Treatment of 198 Cases of Thyroid Nodules with Sanying Capsule Combined with Xiaoying Patch

Shujing SHI[1], Mingyue YANG[1], Yue HAO[1], Haihui ZHU[2*], Yan QIN[2,3]

1. Shaanxi University of Chinese Medicine, Xianyang 712046, China; 2. Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, China; 3. People's Hospital of Heyang County, Heyang 715300, China

Abstract [**Objectives**] To observe the clinical efficacy of Sanying capsule combined with Xiaoying Patch in treating thyroid nodule (TN). [**Methods**] Two groups were treated similarly, with 200 cases in the control group undergoing basic treatment for 12 weeks and 198 cases in the observation group receiving Sanying capsule combined with Xiaoying patches for the same duration. The clinical symptoms, number of nodules, diameter of the largest nodule, and maximum reduction of nodules were observed before and after treatment. A control analysis was performed, and the underlying mechanisms were explored. [**Results**] The primary symptoms of the observation group exhibited a more favorable improvement than those of the control group. Additionally, the number of nodules decreased, the diameter of the largest nodule decreased, and the maximum reduction of nodules decreased in both groups following treatment. However, the observation group demonstrated a more pronounced improvement than the control group ($P<0.05$). [**Conclusions**] The combination of Sanying capsule and Xiaoying patch has been demonstrated to be an effective treatment for TN, with a high degree of reliability in terms of safety.

Key words Thyroid nodule, Sanying Capsule, Xiaoying Patch, Clinical efficacy

1 Introduction

A thyroid nodule (TN) is defined as a localized, scattered lesion caused by abnormal growth of thyroid cells[1]. It is one of the most common clinical thyroid diseases. The incidence of TN is on the rise[2]. The palpation-based incidence rate is 3% - 7%, while the incidence rate diagnosed with the help of high-resolution ultrasound can be as high as 20% - 76%[3]. Of these, the incidence rate of malignancy is estimated to be 5% - 15%[1]. In addition to surgical intervention for benign TN, there is currently no effective treatment in Western medicine. Consequently, the treatment of TN with traditional Chinese medicine (TCM) has become a focus of current clinical research[4]. This study examined the treatment of 198 cases of TN using a combination of Sanying capsules and Xiaoying patches. The results are presented below.

2 Data and methods

2.1 General data A total of 200 TN patients were selected from the outpatient clinic of the Department of Endocrinology of the People's Hospital of Heyang County to serve as the control group. In addition, 198 TN patients were selected from the outpatient clinic of the Department of Endocrinology of the Shaanxi Provincial Hospital of Traditional Chinese Medicine to serve as the observation group. Patients with TN diagnosed as malignant lesions were excluded from both groups. The control group consisted of 76 males and 124 females, with an age range of 21 to 68 years and a mean age of (43.6 ± 7.8) years. The duration of the disease ranged from 1 to 7 years, with a mean duration of (4.5 ± 1.8) years. There were 12 cases with nodules greater than 30 mm, 57 cases with nodules between 10 and 30 mm, and 131 cases with nodules less than 10 mm. Additionally, 56 cases had single nodules and 144 cases had multiple nodules. Finally, 131 cases had normal thyroid function tests and 69 cases had high FSH. The observation group consisted of 63 males and 135 females, with an age range of 23 to 67 years and a mean age of (45.3 ± 6.4) years. The duration of the disease ranged from 1 to 6 years, with a mean duration of (5.1 ± 2.2) years. There were 13 cases with nodules greater than 30 mm, 63 cases with nodules between 10 and 30 mm, and 122 cases with nodules less than 10 mm. Additionally, 45 cases had single nodules and 153 cases had multiple nodules. Finally, 128 cases had normal thyroid function tests and 70 cases had high FSH. The observed differences between the two groups in terms of gender, age, disease duration, nodule size, number of nodules, and thyroid function were not statistically significant ($P>0.05$) and were comparable.

