ORIGINAL RESEARCH

# Clinical Effect of Rehabilitation New Fluid Combined with Sanjie Analgesic Capsules in the Treatment of Granulomatous Mastitis and Thyroiditis and Impact on Immune Indexes of Patients

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## ABSTRACT

**Objective** • To analyze the clinical effect of rehabilitation new fluid combined with Sanjie analgesic capsules in the treatment of granulomatous lobular mastitis (GLM) and thyroiditis and the impact on immune indexes of patients.

**Methods** • For a retrospective study, we selected 150 patients with GLM and 150 patients with thyroiditis admitted to The Fourth Hospital of Shijiazhuang from January 2021 to January 2022. We divided them into three groups based on the treatment methods. Control group 1 (CG1) included patients treated with rehabilitation new fluid alone, while control group 2 (CG2) included patients treated with the Sanjie analgesic capsules alone. The third group, the observation group (OG), included patients treated with rehabilitation new fluid (extract of drying body from Periplaneta americana) at an oral dose of 10 ml combined with Sanjie analgesic capsules. There were 50 patients in each group. The clinical efficacy, symptom improvement, the level changes of free triiodothyronine (FT3), free tetraiodothyronine (FT4), and thyroid stimulating hormone (TSH), and the changes of immune indexes such as CD4+ (cluster of differentiation 4+), CD25+ (cluster of differentiation 25+), CD68+ (cluster of differentiation 68+) and CD138+ (cluster of differentiation 138+) were analyzed.

**Results** • After treatment, the total treatment effectiveness of GLM in the OG was 94%, which was significantly higher than 80% in the CG1 and 78% in the CG2 ($P$ = .037, .021), while the total treatment effectiveness of thyroiditis in the OG was 92%, which was significantly higher than 76% in the CG1 and 74% in the CG2 ($P$ = .029, 0.017). The scores of breast pain, breast overflow, tumor size, local skin changes, and axillary fossa lymphadenectasis of the affected side in the OG of GLM were better than those in CG1 ($P_{\text{breast pain}}$ < .001, 95%CI: 0.573-1.747; $P_{\text{breast overflow}}$ = .022, 95%CI: 0.074-0.905; $P_{\text{tumor size}}$ = .008, 95%CI: 0.231-1.489; $P_{\text{local skin changes}}$ = .001, 95%CI: 0.382-1.498; $P_{\text{axillary fossa lymphadenectasis of the affected side}}$ = .011, 95%CI: 0.096-0.704) and CG2 ($P_{\text{breast pain}}$ = .001, 95%CI: 0.449-1.711; $P_{\text{breast overflow}}$ = .049, 95%CI: 0.002-0.798; $P_{\text{tumor size}}$ =0.019, 95%CI: 0.132-1.428; $P_{\text{local skin changes}}$ < .001, 95%CI: 0.563-1.517; $P_{\text{axillary fossa lymphadenectasis of the affected side}}$ = .001, 95%CI: 0.202-0.678). The levels of FT3 and FT4 in the OG of thyroiditis were higher than CG1 ($P_{FT3}$ < .001, 95%CI: 0.951-1.590; $P_{FT4}$ < .001, 95%CI: 1.421-2.618) and CG2 ($P_{FT3}$ < .001, 95%CI: 0.943-1.643; $P_{FT4}$ < .001, 95%CI: 1.521-2.758), and the TSH level was lower compared with CG1 ($P_{TSH}$ < .001, 95%CI: 2.409-3.070) and CG2 ($P_{TSH}$ < .001, 95%CI: 2.540-3.230). The immune indexes of GLM were improved, and the levels of CD4+, CD25+, CD68+, and CD138+ in the OG were better than those in the CG1 ($P_{CD4+}$ < .001, 95%CI: 2.967-4.912; $P_{CD25+}$ < .001, 95%CI: 3.707-5.212; $P_{CD68+}$ < .001, 95%CI: 1.445-2.200; $P_{CD138+}$ < .001, 95%CI: 3.922-5.510) and CG2 ($P_{CD4+}$ < .001, 95%CI: 3.093-4.995; $P_{CD25+}$ < .001, 95%CI: 3.527-4.904; $P_{CD68+}$ < .001, 95%CI: 1.334-2.216; $P_{CD138+}$ < .001, 95%CI: 3.878-5.352). The immune indexes of thyroiditis were improved, and the levels of CD4+, CD25+, CD68+, and CD138+ in the OG were better than those in the CG1 ($P_{CD4+}$ < .001, 95%CI: 4.235-6.117; $P_{CD25+}$ < .001, 95%CI: 3.300-4.810; $P_{CD68+}$ < .001, 95%CI: 1.173-1.939; $P_{CD138+}$ < .001, 95%CI: 3.704-4.881) and CG2 ($P_{CD4+}$ < .001, 95%CI: 3.136-5.422; $P_{CD25+}$ < .001, 95%CI: 3.182-4.615; $P_{CD68+}$ < .001, 95%CI: 1.216-2.113; $P_{CD138+}$ < .001, 95%CI: 4.145-5.527).

**Conclusion** • The clinical effect of rehabilitation new fluid combined with Sanjie analgesic capsule in the treatment of GLM and thyroiditis is remarkable, which enables enhancement of the treatment efficiency, and improves patients' clinical symptoms, functional indexes, and the levels of immune indexes, as a direction for the follow-up treatment in the clinic. (*Altern Ther Health Med.* 2024;30(7):233-239).


