

Zhang, X.; Ji, Y.; Li, S.; Sha, S.; Hu, M.; Lu, Q.; Li, Q.; 1, Chen, W.; Yu Liu, Y.; Xue, X. (2022) Study on Yanghe Decoction in Improving mTOR Pathway and Expression of Inflammatory Factors in Patients with Acne Mastitis. Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 23 (89) pp. 377-387
DOI: <https://doi.org/10.15366/rimcafd2023.89.026>

ORIGINAL

STUDY ON YANGHE DECOCTION IN IMPROVING MTOR PATHWAY AND EXPRESSION OF INFLAMMATORY FACTORS IN FEMALE ATHLETIC PATIENTS

Xinyue Zhang^{1a}, Yajie Ji^{1a}, Siyu Li¹, Shanyan Sha¹, Minhao Hu¹, Qing Lu¹, Qiong Li¹, Weili Chen¹, Yu Liu¹, Xiaohong Xue*

¹: Department of Breast Surgery, Yueyang Hospital of Integrated Traditional Chinese & Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China

^a: These authors contributed equally to this work

Spanish-English translators:

UNESCO Code / UNESCO Code:

Council of Europe classification / Council of Europe classification:

Recibido 30 de abril de 2020 **Received** April 30, 2020

Aceptado 26 de junio de 2020 **Accepted** June 26, 2020

ABSTRACT

Purpose: A study to explore Yang He Tang chemotherapy to improve mTOR pathway and inflammatory factor expression levels in patients with acne vulgaris. **Methods:** Fifty-seven patients with prickly heat treated in our facility from January 2020 to June 2021 were elected as the observation group, and 20 healthy individuals from a similar period were selected as the control group. The test examined the expression levels of mTOR pathway-related proteins and inflammatory factors in both groups to explore the relationship between the mTOR pathway, inflammatory factors and the development of acne vulgaris.; The patient in the monitoring group received Yanghe Tang chemotherapy, and the expression levels of inflammatory factors of mTOR pathway-related proteins were differentiated before and after treatment to study the value of Yang He Tang chemotherapy in acne vulgaris. **Results:** The observation group (inflamed tissue) had higher levels of mTOR pathway protein expression compared to the control group (normal tissue) ($p < 0.05$); There was no statistically significant change in IL-10 between the two groups ($p > 0.05$), but the observation group had higher levels of IL-2/6/8/1 β compared to the control group ($P < 0.05$); compared with the pre-treatment, the mTOR pathway protein

expression level was lower after treatment ($P < 0.05$); Levels of IL-2/6/8/10/1 β were lower after treatment than before treatment ($p < 0.05$); the efficiency rate of the observation group after treatment was 91.23%. **Conclusion:** The mTOR pathway and inflammatory factor expression are involved in the pathogenesis of acne vulgaris, and Yang He Tang chemotherapy can effectively inhibit their horizontal expression, with high therapeutic effect, which is worth promoting.

KEYWORDS: Yanghe soup; Acne mastitis; MTOR access; Inflammatory factor

1 INTRODUCTION

Acne vulgaris is a disease of chronic, aseptic mastitis characterised by dilated milk ducts and plasma cell infiltration, including "plasma cell mastitis", "granulomatous mastitis", "mammary duct dilatation", etc. in Western medicine. It usually occurs in non lactation and non pregnancy. After the disease, it can show symptoms such as breast lump, nipple depression and overflow, periareolar abscess, and multiple duct formation, Because the nipple secretion is characterized by acne like substances or pus with acne like substances, it is named as acne mastitis (Ramalingam, Vuthaluru, Srivastava, Dinda, & Dhar, 2017). According to relevant data statistics, acne mastitis accounts for 4% - 5% of the total incidence of benign breast diseases. Its condition is easy to repeat and difficult to cure, Gravely impacts women's bodily and mental health. Therefore, its treatment is highly concerned by the society (Zhang, Xu, Zhang, & Ren, 2020).