2.2 Diagnostic criteria

2.2.1 Diagnostic criteria of Western medicine. In accordance with the *Chinese Guidelines for the Diagnosis and Treatment of Thyroid Diseases*, the diagnostic criteria of Western medicine are defined as the presence of one or more nodules identified by thyroid B-ultrasound or isotope scanning, or the fulfillment of the following conditions. (i) Symptoms: nodules may exhibit movement during swallowing, without the presence of redness, swelling, heat, or pain. Additionally, pressure symptoms such as hoarseness, suffocation, and difficulty breathing or swallowing may manifest in larger nodules. (ii) Signs: the palpation examination reveals the presence of unilateral or bilateral thyroid enlargement, which can be palpated as a swelling with clear boundaries. This

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* Corresponding author. E-mail: 1040610170@qq.com

enlargement moves up and down with swallowing, and there is no pressure pain, tremor, or vascular murmur. (iii) Laboratory tests: there are no abnormalities in thyroid function and autoantibodies, or the single TSH level is elevated.

2.2.2 Diagnostic criteria of Chinese medicine. In accordance with the *Diagnostic and Therapeutic Efficacy Criteria of Traditional Chinese Medicine*[5] and *Modern Clinical Endocrinology of Traditional Chinese Medicine*[6], this condition is recognized as phlegm knotting and blood stasis. The following symptoms may be indicative of TN: a palpable mass in front of the neck, a firm or rigid consistency upon palpation, a gradual accumulation over time, a tendency to ascend and descend with swallowing, a tingling sensation and distension of the neck, discomfort, dyspnea or an unfavorable swallowing experience. Secondary symptoms include depressed mood, irritability, chest and abdominal distension, sighing, phlegm in the throat or breast distension. The tongue pulse is manifested as a dark or purple tongue, thin white or white greasy moss, smooth or astringent pulse.

2.3 Exclusion criteria The following cases should be excluded from the study: malignant lesions of the thyroid gland; rapidly enlarging thyroid nodules in a short period of time; Graves' disease, hypothyroidism, acute and subacute thyroiditis, and other diseases of the thyroid gland; patients with severe combined heart, brain, liver, and kidney damage. In addition, patients who have experienced severe trauma or undergone major surgery, those with redness, swelling, heat, pain, and itching of the skin, pregnant women or women who are breastfeeding, patients with psychiatric disorders, patients with an allergy to adhesive tapes, patients with an allergy to traditional Chinese medicines, and those who do not cooperate with the study must be excluded.

2.4 Therapeutic methods Both groups received emotional relief treatment. The observation group was treated with a combination of oral administration of Sanying capsule and external application of Xiaoying patch. The Sanying capsule is composed of Radix Bupleuri (9 g), Fructus Aurantii (12 g), Pericarpium Citri Reticulatae Viride (12 g), Spica Prunellae (12 g), Radix Angelicae Sinensis (9 g), Radix Scrophulariae (9 g), Poria (12 g), Rhizoma Curcumae (12 g), and Rhizoma Curcumae Longae (12 g). The preparation is an in-hospital formulation of Shaanxi Provincial Hospital of Traditional Chinese Medicine in the form of a capsule, bearing the approval number 220150052. It is recommended that two capsules should be taken twice a day for a period of 12 weeks. The Xiaoying patch is composed of Rhizoma Sparganii, Thunberg Fritillary Bulb, Spica Prunellae, Laminariae Thallus, Pericarpium Citri Reticulatae Viride, Fructus Aurantii Immaturus, Flos Carthami, Chuanxiong Rhizoma, and Semen Brassicae. The patch is administered once per day for a period of 12 weeks. The dosage is 1 patch per treatment, with each patch being applied for 4 – 8 h.

2.5 Security indicator Prior to and following treatment, a comprehensive examination of liver function, renal function, blood routine, thyroid function, and other general physical examinations was conducted. Adverse events were recorded in detail.

2.6 Observation indicator TCM syndrome score: in accordance with the *Guiding Principles for Clinical Research of New Chinese Medicines (Trial Implementation)*[7], the main symptoms and signs were scored as 0, 2, 4 and 6, respectively, according to none, light, moderate, and severe. The number of nodules, the diameter of the largest nodule, and the maximum reduction of nodules before and after treatment in the two groups were recorded.

