

Meta-analysis of Integrative Traditional Chinese and Western Medicine in the Treatment of Plasma Cell Mastitis

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Abstract:

The objective is to evaluate the therapeutic effect of integrative traditional Chinese and Western medicine on plasma cell mastitis. The applied methods are to search related literature in China National Knowledge Infrastructure (CNKI), China Biology Medicine Literature Database (CBM), Chinese Science and Technology Journal Full-text Database VIP (VIP), according to the inclusion criteria, we collect the randomized controlled trial in the treatment of plasma cell mastitis, using integrative traditional Chinese and Western medicine treatment or traditional Chinese medicine treatment alone, in comparison to Western medicine treatment alone. We perform Meta-analysis using Revman software to evaluate quality of the included literature. The results show that total efficacy difference between the integrative traditional Chinese and Western medicine treatment group and the Western medicine treatment alone group is statistically significant (RR and 95% CI=1.25 (1.20, 1.30)), and of less heterogeneity. So we draw the conclusion that in the treatment of plasma cell mastitis, the integrative traditional Chinese and Western medicine treatment is superior to the Western medicine treatment alone.

Keywords: Plasma cell mastitis, Serum milk, Integrative traditional Chinese and Western medicine treatment, Randomized controlled trial, Meta-analysis

I. INTRODUCTION

Plasma cell mastitis (PCM), also known as mammary duct dilation (MDE), is a chronic, non-bacterial inflammation of the breast characterized by duct dilation and plasma cell infiltration. The clinical manifestations of this disease are nipple discharge, breast mass, breast pain, abscess, ductal fistula and axillary lymph node enlargement etc.[1] According to research result, autoimmune disorders, lactation disorders, degenerative changes of mammary gland, infection, mammary gland trauma, hormone secretion disorders, closely related with its etiology[2]. Western medicine treatment mainly choose surgery[3], or surgery combined with oral anti-tuberculosis drug treatment[4], some patients oral antibiotics and hormone therapy[5]. In Traditional Chinese medicine, the disease is called "acne mammary carbuncle". The etiology and pathogenesis are liver and stomach disorder and blood stasis in meridian, and the therapeutic method is to sooth the liver and stomach, activate the blood circulation[6]. The advantages of traditional Chinese medicine treatment gradually emerge in recent years, such as fewer side effects, low recurrence rate, shorter course of disease, reduced inflammatory range and so on[7-9]. Therefore, the therapeutic effect of integrative traditional Chinese and Western medicine on plasma cell mastitis is studied and analyzed. A randomized controlled trial (RCT) is selected to conduct a Meta-analysis of the clinical efficacy of integrative Chinese and Western medicine in the treatment of this disease, in order to evaluate the efficacy and advantages of integrative Chinese and Western medicine treatment.

II. MATERIALS AND METHODS

2.1 Literature Source and Search Database

China National Knowledge Infrastructure (CNKI), China Biology Medicine Literature Database (CBM), Chinese Science and Technology Journal Full-text Database VIP (VIP). Time span: 2010-2019. Search keywords: Plasma cell mastitis, integrative traditional Chinese and Western medicine, Randomized clinical trial, Randomized.

2.2 Data Extraction and Quality Assessment

The "Cochrane Risk Bias Assessment Table" in the Cochrane Systematic Evaluator's Manual (5.3) was used to evaluate the quality of the literature, and the Jadad three-item 5-point scale was used to evaluate the quality of the included subjects. Although the included studies had various degrees of randomness and blindness, but the overall research quality is high. Please see results in Fig 1.

