63	Self-prepared Rupi Quyu Decoction, twice/day, 100ml/day	Self-prepared Rupi Quyu Decoction, twice/day, 100ml/day + acupuncture once/day	30 days	①②③④⑥	《Modern TCM breast epidemiology》 《Expert in diagnosis and treatment of milk gland hyperplasia》
Liu Chaonan 2019	30	30	32.52±2.12	33.22±2.43	Chinese medicine granules, 2 times/day	Chinese medicine granules, 2 times/day + acupuncture once/day	30 days	①②③	NR
Shan Xingyu 2021	25	25	35.7± 3.86	35.86±3.81	Xiao Pi Decoction, 2 times/day	Xiao Pi Decoction, 2 times/day + acupuncture once /2 days	3 months	①②③④	《Diagnostic and therapeutic criteria for breast hyperplasia》、 Diagnostic criteria of western medicine

T-experimental group, C-control group, NR- not reported, Outcome indicators: ① : total effective rate after treatment; ② : breast pain after treatment; ③ : size of breast mass after treatment; ④ : changes in related hormone levels; ⑤ : adverse reactions; ⑥ : patient's recovery;

4.3 Results of individual studies

Figure 3 shows that among the 16^[5-20] included randomized trials of acupuncture for the treatment of MGH, the experimental group had a total sample size of 610 and a significant effect of 562, while the control group had a total sample size of 622 and a significant effect of 467. Heterogeneity test results ($I^2=0\%$, $P=0.51$) were based on a fixed-effect model. $RR=1.22$, 95%CI: 1.16-1.28,, $Z=7.79$, $P<0.00001$, indicating that the total effective rate of the experimental group was better than that of the control group.

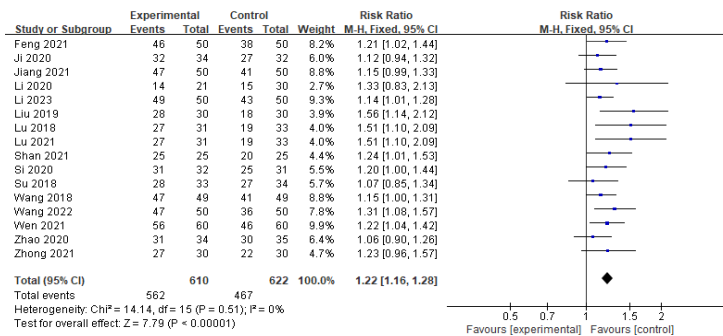


Figure 3: Meta-analysis of efficacy of experimental group and control group in treating MGH

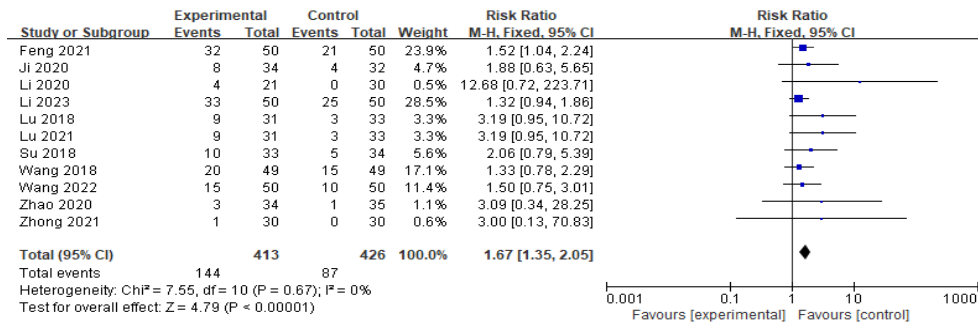


Figure 4: Meta-analysis of cure rates of experimental group and control group in treating MGH

Figure 4 shows that among the 11^[5-7,9,11-15,17-18] included randomized trials of acupuncture for the treatment of MGH, the experimental group had a total sample size of 413 and 144 were cured, while the control group had a total sample size of 426 and 87 were cured. Heterogeneity test results ($I^2=0\%$, $P=0.67$) were based on a fixed-effect model. $RR=1.67$, $95\%CI: 1.35-2.05$, $Z=4.79$, $P<0.00001$ indicates that the cure rate of the experimental group is better than that of the control group.

5. Discussion

The above results proved that the effect of acupuncture group on MGH was more significant than that of drug group, in the included studies, several acupuncture points frequently appeared in the selection of acupuncture prescriptions. It can be seen from the following figure (Figure 5) that Danzhong point appeared the most frequently. Danzhong point is located on the anterior median line of the body, level with the fourth intercostal space, and at the intersection of the line between the two nipples and the anterior median line. The main therapeutic effects of Danzhong point include: cough, asthma, chest tightness, heartache, choking, hiccup, etc. And puerperal breast diseases such as low milk secretion, mastitis, intramammary nodules, etc. The main acupuncture technique of Danzhong point is the direct acupuncture of 0.3-0.5 inch, or the flat acupuncture.

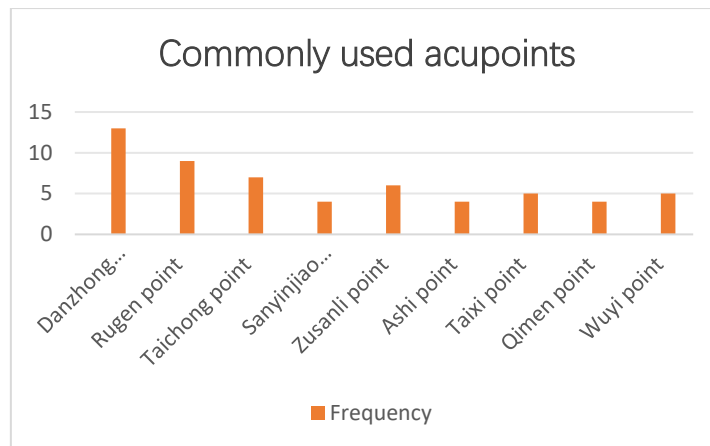


Figure 5: Frequency distribution of acupuncture points

6. Conclusion

Acupuncture can effectively treat breast pain in patients with MGH and reduce the volume and hardness of breast lumps. In addition to improving the quality of life of patients, it can also regulate the emotional changes of patients and menstrual abnormalities^[3, 22]. In addition, taking prunella also has a certain effect on the treatment of MGH. Shi et al.(2021) pointed out that for the treatment of patients with MGH, prunella has ideal effects, which can not only promote the relief of clinical symptoms of patients, but also improve the level of sex hormones in patients, so it has high clinical application value and can be promoted more vigorously^[21]. This research provides an important reference for the clinical treatment of MGH. However, due to the small number of literatures included in this study and the relatively low quality of literatures, the analysis results may be affected to some extent. Therefore, this paper can provide certain references for clinical acupuncture in the treatment of MGH. However, more randomized

controlled experiments are still needed to strictly implement the blind principle to verify the efficacy of acupuncture in the treatment of MGH.

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