At present, the pathogenesis of acne mastitis has not been clarified (Zuo et al., 2021). It is believed that it is caused by the interaction of multiple factors, and there are many treatment schemes, including surgery, conservative treatment, and traditional Chinese medicine therapy (Beale & Cunningham, 2018). Among them, the advantages of both internal and external treatment of traditional Chinese medicine occupy a low position in the treatment of acne mastitis (Cebron et al., 2020). The traditional Chinese medicine treatment of acne mastitis is mainly to eliminate blood stasis and dissipate knots. Yanghe decoction has the effect of dispelling cold and removing stagnation, so it can be used for treatment (Wang et al., 2019). Relevant studies have confirmed that inflammatory reaction and mTOR pathway related proteins are involved in the pathogenesis and progress of acne mastitis, and there are few studies on Yanghe decoction to improve mTOR pathway in acne mastitis patients (Nan et al., 2022; Ojeyinka & Ajide, 2022). Therefore, this paper takes it as the focus of research, which is reported as follows.

2 DATA AND METHODS

2.1 General information

Fifty-seven patients with common acne admitted to our institute from January 2020 to June 2021 were chosen as the study group, and 20 healthy

people in the same period were taken as the control group. All subjects were female and signed the study informed agreement form. The age of the observation group was 25-42 years, with a mean age of (32.5±3.8) years. Duration of illness was 5-66 days with a mean of (35.5±10.5) days; The control group was 25-41 years old with a median age of (30.6±4.3) years. There was no major change in age observed among the two groups ($p>0.05$). The study was endorsed for approval by the Hospital Ethics Association.

Inclusion criteria: (1) The observation group was diagnosed as acne mastitis by pathological examination, while the control group was proved healthy by physical examination; (2) Non lactating period, aged 18-50 years; (3) No contraindication for treatment; (4) The spirit, consciousness and communication ability are normal.

Exclusion criteria: (1) immune diseases; (2) Heart, liver and kidney dysfunction; (3) Complicated with other breast diseases; (4) Complicated with intracranial injury.

2.2 Methods

2.2.1 Control group:No drug treatment and no intervention.

2.2.2 Observation group:Yanghe decoction was cut into pieces, and the drug was taken warm after decoction, twice a day, 100ml/time. Yanghe Decoction is composed of 10 g antler slices, 12 g prepared ground, 3 g cinnamon, 6 g roasted ephedra, 12 g white mustard seed, 3 g turmeric charcoal, 12 g dried tangerine peel, 12 g green peel, 15 g saponification thorn, 9 g angelica dahurica, 9 g herba artemisiae, 6 g Jiaoshan Gardenia jasminoides, and 9 g rhubarb. The liquid taken is decocted in the Chinese medicine room of our hospital. All patients continued to use the drug for 3 months.

2.3 Observed indicators

2.3.1 Inflammatory factors.

Interleukin-1 β /2/6/8/10 (IL-1 β /2/6/8/10), 3ml of fasting venous blood was drawn, centrifuged, and the upper serum was extracted for enzyme-linked immunosorbent assay(Wu, Yang, & Ma, 2022).

2.3.2 mTOR pathway-related protein expression: PI3K, AKT, mTOR, specimens of breast inflammation tissue from the observation group and normal breast tissue from the control group were taken and detected by Envision two-step method (Kong et al., 2020).

2.2.3 Treatment effect: cured: disappearance of breast lumps, abscesses, red and hot symptoms and healing of fistula; improved: significant reduction or basic disappearance of lumps, relief of symptoms and almost

healing of fistula; not cured: not meeting the above criteria. Effective rate = (cured + improved)/total x 100% (Ahmed et al., 2021).

2.4 Statistical methods

A software package SPSS 25.0 was used to process the data. The statistical data are indicated by $(\bar{x} \pm s)$ with t-test and the count data are indicated by n (%) with χ^2 test $P < 0.05$ indicates a statistically meaningful difference and the study used GraphPadPrism8 as the graphing software.