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## INTRODUCTION

Granulomatous mastitis (GLM) and thyroiditis are both autoimmune diseases, and morbidity has had an upward trend in recent years.[1] GLM often appears in non-lactating women, with the characteristic performance of non-caseous necrosis, and the lesions occur in the lobules of the mammary gland, performing granulomatosis eventually. At present, surgical resection is used in clinical treatment, accounting for about 50%, but the recurrence rate is 20%-30% and can lead to sequelae such as hypertrophic scars and breast deformation, with a low acceptance rate in patients.[2] Thyroiditis is common in women, which is manifested as goiter and pain, and thyroid function is reduced with the aggravation of the disease. Hormone treatment is often unable to cure this disease, and the condition is easy to repeat, increasing the pain of patients so the key topic of study is to explore new and effective treatment methods for medical staff worldwide.[3] In recent years, regulatory T cells like CD4+ (cluster of differentiation 4+), CD25+ (cluster of differentiation 25+), CD68+ (cluster of differentiation 68+), and CD138+ (cluster of differentiation 138+) are abnormally expressed in GLM and thyroiditis, so it is suspected that regulatory T cells can participate in the occurrence and development of inflammation via immune regulation of patients.[4,5] From the perspective of traditional Chinese medicine (TCM), these two diseases belong to the category of yin asthenia, and kidney-yang deficiency forms the state of deficient vital Qi leading to the lingering pathogen. Yang from yin likes inexhaustible spring, which needs to start by nourishing yin, and then warming yang to eliminate evil.[6,7] Rehabilitation new fluid and Sanjie analgesic capsules belonging to TCM, rehabilitation new fluid have the effect of promoting blood circulation, nourishing, and promoting granulation, and modern medicine has also proven its anti-inflammatory effect, while Sanjie analgesic capsules have the effect of softening hardness and dissipating mass, dispersing blood stasis and analgesic therapy, and inhibiting the aseptic inflammation.[8] The combination of these drugs can achieve the effects of nourishing, warming the kidney, supporting, activating blood, and eliminating stasis. Restoring vital energy as the root and eliminating pathogens as the standard, simultaneous application of attacking pathogen and tonifying Qi (the invasion of pathogen leads to the diseases if people lacks healthy energy, so the body can not maintain balance if they only received the treatment of attacking pathogen, without the supplement of Qi) keeps evils away through supplementing healthy energy (namely, human body's ability to resist evil, with the functions of defense, immune supervision and the maintenance of internal balance), and also reflects the effect on improving the immunity of the body to resist diseases in Western medicine. A study has shown that the application of rehabilitation of new fluid in patients with ulcerative colitis can improve the inflammation level and enhance the immune function, with a significant curative effect.[9] According to the studies of surgery patients with plasma cell mastitis,[10] rehabilitation new fluid combined with Sanjie analgesic capsules can promote the illness recovery of surgery patients with plasma cell mastitis, improving the immune function. However, the current clinical study on the rehabilitation of new fluid combined with Sanjie analgesic capsules in the treatment of GLM and thyroiditis is rare, and the therapeutic effect needs to be further explored. Based on this, 150 patients with GLM and 150 patients with thyroiditis were selected for the retrospective study to analyze the clinical effect of rehabilitation new fluid combined with Sanjie analgesic capsules in the treatment of GLM and thyroiditis and the impact on immune indexes.

## MATERIALS AND METHODS

### Case data and grouping

150 patients with GLM and 150 patients with thyroiditis admitted to The Fourth Hospital of Shijiazhuangour from January 2021 to January 2022 were selected for the retrospective study, and they were divided into three groups according to different treatment methods. The patients treated with rehabilitation new fluid alone and Sanjie analgesic capsules alone were included in control group 1 (CG1) and control group 2 (CG2), respectively, while the patients treated with rehabilitation new fluid combined with Sanjie analgesic capsules were included in the observation group (OG), with 50 cases in each group. Among them, the patients with GLM in the CG1 were 21-32 years old, with an average age of (28.30±2.26) years old, a disease duration of 2-12 months, and an average disease duration of (8.23±2.28) months, and in terms of pathogenetic locations, there were 22 cases on the left side and 28 cases on the right side. Education level. There were 24 cases of senior high school and above, 19 cases of junior high school, and 7 cases of primary school and below. The patients with GLM in the CG2 were 20-31 years old, with an average age of (28.34±2.03) years old, a disease duration of 2-11 months, and an average disease duration of (8.47±2.35) months, and 20 cases had focal lesions on the left side and 30 cases had focal lesions on the right side. Education level. There were 22 cases of senior high school and above, 20 cases of junior high school, and 8 cases of primary school and below. The patients with GLM in the OG were 21-30 years old, with an average age of (27.98±2.09) years old, a disease duration of 1-12 months, and an average disease duration of (7.93±2.57) months, and there were 24 cases on the left side and 26 cases on the right side. In terms of education level, there were 25 cases of senior high school and above, 18 cases of junior high school, and 7 cases of primary school and below. All patients were female, and there was no statistical difference in the general data of each group ($P > .05$).

In the CG1 of thyroiditis, there were 8 males and 42 females aged 26-47 years old, with an average age of (34.94±3.09) years old, a disease duration of 0.3-2 years, and an average disease duration of (1.18±0.61) years. As for education level, there were 31 cases of senior high school and above, 11 cases of junior high school, and 8 cases of primary school and below. In the CG2 of thyroiditis, there were 9 males and 41 females aged 24-48 years old, with an average age of

(35.40±3.04) years old, disease duration of 0.2-2 years, and the average disease duration of (1.14±0.54) years. Regarding education level, there were 32 cases of senior high school and above, 11 cases of junior high school, and 7 cases of primary school and below. In the OG of thyroiditis, there were 11 males and 39 females aged 24-46 years old, with an average age of (34.84±2.93) years old, a disease duration of 0.4-2.5 years, and an average disease duration of (1.18±0.54) years. Education level. There were 30 cases of senior high school and above, 24 cases of junior high school, and 6 cases of primary school and below. There was no statistical difference in the general data of each group ($P > .05$), with a comparison.