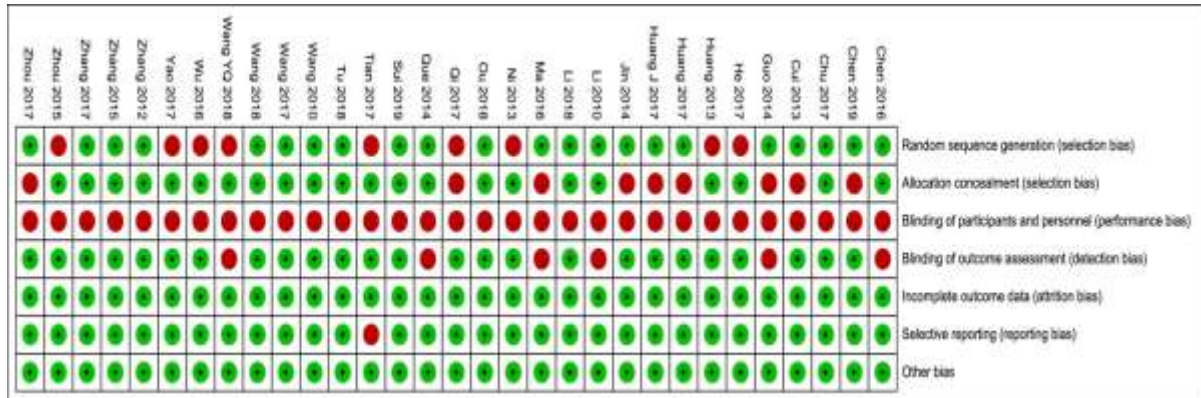


Fig 1: Cochrane risk bias evaluation chart

2.3 Research Object

The research object conforms to the criteria established by the Surgical Institute of Chinese Traditional Chinese Medicine Association in 1997 or the pathological diagnosis of plasma cell mastitis, and adopts integrative traditional Chinese and Western medicine treatment and Western medicine treatment alone, regardless of whether blind or distributed concealment is used in the trial design.

2.4 Diagnostic Criteria

The diagnostic criteria of plasma cell mastitis is according to the "Diagnostic and Efficacy Standards for Syndrome in Traditional Chinese Medicine" issued in 1997: There is uncomfortable local pain and touchable lump in the breast. The lump is located around the areola or stretches to a certain quadrant, which is tough or hard. The surface of lump is nodular. The boundary of lump is unclear. The lump has no adhesion to the chest wall. The lumps may have varying degrees of redness, swelling, heat, pain, and mild systemic inflammatory response. During the anti-infective treatment, the lump can be reduced or enlarged. The ipsilateral axillary lymph nodes are swollen, soft in texture, accompanied by tenderness. The lymph nodes can shrink or subside as the disease progresses. Plasma cell mastitis can be recurrent and gradually form scars, causing the nipple to sink. A small number of patients have bloody or watery nipple discharges.

2.5 Intervention

The type of intervention is randomized controlled trial (RCT) in the treatment of plasma

cell mastitis, using integrative traditional Chinese and Western medicine treatment, in comparison to Western medicine treatment alone. Western medicine treatment includes Western medicine for oral and external usage e.g. antibiotics, surgery and other treatments. The integrative traditional Chinese and Western medicine treatment is based on the treatment of Western medicine and the internal and external treatment of traditional Chinese medicine.

2.6 Efficacy Index

According to the "Diagnostic and Efficacy Standards for Traditional Chinese Medicine Diseases" promulgated by the Traditional Chinese Medicine Administration: Cure means after stopping usage of drug, it does not recur within 6 months. Breast lumps is significantly reduced and pain completely dissipates. Effective means breast lumps is reduced more than half by size and pain significantly dissipates. Invalid means clinical symptoms do not improve or even aggravate.

2.7 Exclusion Criteria

There are no clinical observations, clinical experience, reviews, animal experiments, and clinical studies without statistical analysis.

2.8 Statistical Method

RR and its 95% CI are selected as the effect indicators, and the Chi-square test and I^2 test are performed to evaluate the heterogeneity of the combined results. If $I^2 > 50\%$, it is considered to be of high heterogeneity. The combined results are of less heterogeneity through this whole study, so a fixed effect model is performed to combine the results. A funnel plot is applied to assess the publication bias. The above analysis is performed using Revman software. As $P < 0.05$, the analysis is considered statistically significant.

III. Results

3.1 Literature Search Results

After de-weighting, there are 31 articles in total that meet the inclusion and exclusion criteria. There is no English literature that meet the requirements. The literature list is as follows:

TABLE I. Characteristics of included studies

Author	Publication year	Age	No. of intervention group	No. of comparison group	Intervention	Control	Outcomes
Chen	2016	22-58	60	60	Qingre Jiedu Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical treatment	Overall response rate, complete response rate, recurrence rate
Chen	2019	22-56	32	24	Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical treatment	Complete response rate, recurrence rate
Chu	2017	18-46	42	41	Qingre Jiedu Chinese medicine treatment + Control treatment	Ruyi gold paste and prednisone	Overall response rate, complete response rate, recurrence rate
Cui	2013	22-61	35	28	Chinese medicine treatment + Control treatment	Surgical treatment	Overall response rate, complete response rate, recurrence rate
Guo	2014	19-45	22	15	Compound sophora injection plus traditional Chinese medicine treatment	Conventional western medicine treatment	Overall response rate, complete response rate
He	2017	32-44	41	41	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate
Huang	2013	23-58	32	32	Chinese medicine treatment + Control treatment	Surgical treatment	Overall response rate, complete response rate, recurrence rate
Huang	2017	20-60	42	42	Chinese medicine on the basis of the control group	Hormone shock therapy and operation	Overall response rate, complete response rate, recurrence rate
Huang J	2017	17-65	48	48	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate

Jin	2014	20-60	20	20	Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical treatment	Overall response rate, complete response rate
Li	2010	17-55	54	52	Qingre Jiedu Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical treatment	Overall response rate, complete response rate, recurrence rate
Li	2018	27-58	30	30	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate, recurrence rate
Ma	2016	22-45	50	50	Traditional Chinese medicine on the basis of the control group	Conventional ductal lavage combined with partial closure	Recurrence rate
Ni	2013	30-50	30	30	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate
Ou	2018	20-57	48	48	modified Qinggan Jieyu decoction	antibiotics and external therapy treatment	Overall response rate, complete response rate
Qi	2017	20-45	30	30	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate, recurrence rate
Que	2014	25-50	40	38	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate
Sui	2019	23-51	35	35	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate
Tian	2017	19-57	45	45	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate
Tu	2018	18-56	38	38	Qingre Jiedu Chinese medicine treatment +	antibiotics and external therapy	Overall response rate, complete response

					Control treatment	treatment	rate
Wang	2010	21-50	31	28	Traditional Chinese medicine on the basis of the control group	Conventional ductal lavage combined with partial closure	Overall response rate, complete response rate
Wang	2017	24-56	33	33	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate
Wang	2018	23-47	30	30	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate, recurrence rate
Wang YQ	2018	34-68	34	34	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate, recurrence rate
Wu	2016	22-63	45	44	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate
Yao	2017	24-54	33	33	Chinese medicine treatment + Control treatment	Conventional western medicine treatment	Overall response rate, complete response rate, recurrence rate
Zhang	2012	19-50	40	40	Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical treatment	Overall response rate, complete response rate, recurrence rate
Zhang	2015	22-54	72	48	Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical treatment	Overall response rate, complete response rate, recurrence rate
Zhang	2017	23-47	60	60	Acupuncture + Control treatment	Surgical treatment	Overall response rate, complete response rate
Zhou	2015	26-52	38	30	Chinese medicine treatment + Control treatment	Hormone and antibacterial drugs and surgical	Overall response rate

						treatment	
Zhou	2017	20-45	60	60	Chinese medicine treatment + Control treatment	Breast duct endoscopic intervention	Overall response rate, complete response rate, recurrence rate

3.2 Meta-analysis:

Inclusion criteria: randomized controlled trials; the control group is Western medicine treatment, the intervention group is traditional Chinese medicine plus Western medicine; the outcome is cure rate, effective rate and recurrence rate of plasma cell mastitis; the shedding rate is higher than 50%.

3.2.1 Efficacy meta-analysis

The efficacy Meta-analysis includes 2,245 people. The analysis indicates that the integrative traditional Chinese and Western medicine treatment is 25% more efficient than the Western medical treatment alone (RR and 95% CI=1.25 (1.20, 1.30)), and it is of less heterogeneity. It demonstrates that the therapeutic effect of the integrative Chinese and Western medicine treatment group is superior to the Western medicine alone. Please see results in Fig 2.