3 RESULTS

3.1 Comparison of mTOR pathway protein expression levels between the two groups

Versus control group (normal tissue), the observation group (inflamed tissue) had high levels of mTOR pathway protein expression ($P < 0.05$) (see Figure 1).

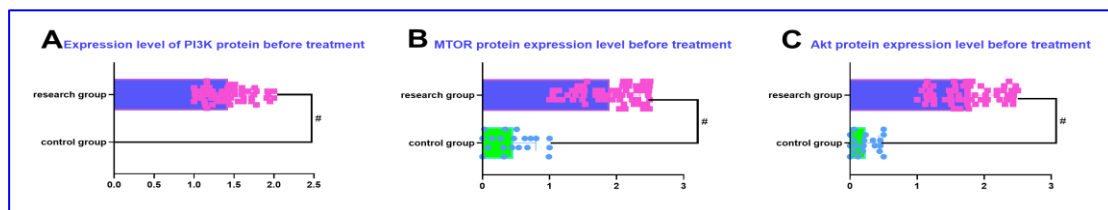


Fig. 1 Comparison of mTOR pathway protein expression levels between the two groups (Note: PI3K, AKT, mTOR ratio, # $P < 0.05$, statistically significant compared to the control group, indicating that the expression of mTOR pathway protein in inflammatory tissue is higher than that in normal tissue)

3.2 Comparison of inflammatory factor levels between the two groups

IL-10 was not elevated significantly in either arm ($P > 0.05$), but IL-2/6/8/1 β levels were higher in the observation arm versus the control arm ($P < 0.05$) (see Figure 2).

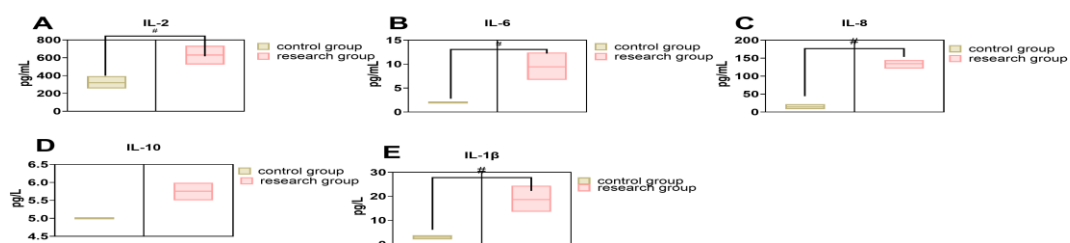
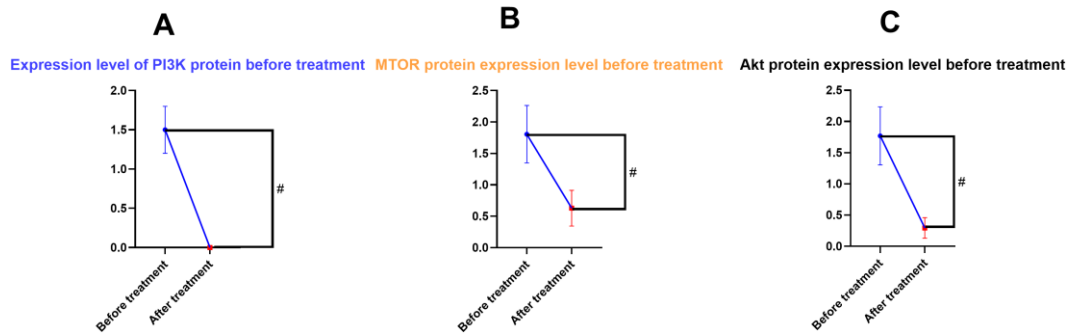


Fig. 2 Comparison of inflammatory factor levels between the two groups (Note: IL-2/6/8/1 compared with the control group β Ratio, # $P < 0.05$, the difference between the two groups is statistically significant, indicating that the serum level of acne mastitis patients is higher than that of normal patients)

3.3 Comparison of mTOR pathway protein expression before and after treatment in the observation group

After being treated, the expression level of mTOR pathway protein was lower than before therapy ($p < 0.05$) (see Figure 3).