### Inclusion criteria and exclusion criteria

**Inclusion criteria**. 1) The included patients were diagnosed with GLM and thyroiditis by pathology biopsy and iconography, respectively, and met the diagnostic criteria of GLM in Exert Consensus on Diagnosis and Treatment of Non-lactating Mastitis[9] and the diagnostic criteria of thyroiditis in Diagnosis and Treatment Guidelines of Thyroiditis in China.[11] 2) Patients had no immune diseases such as rheumatoid arthritis and dermatomyositis. 3) Patients had clinical manifestations like obvious swelling, hot, pain, and pressing pain in the breast. 4) Patients with thyroiditis had different degrees of goiter. 5) This study was in line with the declaration of Helsinki (2013),[12] patients and their families who understood the purpose, significance, content, and confidentiality signed informed consent.

**Exclusion criteria**. 1) Patients with severe functional disorders in the heart, liver, and kidney; 2) patients who used other medical treatment recently; 3) patients with allergy to drugs used in this study; 4) patients with breast fibroma, breast cancer, breast tuberculosis, and breast hyperplasia; 5) patients with other internal medicine diseases like hepatitis, tuberculosis, diabetes, and nephropathy; 6) patients with no obvious purulent sign and symptom and who had simple lump; and 7) patients in the gestation period.

## METHODS

### Treatment method

CG1 received rehabilitation new fluid (manufacturer: Sichuan Good Doctor Panxi Pharmaceutical Co., Ltd.; NMPA approval No.: Z51021834; specification: 10ml*6 piece) alone for treatment at an oral dose of 10 ml/dose 3 times a day, CG2 simply used Sanjie analgesic capsules (manufacturer: Jiangsu Kanion Pharmaceutical Co., Ltd.; NMPA approval No.: Z20030127; specification: 0.4 g × 30 s) at an oral for 4 capsules/dose for 3 times daily, and the OG was treated with rehabilitation new fluid combined with Sanjie analgesic capsules, with the same usage and dosage as above. All patients were treated for 3 months continuously.

### Detection method

Fasting peripheral blood (5ml) was collected before and after treatment and sent to the laboratory department for testing to detect the CD4+ T cells, CD25+ T cells, CD68+ T cells, and CD138+ T cells in inflammatory tissues extracted from lesions using immunohistochemical staining method, fixed in 10% formalin solution. The routine paraffin embedding and serial slices were taken and then stored at normal temperature. The paraffin sections were placed in a container containing citrate buffer (specification: 500ml; manufacturer: Beijing Yita Biotechnology Co., Ltd.; batch No.: 125-62-6) for boiling for 5 minutes after the routine de-paraffin and washing, followed by the incubation in 3% hydrogen peroxide at room temperature for 15 min, then washing with PBS 3 times in 5 min, and the sealing was performed with 5% goat serum (specification: 50T/645T; manufacturer: Shanghai Yaji Biotechnology Co., Ltd.; Batch No.: UI89-1018) for the incubation at room temperature lasting for 30 min. The diluted appropriate proportion of the first antibody was added at 4°C overnight, with PBS for rinsing 3 times 5 minutes, then dropwise the biotin-labeled second antibody for the incubation at room temperature lasting for 20 min, with PBS for rinsing 3 times 5 min. The horseradish peroxidase-labeled pronase avidin (specification: 100 μl; manufacturer: Yeasen Biotechnology (Shanghai) Co., Ltd.; batch No.: 35105ES60) was added for the incubation at room temperature lasting for 20 min, with PBS for rinsing 3 times 5 minutes, using diaminobenzidine (DAB) chromogenic agent (specification: 60 ml; manufacturer: Beijing Solarbio Science and Technology Co., Ltd.; batch No.: DA1016) for coloration to observe by a microscope. The rinse using tap water, double staining with hematoxylin, alcoholic dehydration at gradient level, transparency using xylene, and mounting by neutral tree gum were performed. An inverse microscope was used to observe the staining section via the immunohistochemical method (S-P), with 3 doctors in the pathology department observing the slice independently by a light microscope.

### Observation indices

The clinical efficacy of patients was observed in the three groups, and the evaluation criteria of curative effect on GLM[14] were as below. If the constitutional symptom and local masses disappeared, with a favorable cure of traumatism, the treatment was markedly effective. If the constitutional symptom disappeared, while local swelling and pain were alleviated, the scope was reduced or traumatism was improved, the treatment was effective. If the symptom did not disappear, and the abscess was recurring and even formed the galactorrhea, the treatment was invalid. The evaluation criteria for curative effect on thyroiditis were as follows. If the symptoms and signs such as fever and thyroid neoplasms disappeared or returned to normal, with a normal ultrasound examination and the curative effect maintained for more than 3 months, the treatment was markedly effective. If the symptoms and signs such as fever and thyroid neoplasms disappeared basically or dramatically improved, and the ultrasound examination showed a reduction in sporadic flake-like lower echo lesions, the treatment was effective. If the symptoms and signs such as fever and thyroid neoplasms were not improved, and the ultrasound examination showed a hypoechoic lesion, the

**Table 1.** Integral rating table of symptoms and signs in patients with GLM

| Symptoms | Signs | Scores |
|---|---|---|
| Breast pain | No pain and pressing pain | 0 |
| | Mild self-conscious pain and pressing pain | 2 |
| | Self-conscious pain and pressing pain, mainly before menstruation, with paroxysm | 4 |
| | Obvious self-conscious pain and pressing pain or cannot press, with persistence and radioactivity, affecting daily life | 6 |
| Breast overflow | No | 0 |
| | Yes | 2 |
| Changes in local skin | Normal local skin | 0 |
| | Local skin with dull red | 2 |
| | Local skin with blush | 4 |
| | Local skin with scarlet red | 6 |
| Tumor size | No | 0 |
| | < 2 cm × 2 cm | 2 |
| | 2 cm × 2 cm ≤ tumor mass < 5 cm × 5 cm | 4 |
| | ≥5 cm × 5 cm | 6 |
| Axillary fossa lymphadenectasis of the affected side | No | 0 |
| | Yes | 2 |