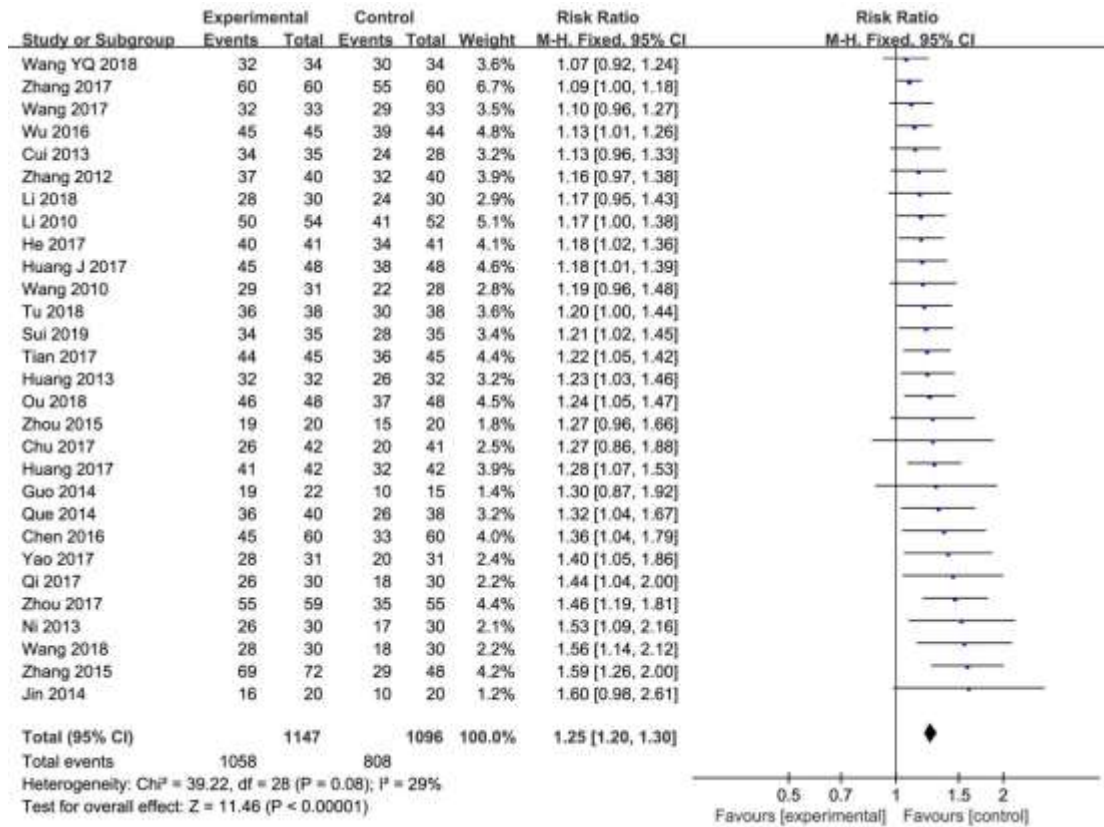


Fig 2: efficacy Meta-analysis chart and Forest plot

3.2.2 Cure rate meta-analysis

The cure rate Meta-analysis includes 2,071 people. The analysis indicates that the cure rate of integrative traditional Chinese and Western medicine treatment is 53% higher than the Western medical treatment alone (RR and 95% CI=1.53 (1.40, 1.67)), and it is of of less heterogeneity. According to statistical data, the cure rate of integrative Chinese and Western medicine treatment is much higher than the Western medical treatment alone. Please see results in Fig 3.