Graph 3 Expression level of mTOR pathway protein before and after treatment in the observation group (Note: Compared with PI3K, AKT, mTOR ratio before treatment, # $P < 0.05$, the difference before and after treatment is statistically significant, suggesting that Yanghe decoction can improve the mTOR pathway protein surface in the serum of patients with acne mastitis to the level)

3.4 Comparison of levels of inflammatory factors in the observation group before and after treatment

Versus before the procedure, IL-2/6/8/10/1 after treatment β Low level ($P < 0.05$) (see Figure 4).

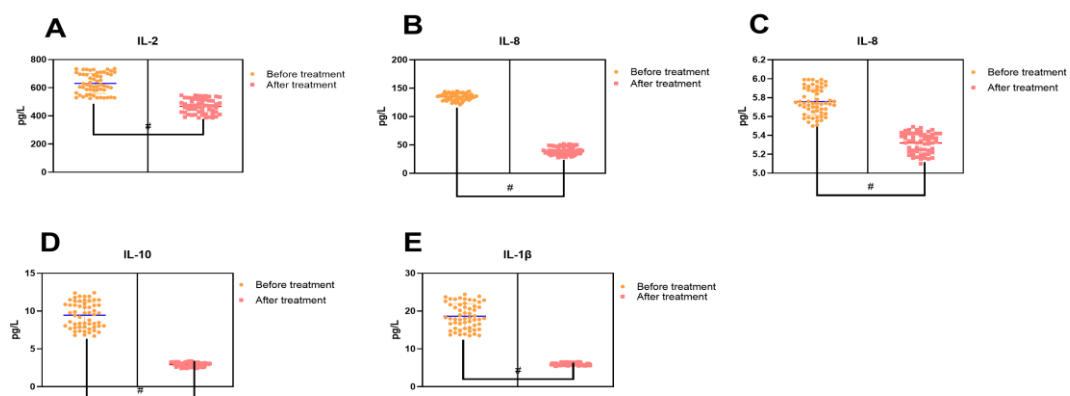


Fig. 4 Comparison of inflammatory factor levels in the monitoring group pre and post treatment (Note: compared with the control group, IL-2/6/8/10/1 β Ratio, # $P < 0.05$, The statistical significance of the difference prior to and after therapy indicates that Yanghe water decoction could improve the serum levels of flammatory factors in patients with acne vulgaris.)

3.5 Treatment effect of observation group

After treatment in the observation group, 6 patients were healed (10.53%) and 46 improved (80.70%), 5 cases were not healed (8.77%), and the effective rate was 91.23% (see Figure 5).

treatment effect



Total=91.23%

4 DISCUSSION

According to relevant data, the incidence of acne mastitis is increasing year by year, and its pathogenesis has not been unified in the medical community at present (Lin et al., 2022). However, many mathematicians at home and abroad believe that acne mastitis is an immune disease, mTOR pathway, IL-2/6/8/10/1 beta and many other inflammatory elements are responsible for the onset and progression of disease (Sawuer, Wu, Sun, & Liu, 2022). This study found that mTOR pathway, The concentration of IL-2/6/8/10/1 β -lactamase was markedly higher in normal tissues. Relevant studies have found that abnormal mTOR signal pathway is involved in the formation of various breast pathology. Through the study of patients with granulomatous mastitis, it is found that PI3K, AKT, mTOR in their serum are highly expressed, which is consistent with the conclusions of this study (Coombe & Hamed, 2021; Omranipour & Vasigh, 2020). IL-8 is engaged in processes of pro-inflammation and immunosuppression, and IL-1 β play an active role in cell differentiation, cell proliferation and apoptosis. It has been found that IL-1 β / It was highly expressed in patients with acne mastitis, and its expression level was positively correlated with the stage. IL-8 mediates local inflammation and is the main mediator of acute phase response (Steuer et al., 2020). IL-10 is an anti-inflammatory element that suppresses the release of pro-inflammatory factors. It can inhibit inflammation by regulating the secretion and synthesis of IgE and IgG4 (Lei et al., 2017). In China, studies have found that IL-10 is expressed at a low level in plasma cell mastitis patients, which is different from the conclusions of this study. Analysis may be related to patient stage, disease type and other factors. IL-6 plays an effective role in stress