**Table 2.** Comparison of clinical efficacy in patients with GLM among the three groups [n(%)]

| Groups | Cases | Markedly effective | Effective | Invalid | Total effectiveness |
|---|---|---|---|---|---|
| CG1 | 50 | 22 (44.00) | 18 (36.00) | 10 (20.00) | 40 (80.00)[a] |
| CG2 | 50 | 20 (40.00) | 19 (38.00) | 11 (22.00) | 39 (78.00)[b] |
| OG | 50 | 36 (72.00) | 11 (22.00) | 3 (6.00) | 47 (94.00) |

[a]indicated a significant difference in the CG1 compared with OG ($P < .05$)
[b]indicated a mark difference in the CG2 than OG ($P < .05$).

**Table 3.** Comparison of clinical efficacy in patients with thyroiditis among the three groups [n(%)]

| Groups | Cases | Markedly effective | Effective | Invalid | Total effectiveness |
|---|---|---|---|---|---|
| CG1 | 50 | 21 (42.00) | 17 (34.00) | 12 (24.00) | 38(76.00)[a] |
| CG2 | 50 | 20 (40.00) | 17 (34.00) | 13 (26.00) | 37 (74.00)[b] |
| OG | 50 | 34 (68.00) | 12 (24.00) | 4 (8.00) | 46 (92.00) |

[a]indicated a significant difference in the CG1 compared with OG ($P < .05$)
[b]indicated a mark difference in the CG2 than OG ($P < .05$).

**Table 4.** Comparison of symptoms and signs integral among the three groups ($\bar{x} \pm s$, points)

| Evaluation indicators | | CG1 | CG2 | OG | *t* | *P* value |
|---|---|---|---|---|---|---|
| Breast pain | Before treatment | 4.52±1.45 | 4.32±1.63 | 4.40±1.28 | 0.439 | .662 |
| | After treatment | 3.76±1.49[a] | 3.68±1.42[a] | 2.60±1.58[a] | 3.777 | <.001 |
| Breast overflow | Before treatment | 1.56±0.84 | 1.52±0.86 | 1.60±0.81 | 0.242 | .809 |
| | After treatment | 0.96±1.01[a] | 0.92±1.01[a] | 0.52±0.89[a] | 6.126 | .047 |
| Tumor size | Before treatment | 4.48±1.49 | 4.44±1.30 | 4.52±1.45 | 0.136 | .892 |
| | After treatment | 3.32±1.54[a] | 3.24±1.61[a] | 2.46±1.75[a] | 8.095 | .017 |
| Changes in local skin | Before treatment | 4.64±1.37 | 4.68±1.32 | 4.72±1.33 | 0.296 | .768 |
| | After treatment | 3.30±1.49[a] | 3.40±1.53[a] | 2.36±1.44[a] | 13.675 | .001 |
| Axillary fossa lymphadenectasis of the affected side | Before treatment | 1.44±0.91 | 1.48±0.89 | 1.52±0.86 | 0.452 | .652 |
| | After treatment | 0.80±0.99[a] | 0.84±1.00[a] | 0.40±0.81[a] | 6.551 | .038 |

[a]represented a significant difference in the comparison before and after treatment in the same group ($P < .05$).

treatment was invalid. The total treatment effectiveness = the number of markedly effective cases + the number of effective cases/total cases %.

According to the integral table of the symptoms and signs of GLM in TCM from the Comprehensive Method of Combining TCM Classification with Biomedical Diagnosis,[15] the symptoms and signs were recorded before and after treatment using the integral method, as shown in Table 1.

Thyroid function indicators. The levels of free triiodothyronine (FT3), free tetraiodothyronine (FT4), and thyroid stimulating hormone (TSH) were detected by the radioimmunoassay method.

The index changes of regulatory T cells CD4+, CD25+, CD68+, and CD138+ were compared in patients among the three groups before and after treatment.

### Statistical analysis

The data processing software was Statistical Product and Service Solutions SPSS version 22.0 (IBM company, Armonk, State of New York, USA), and GraphPad Prism version 7 (GraphPad Software, San Diego, CA, USA) was used to draw pictures. The enumeration data and measurement data were tested by $\chi^2$ and *t* test, indicated by [n (%)] and ($\bar{x} \pm s$). When $P < .05$, the differences were considered to be statistically significant.

## RESULTS

### Comparison of clinical efficacy in patients with GLM among the three groups

The total treatment effectiveness in the OG was markedly higher than that in the CG1 and the CG2, with no statistical significance in difference ($P < .05$), as shown in Table 2.

### Comparison of clinical efficacy in patients with thyroiditis among the three groups

The total treatment effectiveness in the OG was markedly higher than that in the CG1 and the CG2, with no statistical significance in difference ($P < .05$), as shown in Table 3.

### Comparison of symptoms and signs integral to GLM among the three groups

There was no statistical significance in symptoms and signs integral among the three groups before treatment ($P > .05$). After treatment, the scores of breast pain, breast overflow, tumor size, changes of local skin, and axillary fossa lymphadenectasis of the affected side in the OG were better than those in the CG1 and CG2, as detailed in Table 4.