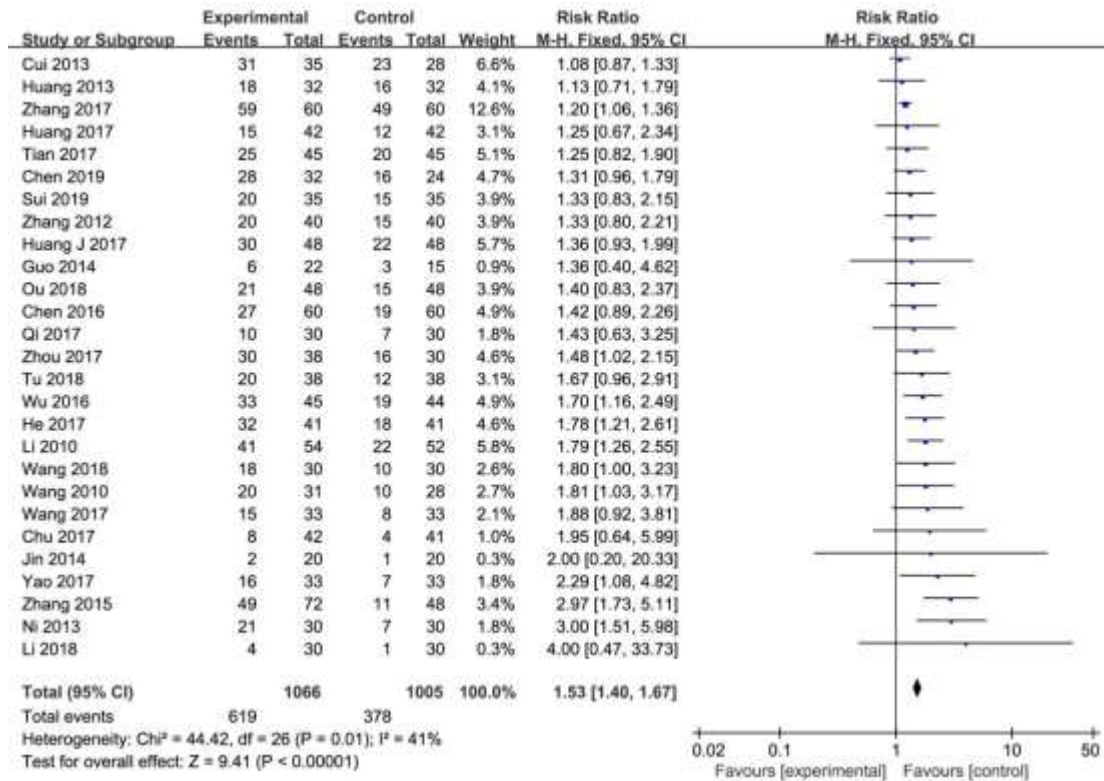


Fig 3: Heal rate Meta-analysis chart and Forest plot

3.2.3 Recurrence rate meta-analysis

The recurrence rate Meta-analysis includes 1,198 people. The analysis indicates that the recurrence of the integrative traditional Chinese and Western medicine treatment is 54% lower than the western medicine alone (RR and 95% CI=0.46 (0.37, 0.57)), and it is of less heterogeneity. It demonstrates that the efficacy of the integrative Chinese and Western medicine treatment group is superior to the Western medicine alone. Please see results in Fig 4.

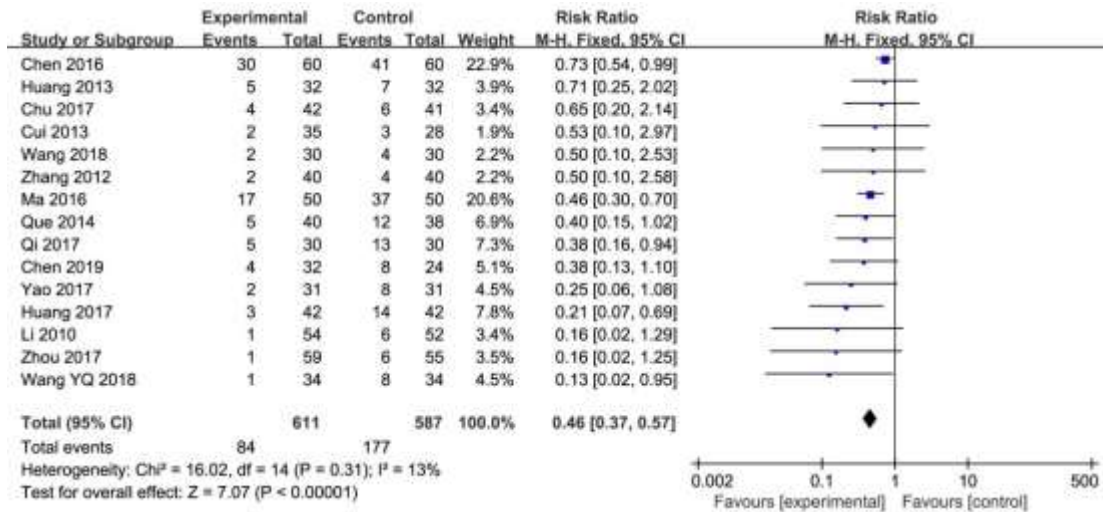


Fig 4: recurrence rate Meta-analysis chart and Forest plot

3.3 Publication Bias

A “funnel plot” analysis is performed on the included literature in the study, and the funnel plot is drawn using statistical analysis software. Analysis of publication bias is performed using the Stata software for Begg test and Egger test. The complete response rate of Begg test is $P=0.09958$. The complete response rate of Egger test is $P = 0.0003618$. The overall response rate of Begg test is $P < 0.001$. The overall response rate of Egger test is $P < 0.001$. The recurrence response rate of Begg test is $P=0.216$. The recurrence response rate of Egger test is $P=0.003762$.

The funnel plot shows that there is no significant publication bias in the Meta-analysis of the three outcomes. Please see results in Fig 5.