response and immune response, both in promoting inflammation and anti infection (Mao, Feng, & Gong, 2018). In the animal experiment, an animal model was established by injecting the tissue homogenate of the patients with acne mastitis into the mice, and IL-6 was injected into the mice. The results showed that the mouse model could show similar breast performance with the patients, and the activity of various inflammatory related signal transduction was also significantly improved (Goulabchand et al., 2020). In some domestic studies, by observing the expression level of IL-6 in patients with acne mastitis at different stages (acute, subacute and chronic), it was found that the level of IL-6 in acute and subacute stage was significantly higher than that in chronic stage, suggesting that IL-6 was involved in disease progression (Liu et al., 2020). Therefore, during treatment, mTOR pathway, IL-2/6/8/10/1 β And other inflammatory factors to evaluate the therapeutic effect.

Acne mastitis is a TCM disease, including plasma cell mastitis, granulomatous mastitis, acute and chronic inflammatory cell infiltration in Western medicine (Xing, Zhang, Zha, & Zhang, 2022). According to Chinese medicine, acne vulgaris occurs mainly due to congenital deficiencies, depression and deformity of the nipple causing emotional discomfort, stagnation of liver qi, coupled with exogenous evil, excessive eating fat and sweet taste causing poor spleen and stomach movement, stagnation of qi and blood stasis, damp heat and phlegm stasis, resulting in loss of nourishment of the breast orifice, lack of qi supply, and the formation of carbuncle. Therefore, the treatment should be based on the principles of reducing swelling and dispersing knot, clearing heat and detoxifying, and supplementing qi and warming yang (Li et al., 2021). Yanghe decoction can treat a variety of diseases, including bone tuberculosis, periostitis, bronchitis, asthma, hyperplasia of mammary lobule (female), dysmenorrhea, etc. In recent years, with the research of its application in gynecology, It has also been found to play an essential role in polycystic ovary syndrome, endometriosis, breast cancer, plasma cell mastitis and other diseases. Yanghe Decoction is a traditional Chinese medicine prescription composed of staghorn slices, prepared rehmannia, cinnamon, roasted ephedra, white mustard seed, baked ginger charcoal, dried tangerine peel, green peel, saponin thorn, angelica dahurica, herba artemisiae, Jiaoshanzhi and rhubarb. Modern pharmacology has confirmed that Yanghe decoction can exert effective anti-inflammatory effects and lowers the levels of various elements of the inflammatory response during disease progression, so it has practical value in the treatment of chronic inflammatory diseases. The deer horn tablets in this formula are effective in tonifying Yang and benefiting the essence, invigorating the blood and detoxifying the body. Modern pharmacology has confirmed that it has anti-inflammatory effect. Radix Pseudostellariae is known to nourish the blood and nourish the Yin, tonify the essence and fill the marrow, and unblock the blood vessels. Modern pharmacology has confirmed that it has the functions of enhancing immunity, promoting blood coagulation, and regulating immunity.