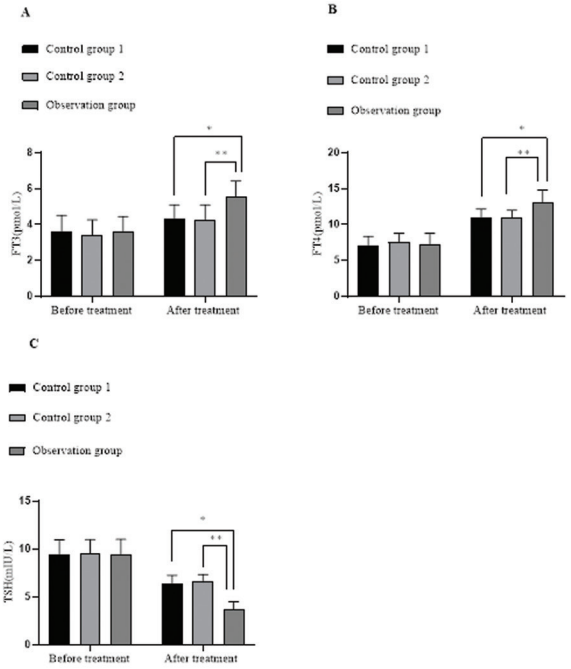
### Comparison of thyroid function indicators among the three groups of thyroiditis

There was no statistical difference in the levels of FT3, FT4, and TSH among the three groups before treatment ($P > .05$). After treatment, the three groups were improved, and the levels of FT3 and FT4 in the OG were markedly higher than those in the CG1 and CG2, and the TSH level was visibly lower than that in the CG1 and CG2 ($P < .05$), as shown in Figure 1.

### Levels of immune indexes in patients with GLM

Before treatment, there was no statistical difference in the levels of immune indexes among the three groups ($P > .05$). After treatment, the levels of CD4+, CD25 +, CD68+, and CD138+ in the OG were better than those in the CG1 and CG2, with statistical significance in difference ($P < .05$), as shown in Table 5.

**Figure 1.** Comparison of thyroid function indicators among the three groups of thyroiditis ($\bar{x} \pm s$). Notes. The horizontal coordinate indicates before and after treatment, and the vertical coordinate indicates the level values of FT3, FT4, and TSH.




Note: (A) * represented that the FT3 level in the OG was markedly higher than that in the CG1 (5.56±0.86 vs. 4.29±0.81, $t$ = 7.601, $P$ < .001). ** represented that the FT3 level in the OG was markedly higher than that in the CG2 (5.56±0.86 vs. 4.27±0.81, $t$ = 7.721, $P$ < .001). (B) * represented that the FT4 level in the OG was markedly higher than that in the CG1 (13.01±1.78 vs. 10.99±1.17, $t$ = 6.706, $P$ < .001). ** represented that the FT4 level in the OG was markedly higher than that in the CG2 (13.01±1.78 vs. 10.88±1.09, $t$ = 7.216, $P$ < .001). (C) * represented that the TSH level in the OG was markedly higher than that in the CG1 (3.65±0.85 vs. 6.39±0.86, $t$ = 16.023, $P$ < .001). ** represented that the TSH level in the OG was markedly higher than that in the CG2 (3.65±0.85 vs. 6.54±0.81, $t$ = 17.405, $P$ < .001).

**Table 5.** Levels of immune indexes in patients with GLM ($\bar{x} \pm s$)

| Evaluation indicators | | CG1 | CG2 | OG | $t$ | $P$ value |
|---|---|---|---|---|---|---|
| CD4+ (%) | Before treatment | 38.08±2.98 | 37.42±3.26 | 37.99±3.51 | 0.138 | .890 |
| | After treatment | 34.06±2.40[a] | 34.16±2.35[a] | 30.12±2.42[a] | 8.174 | <.001 |
| CD25+ (%) | Before treatment | 18.86±3.40 | 18.99±3.43 | 19.04±3.22 | 0.272 | .786 |
| | After treatment | 16.78±2.13[a] | 16.54±2.07[a] | 12.32±1.44[a] | 12.266 | <.001 |
| CD68+ (%) | Before treatment | 5.44±1.39 | 5.38±1.51 | 5.42±1.47 | 0.070 | .944 |
| | After treatment | 3.67±1.26[a] | 3.62±1.40[a] | 1.85±0.55[a] | 9.361 | <.001 |
| CD138+ (%) | Before treatment | 14.58±2.17 | 14.41±2.15 | 14.53±2.02 | 0.119 | .905 |
| | After treatment | 11.97±2.27[a] | 11.87±2.32[a] | 7.26±1.34[a] | 16.635 | <.001 |

[a]showed a significant difference in the same groups before and after treatment ($P$ < .05).

**Table 6.** Levels of immune indexes in patients with thyroiditis ($\bar{x} \pm s$)

| Evaluation indicators | | CG1 | CG2 | OG | $t$ | $P$ value |
|---|---|---|---|---|---|---|
| CD4+ (%) | Before treatment | 37.80±3.43 | 37.97±3.25 | 37.43±2.98 | 0.576 | .566 |
| | After treatment | 35.62±2.90[a] | 34.72±3.15[a] | 30.44±2.00[a] | 10.397 | <.001 |
| CD25+ (%) | Before treatment | 19.88±2.91 | 20.19±2.63 | 20.57±2.93 | 1.181 | .240 |
| | After treatment | 16.29±2.34[a] | 16.13±2.31[a] | 12.23±1.31[a] | 10.705 | <.001 |
| CD68+ (%) | Before treatment | 5.30±1.48 | 5.59±1.54 | 5.37±1.48 | 0.236 | .814 |
| | After treatment | 3.49±1.30[a] | 3.60±1.40[a] | 1.94±0.58[a] | 7.699 | <.001 |
| CD138+ (%) | Before treatment | 15.99±2.15 | 16.18±2.35 | 16.34±2.21 | 0.803 | .424 |
| | After treatment | 12.24±1.83[a] | 12.79±1.99[a] | 7.95±1.32[a] | 13.444 | <.001 |

[a]showed a significant difference in the same groups before and after treatment ($P$ < .05).