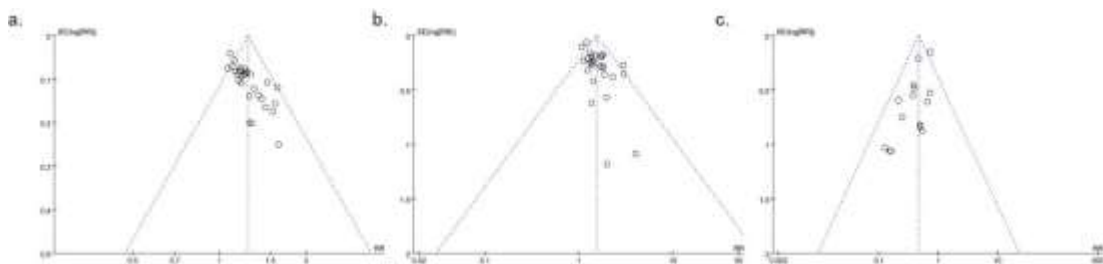


Fig 5: funnel plot

(a: Forest plot-overall response rate; b: Forest plot-complete response rate;

c: Forest plot-recurrence rate)

3.4 Efficacy Evaluation

The results of Meta-analysis charts indicate the integrative traditional Chinese and Western medicine treatment is superior to the Western medicine alone in the treatment of plasma cell mastitis. The included literature in the study demonstrates that the integrative traditional Chinese and Western medicine treatment is not only effective in improving the short-term efficacy, but also has a significant effect on long-term efficacy.

IV. CONCLUSION

Plasma cell mastitis is a chronic non-bacterial and non-infectious breast inflammation caused by secretion retention, nipple depression, breast duct stenosis, occlusion, and obstructive duct excretion. It is more common in non-lactation or non-pregnancy women aged 30-40 years old[10]. This disease is often accompanied by nipple discharge and depression. After suppurative ulceration, pus will occur, which is easy to repeatedly redness, swelling and ulcerate, forming fistula. The course of this disease is long and difficult to recover. If it is not treated in time, it will gradually damage the breast shape and seriously damage the physical and mental health of the patient[11].

Although plasma cell mastitis is a benign disease, its pathological characteristics are complex and changeable, and it is easy to cause misdiagnosis and missed diagnosis in clinic[12]. Research shows that most of the bacteria infected with plasma cell mastitis are *Mycobacterium tuberculosis*, and the effect of ordinary antibiotic treatment is not obvious. Surgical treatment is still the main clinical treatment measure at present, but some research reports believe that surgical treatment is not the standard treatment measure for non-lactation mastitis treatment. If the scope of surgery is too small, the postoperative recurrence rate will be extremely high, and the scope of surgery is too large, which has a greater impact on the appearance of the breasts. After surgery, due to breast deformation and other problems, women are also taken care of. It becomes a big trauma[13]. At present, more and more clinical studies show that according to the etiology and pathogenesis of plasma cell mastitis and based on the principle of syndrome differentiation and treatment, traditional Chinese medicine internal and external application combined with Western medicine anti-inflammatory, surgery and other treatments have unique advantages in the treatment of plasma cell mastitis[14-17]. This study uses meta-analysis to systematically evaluate the treatment of plasma cell mastitis with integrated traditional Chinese and western medicine. Through systematic, objective and quantitative comprehensive analysis of many research results of the same category, the

heterogeneity between different research results is explained, the credibility of the research conclusions is increased, and evidence-based medical evidence for its next clinical treatment is provided.

Further statistical literature refers to the advantages of the treatment plan of integrated traditional Chinese and western medicine, and the recurrence rate of its treatment is statistically analyzed. Compared with pure Western medicine treatment, integrated traditional Chinese and western medicine treatment has the advantages of reducing the recurrence rate of the disease and prolonging the recurrence time. It shows that the therapeutic effect of this treatment plan is accurate, suggesting that the treatment of plasma cell mastitis with the combination of traditional Chinese and western medicine can not only give full play to the unique advantages of traditional Chinese medicine in the treatment of plasma cell mastitis, but also further improve the therapeutic effect of western medicine and provide patients with a more optimized treatment plan.

In addition, at the time of this study, it was found that none of the foreign literatures included in the literature conformed to the treatment of plasma cell mastitis with the combination of traditional Chinese and western medicine. The reason may be that the treatment plan is in the exploration stage and lacks recognized evaluation standards for efficacy. Therefore, no English literature that meets the inclusion standard RCT was found in this study. Therefore, in future studies, we should pay attention to standardized treatment and clinical research, use objective indicators to evaluate the curative effect, and carry out large-sample clinical randomized controlled trials to further improve the quality of the study.

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