Cinnamomum cassia has the effects of warming the middle and dispersing cold, activating blood circulation and dredging channels, promoting qi and relieving pain. Modern pharmacology has confirmed that it has anti ulcer, anti-inflammatory and other effects. The roasted ephedra has the effects of sweating, relieving superficialities, promoting water and reducing swelling. Modern pharmacology has confirmed that it has the effects of diuresis, inhibiting smooth muscle and anti inflammation. White mustard seed has the effects of regulating qi, dispersing knots, dredging collaterals and relieving pain. Modern pharmacology has confirmed that it has bactericidal, anti lipid peroxidation and other effects. Processed ginger charcoal has the effect of warming the meridians and stopping bleeding. Modern pharmacology has confirmed that it has the effect of anti ulcer and hemostasis. Chenpi has the effects of regulating qi, drying dampness and removing phlegm. Modern pharmacology has proved that it has analgesic, anti-inflammatory, antioxidant and other effects. Qingpi has the effects of soothing the liver and breaking qi, eliminating accumulation and resolving stagnation, and Zaojiao thorn has the effects of detumescence, supporting toxin and expelling pus. Modern pharmacology has confirmed that it has the functions of sterilization, anti-inflammatory, immune regulation, etc. Angelica dahurica has the effects of relieving exterior cold, drying dampness, removing wind, relieving pain, reducing swelling and expelling pus. Modern pharmacology has confirmed that it has anti-inflammatory, antipyretic, analgesic, antibacterial and other effects. Herba Artemisiae Scopariae has the functions of clearing away dampness and heat, nourishing yin and kidney, detoxifying and healing sores. Modern pharmacology has confirmed that it has the functions of analgesia, anti-inflammatory, cholagogic, immune regulation, etc. Jiaoshan Gardenia has the effects of purging fire and removing annoyance, clearing heat and removing dampness. Modern pharmacology has confirmed that it has the effects of sedation, cholagogic, blood coagulation, etc. Rhubarb is effective in clearing heat and fire, resolving blood stasis and detoxifying toxins, diuretic and decongesting. Modern pharmacology has proved that rhubarb has the effects of purging, Antibacterial and antinflammatory, activates blood circulation and dissolves blood clots. A variety of medicinal materials play a synergistic role, so that the whole prescription can be used to warm yang and replenish blood, dispel cold and eliminate knots, detoxify and detumescence, regulate qi and promote blood circulation. This study found that 57 cases of acne mastitis were treated with Yanghe Decoction, the effective rate was as high as 91.23%, and the expression levels of mTOR pathway related proteins and inflammatory factors decreased significantly after treatment compared with those before treatment.

In a domestic study, 59 patients with plasma cell mastitis were treated with modified Yanghe Decoction and Toupus Powder. The total effective rate of PRL, FSH, IL-1 β , IL-6 and TNF- α therapy was 91.5% after treatment compared to before treatment, which is consistent with the findings of this study. In another

study, the patients were treated with routine western medicine and modified Yanghe decoction in combination with traditional Chinese medicine for plasma cell mastitis respectively. The results showed that the total rate of effectiveness of the modified Yanghe decoction combined group was 92.0% better than that of the conventional western medicine group (66.7%), and the course of treatment was also shorter than that of the conventional treatment. All of them can be said that the treatment value of Yanghe decoction in acne mastitis. However, it should be noted that due to the diversity of the manifestations of acne mastitis and the large differences in the manifestations of different stages, it is necessary to conduct a reasonable syndrome differentiation in the treatment of traditional Chinese medicine, appropriately select the appropriate external treatment of traditional Chinese medicine while treating internally, and give full play to the characteristics of internal and external treatment, so as to effectively control the disease.

5 CONCLUSION

The occurrence of acne mastitis will increase the expression level of mTOR pathway related proteins and inflammatory factors, and are complicit in the creation and development of disease. After the treatment with Yanghe decoction, its level expression decreased significantly, and the effective rate of treatment reached 91.23%. Comprehensive analysis showed that the application of Yanghe decoction in the treatment of acne mastitis was of great value, but there were still many shortcomings in this study. The patient's disease stage and type were not differentiated, and the recurrence of the disease after treatment was not studied, This may lead to some deviation in the experimental data. Therefore, in the later research, the above problems should be improved, and the number of research samples, observation and treatment should be continuously expanded to obtain accurate experimental data and conclusions.

Funding

Yueyang Hospital of Integrated Traditional Chinese and Western Medicine Affiliated to Shanghai University of Traditional Chinese Medicine (No.2019YYQ24); Cultivation Project of Dominant Diseases of Traditional Chinese Medicine of Shanghai TCM Development Office(No.ZYBZ-2017008)

Competing interests

The authors declare that they have no competing interests.

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