**Levels of immune indexes in patients with thyroiditis**

Before treatment, there was no statistical difference in the levels of immune indexes among the three groups ($P$ > .05). After treatment, the levels of CD4+, CD25+, CD68+, and CD138+ in the OG were better than those in the CG1 and CG2, and the difference was statistically significant ($P$ < .05), as shown in Table 6.

## DISCUSSION

GLM is a chronic breast inflammation, with the formation of granulomatosis in breast tissue as the main pathological manifestation, It has a long disease duration and is easy to repeat, and the treatment by surgery or hormone is not the best method because of possible side effects and high recurrence rate, damaging the immune function of patients.[16] Thyroiditis, as a heterogeneous disease involving the thyroid, the structural damage of thyroid follicles caused by autoimmunity, viral infection, bacterial or fungal infection, radiation injury, drugs and other factors leads to goiter producing inflammation, and excessive thyroid hormones produce the symptoms of hyperthyroidism, while low thyroid hormones cause the hypothyroidism.[17,18] The oral administration of thyroid hormone was usually taken in the clinical treatment, without an ideal efficacy, but patients with this disease cannot recover often, bringing troubles to patients.[19] The essence of inflammation is the imbalance of yin (the substantial substance of the human body, that is, body fluids, including blood, saliva, tears, watery nasal secretion, endocrine, and even male semen) and yang (insubstantial substance of the human body, namely, physical function and Qi) in the whole body and the break of the internal steady state, leading to the morphological changes caused by the malfunction such as viscera, meridians, and qi-blood-body fluid, ultimately inducing the meridian disorder that is difficult to recover after the coordination between the internal environment of the human body and the outside world is damaged.[20,21] The TCM adheres to the principle of internal and external treatment, with elimination in the early stage, support method in the middle stage, and supplement in the later stage. Syndrome differentiation such as promoting blood circulation to remove blood stasis, resolving phlegm and resolving masses, soothing liver, and promoting qi (dispering and dredging function of liver) is used for the clinical swelling symptoms of early GLM. Traditional Chinese Medicine (TCM) has various therapies to treat GLM ulcers and thyroiditis. In the middle stage, therapies like pus-draining, toxin-expelling, qi-benefiting, toxic-pushing, warming yang, and drawing toxins are applied to prevent the GLM ulcer from breaking or to heal the ulcer and pus. In the later stage, replenishing qi to invigorate the spleen, warming Yang, reducing swelling, and nourishing blood are used to improve the symptoms of a long-term wound that does not heal even after ulceration or swelling and collapse of the affected area. TCM has a wealth of experience in treating GLM and thyroiditis through

comprehensive analysis, personalized precision therapy, and syndrome differentiation therapy. It has unique advantages in reducing recurrent metastasis, controlling the disease, and improving symptoms.[22] The main component of rehabilitation new fluid is the Periplaneta americana extract, and its effect of supplementing Qi and nourishing yin, consolidating root, and promoting granulation is recognized after research and clinical practice for many years, which can improve the immune function of patients, and has anti-inflammation and anti-tumor effects.[23,24] Sanjie analgesic capsules have the main role of softening hardness dissipating mass and dispersing blood stasis, and analgesic therapy, which has been widely used in the treatment of endometriosis.

This study found that the curative effect of rehabilitation of new fluid combined with Sanjie analgesic capsules in the treatment of GLM and thyroiditis was markedly better than that of a single drug. The total treatment effectiveness of GLM in the OG was 94%, which was overtly higher than 80% in the CG1 and 78% in the CG2 ($P < .05$), while the total treatment effectiveness of thyroiditis in the OG was 92%, which was visibly higher than 76% in the CG1 and 74% in the CG2 ($P < .05$). The reason may be that the essence of GLM and thyroiditis is the manifestation of blood stasis and phlegm stagnation, and the method of activating blood circulation to dissipate blood stasis, and dispersing phlegm and eliminating stagnation can help patients further improve clinical symptoms and enhance the curative effect. Scholar Breznik Vesna[25] has pointed out that the combination application of rehabilitation new fluid and Sanjie analgesic capsules in patients with plasma cell mastitis could improve breast pain and incision healing time. In this study, the scores of breast pain, breast overflow, tumor size, changes of local skin, and axillary fossa lymphadenectasis of the affected side in the OG of GLM were better than those in CG1 and CG2. The levels of FT3 and FT4 in the OG of thyroiditis were higher than those in the CG1 and CG2 ($P < .05$), and the TSH level was lower than that in the CG1 and CG2 ($P < .05$), indicating that rehabilitation new fluid combined with Sanjie analgesic capsules could improve the symptoms of patients with GLM and thyroiditis. Rehabilitation of new fluid containing polyols and peptides enables promotion of the regeneration of epidermal epithelium, accelerates the growth of granulation tissue, increases the regeneration of local capillaries by improving the blood circulation of local injured tissue, and makes the necrotic tissue of injured wound detach to generate new epithelium, while peptide constituents could reduce the inflammatory wound pain, protect the new epithelium of wound, and have obvious effect on relieving swelling and analgesic therapy. Sanjie analgesic capsules have the effect of removing blood stasis, promoting granulation, and eliminating stagnation to stop pain, which can reduce the levels of thromboxane and prostaglandin in plasma and inhibit aseptic inflammation.

Regulatory T cells are a type of T cell subset that can regulate the autoimmune reaction in vivo. They have immune energy and immunosuppressive properties, and their role is based on direct contact with other cells rather than cytokine secretion. CD4, CD25, CD68, and CD138 can bind to chemokines, leading to neutrophil aggregation at the site of inflammation. This process inhibits T cell migration and regulates the body's response to leukocyte-endothelial cell interaction, thus participating in the inflammatory response. As a result, Regulatory T cells help prevent the migration and invasion of breast duct epithelial and thyroid follicular epithelial cells.[26] When damage in lesions, CD4, CD25, CD68 and CD138 molecules outside the epithelial cell membrane fell off and bound with bacteria or fibroblasts to participate in the immune response of the body. The degrees of inflammation in patients can be judged by the changes in immune indexes, and in the case of a high proportion of CD68 and CD138, the proportion of multiple and giant cells in GLM and follicular epithelial cells in thyroiditis is obvious. CD4 mainly reflects acute inflammatory response, while CD25 has an increase, indicating that special infection should be paid attention to.[27] Ling Jie et al.[28] have confirmed that patients with non-lactating mastitis had varying degrees of immune dysfunction, and the percentages of CD3 and CD4/CD8 cells in T cell subsets were increased. Koksal Hande et al.[29] have found that CD68, CD163, and IgG4 had high positive expression rates in GLM, and this study showed that the expression of immune indexes in patients with GLM and thyroiditis was abnormal. After treatment, the levels of CD4+, CD25+, CD68+, and CD138+ in the OG were better than those in the GP1 and GP2 ($P < .05$), showing that rehabilitation new fluid combined with Sanjie analgesia capsules have an obvious effect in patients with GLM and thyroiditis, and can improve the immune function of patients. The active substances such as polyols, epidermal growth factor, amino acid, and sticky sugar amino acid contained in rehabilitation new fluid have the effects of anti-inflammatory, de-tumescence, and promoting cell and new granulation proliferation, accelerating the repair of lesion sites and the abscission of necrotic tissues, improving the immunity of the body, helping phagocytes to play the role of phagocytosis and strengthening the body resistance. Sanjie analgesia capsule has strong anti-inflammatory and analgesic effects and improves the immune function of the body, and the combination of these drugs can further improve the clinical efficacy.

In summary, the clinical effect of rehabilitation new fluid combined with Sanjie analgesia capsule in the treatment of GLM and thyroiditis is remarkable, which enables enhancement of the treatment efficiency, and improves patients' clinical symptoms, functional indexes, and the levels of immune indexes, as a direction for the follow-up treatment in the clinic.

There are some limitations of this study. Limited by the actual conditions, this study has a small sample size and sample range. At the same time, the observation indexes selected in this study are more objective, and there is no dynamic study on the long-term quality of life of patients. In the future, the sample size should be increased, the sample range should be expanded, and observation indicators should be enriched to complete the dynamic follow-up study of such patients.

## ETHICAL COMPLIANCE

This study was approved by the ethics committee of The fourth hospital of Shijiazhuang. Signed written informed consents were obtained from the patients and/or guardians.

## CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

## AUTHOR CONTRIBUTIONS

YS, XZ HZ, and LZ designed the study and performed the experiments, YS, XZ, and HL collected the data, HL and YX analyzed the data, and YS, XZ HZ, and LZ prepared the manuscript. All authors read and approved the final manuscript.

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## REFERENCES


1. Wang L, Ni C, Shen H, et al. Comparison of the Detection Windows of Heroin Metabolites in Human Urine Using Online SPE and LC-MS/MS: Importance of Morphine-3-Glucuronide. *J Anal Toxicol*. 2020;44(1):22-28. doi:10.1093/jat/bkz040
2. Martins LB, Rodrigues AMDS, Monteze NM, et al. Double-blind placebo-controlled randomized clinical trial of ginger (*Zingiber officinale Rosc.*) in the prophylactic treatment of migraine. *Cephalalgia*. 2020;40(1):88-95. doi:10.1177/0333102419869319
3. Hu X, Chen Y, Shen Y, Tian R, Sheng Y, Que H. Global prevalence and epidemiological trends of Hashimoto's thyroiditis in adults: A systematic review and meta-analysis. *Front Public Health*. 2022;10:1020709. doi:10.3389/fpubh.2022.1020709
4. Lorenz J, Al-Maawi S, Sader R, Ghanaati S. Individualized Titanium Mesh Combined With Platelet-Rich Fibrin and Deproteinized Bovine Bone: A New Approach for Challenging Augmentation. *J Oral Implantol*. 2018;44(5):345-351. doi:10.1563/aaid-joi-D-18-00049
5. Wang Y, Tian A, Zhang F, Yu J, Ling J. Inflammatory Immune Process and Depression-like Behavior in Hypothyroid Rats: A [$^{18}$F] DPA-714 Micro Positron Emission Tomography Study. *Pharmaceuticals (Basel)*. 2023;16(2):279-279. doi:10.3390/ph16020279
6. Shuyang X, Qiang Y. Bacterial factors of mastitis in lactating women and its effect on the physical properties and chemical composition of breast milk. *Cell Mol Biol (Noisy-le-grand)*. 2021;67(3):172-177. doi:10.14715/cmb/2021.67.3.27
7. Norman C, Walker G, McKirdy B, et al. Detection and quantitation of synthetic cannabinoid receptor agonists in infused papers from prisons in a constantly evolving illicit market. *Drug Test Anal*. 2020;12(4):538-554. doi:10.1002/dta.2767
8. Du L, Du DH, Chen B, Ding Y, Zhang T, Xiao W; Anti-Inflammatory Activity of Sanjie Zhentong Capsule Assessed By Network Pharmacology Analysis of Adenomyosis Treatment. Anti-Inflammatory Activity of Sanjie Zhentong Capsule Assessed By Network Pharmacology Analysis of Adenomyosis Treatment. *Drug Des Devel Ther*. 2020;14:697-713. doi:10.2147/DDDT.S228721
9. Li HB, Chen MY, Qiu ZW, et al. Efficacy and safety of Kangfuxin liquid combined with aminosalicylic acid for the treatment of ulcerative colitis: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97(21):e10807. doi:10.1097/MD.0000000000010807
10. Zhang J, Xu J, Zhang J, Ren Y. Chinese herbal compound combined with western medicine therapy in the treatment of plasma cell mastitis: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(44):e22858. doi:10.1097/MD.0000000000022858
11. Yiğitbaşı MR, Guntas G, Atak T, Sonmez C, Yalman H, Uzun H. The Role of Interleukin-33 as an Inflammatory Marker in Differential Diagnosis of Idiopathic Granulomatous Mastitis and Breast Cancer. *J Invest Surg*. 2017;30(4):272-276. doi:10.1080/08941939.2016.1240270
12. Marin F, Jódar E, Sánchez Del Pozo J. Coexistence of dyschondrosteosis associated to *SHOX* deficiency, pseudohypoparathyroidism 1B, and chronic autoimmune thyroiditis: a case report. *J Pediatr Endocrinol Metab*. 2020;34(4):531-534. doi:10.1515/jpem-2020-0419
13. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194. doi:10.1001/jama.2013.281053
14. Saydam M, Yilmaz KB, Sahin M, et al. New Findings on Autoimmune Etiology of Idiopathic Granulomatous Mastitis: Serum IL-17, IL-22 and IL-23 Levels of Patients. *J Invest Surg*. 2021;34(9):993-997. doi:10.1080/08941939.2020.1725190
15. Lu A, Jiang M, Zhang C, Chan K. An integrative approach of linking traditional Chinese medicine pattern classification and biomedicine diagnosis. *J Ethnopharmacol*. 2012;141(2):549-556. doi:10.1016/j.jep.2011.08.045
16. Patel OA, Bakhshi GD, Nadkarni AR, Rangwala ZS. Granulomatous Mastitis Due to Non-Tuberculous Mycobacteria: A Diagnostic and Therapeutic Dilemma. *Clin Pract*. 2021;11(2):228-234. doi:10.3390/clinpract11020034
17. Naik MA, Korlimarla A, Shetty ST, Fernandes AM, Pai SA. Cystic Neutrophilic Granulomatous Mastitis: A Clinicopathological Study With 16s rRNA Sequencing for the Detection of Corynebacteria in Formalin-Fixed Paraffin-Embedded Tissue. *Int J Surg Pathol*. 2020;28(4):371-381. doi:10.1177/1066896919896021
18. Çetin K, Sıkar HE, Güllüoğlu BM. Idiopathic granulomatous mastitis with erythema nodosum: is it a variant of clinical presentation indicating treatment resistance? A retrospective cohort study. *Breast J*. 2020;26(9):1645-1651. doi:10.1111/tbj.13944
19. Aksan H, Kundaktepe BP, Sayili U, et al. Circulating miR-155, let-7c, miR-21, and PTEN levels in differential diagnosis and prognosis of idiopathic granulomatous mastitis and breast cancer. *Biofactors*. 2020;46(6):955-962. doi:10.1002/biof.1676
20. Zhang H, Ding P, Zhang X, et al. MAC Mediates Mammary Duct Epithelial Cell Injury in Plasma Cell Mastitis and Granulomatous Mastitis. *International Immunopharmacology*. 2022;113(Pt A):109303-109303. doi:10.1016/j.intimp.2022.109303
21. Zheng B, Song J, Lu M, Chen C, Sun S. Current Research Describing the Role of CD4$^+$ T Lymphocyte Subsets in the Pathogenesis of Granulomatous Lobular Mastitis. *J Invest Surg*. 2022;35(10):1790-1795. doi:10.1080/08941939.2022.2090035
22. Tao YX, Li Q, Li CC, Huo JJ. Efficacy of Chinese medicine in the adjuvant treatment of Hashimoto's thyroiditis with hypothyroidism: a systematic review and meta-analysis. *Biotechnol Genet Eng Rev*. 2023;21:1-27. doi:10.1080/02648725.2023.2184959
23. Yang XF, Shi SW, Chen K. Case report: recombinant human epidermal growth factor gel plus kangfuxin solution in the treatment of aplasia cutis congenita in a case with Adams-Oliver syndrome. *Front Surg*. 2023;9:1072021. doi:10.3389/fsurg.2022.1072021
24. Zeng A, Gu G, Deng L. Effect of Kangfuxin Solution Fumigation Bath on Postoperative Patients with Hemorrhoid PPH and Influence on the Postoperative Complications. *Evid Based Complement Alternat Med*. 2021;2021:6473754. doi:10.1155/2021/6473754
25. Breznik V, Marko PB. A Case of Overlapping Clinical Features of Idiopathic Granulomatous Mastitis, Hidradenitis Suppurativa, and Pyoderma Gangrenosum Successfully Treated with Adalimumab. *Case Rep Dermatol*. 2022;14(2):98-106. doi:10.1159/000523801
26. M Braden A, V Stankowski R, M Engel J, A Onitilo A. Breast cancer biomarkers: risk assessment, diagnosis, prognosis, prediction of treatment efficacy and toxicity, and recurrence. *Curr Pharm Des*. 2014;20(30):4879-4898. doi:10.2174/1381612819666131125145517
27. Krysiak R, Szkróbka W, Okopień B. Dehydroepiandrosterone potentiates the effect of vitamin D on thyroid autoimmunity in euthyroid women with autoimmune thyroiditis: A pilot study. *Clin Exp Pharmacol Physiol*. 2021;48(2):195-202. doi:10.1111/1440-1681.13410
28. Ling J, Xie X, Wang Y, et al. Differential expression profiles of miRNA in granulomatous lobular mastitis and identification of possible biomarkers. *Exp Ther Med*. 2022;24(2):500. doi:10.3892/etm.2022.11427
29. Koksal H. The Clinical Utility of Autoantibodies in Patients with Idiopathic Granulomatous Mastitis. *J Invest Surg*. 2022;35(2):325-329. doi:10.1080/08941939.2020.1861666