2.7 Efficacy assessment The effectiveness of the treatment can be classified as follows: markedly effective: syndrome score ratio $\geqslant 70\%$, palpation and B-ultrasound or isotope scanning showed disappearance of the mass; effective: $30\% \leqslant$ syndrome score ratio $< 70\%$, palpation and B-ultrasound or isotope scanning showed significant reduction of the mass; ineffective: syndrome score ratio $< 30\%$, palpation and B-ultrasound or isotope scanning showed no change or enlargement of the mass. The Nimodipine method was employed for the calculation of the score ratio, which was defined as follows: score ratio = (Pre-treatment score – Post-treatment score)/Pre-treatment score $\times 100\%$.

2.8 Statistical method The SPSS 19.0 statistical software was employed for the analysis. The data were expressed as $(\bar{x} \pm s)$ for the measurement data and as cases (%) for the count data. The t test was performed for the former and the χ^2 test for the latter. The difference was considered statistically significant at $P < 0.05$.

3 Results and analysis

3.1 Efficacy comparison The results of the observation group following treatment demonstrated superior efficacy compared to the control group ($P < 0.05$). The findings are presented in Table 1.

Table 1 Comparison of efficacy between the two groups case (%)

Group	*n*	Markedly effective	Effective	Ineffective	Total effective
Observation	198	32 (16.16)	128 (64.65)	38 (19.19)	160 (80.81)*
Control	200	3 (1.50)	41 (20.50)	156 (78.00)	44 (22.00)

NOTE * indicates a statistically significant difference at the 0.05 level in comparison to the control group. The same below.

3.2 Comparison of nodule number A significant reduction in the number of nodules was observed in the observation group following treatment, in comparison to the control group ($P < 0.05$). The results are displayed in Table 2.

3.3 Comparison of the diameter of the largest nodule The diameter of the largest nodule in the observation group following treatment was found to be significantly smaller than that in the control group ($P < 0.05$). The results are shown in Table 3.

Table 2 Comparison of nodule number before and after treatment between the two groups case (%)

Group	*n*	Time	Single nodule	Multiple nodules	Total
Observation	198	Before treatment	45 (22.73)	153 (77.27)	198 (100.00)
		After treatment	34 (17.17)	120 (60.61)	154 (77.78)*
Control	200	Before treatment	56 (28.00)	144 (72.00)	200 (100.00)
		After treatment	44 (22.00)	148 (74.00)	192 (96.00)

Table 3 Comparison of the diameter of the largest nodule before and after treatment between the two groups ($\bar{x} \pm s$)

Group	*n*	Time	Diameter of the largest nodule//mm
Observation	198	Before treatment	13.5 ± 4.9
		After treatment	6.2 ± 3.7*
Control	200	Before treatment	13.4 ± 5.1
		After treatment	11.8 ± 3.6

3.4 Comparison of the maximum reduction of nodules A statistically significant improvement in the maximum reduction of nodules in the observation group following treatment was observed in comparison to the control group ($P < 0.05$). The results are shown in Table 4.

Table 4 Comparison of the maximum reduction of nodules case

Group	*n*	>10 mm	5 – 10 mm	<5 mm
Observation	198	30.0*	124.0*	44
Control	200	2.0	34.0	164

3.5 Comparison of adverse events No adverse events were observed in either group.

4 Discussion

The pathogenesis of benign TN is complex. Western medical treatment includes psychological comfort, close follow-up, thyroid-stimulating hormone (TSH) suppression, radioactive iodine (131I) therapy, anhydrous alcohol injection, radiofrequency ablation, and surgical intervention. Surgical resection is the most commonly employed surgical approach, but it is more traumatic and prone to recurrence. It also has certain disadvantages, and the results are not yet satisfactory. Chinese medicine offers a distinctive set of advantages and efficacy in the treatment of TN. The concept of "preventing disease before it occurs and preventing change when it has already occurred" in Chinese medicine is of particular significance in the treatment of benign TN[8]. The administration of traditional Chinese medicine orally, in conjunction with the external application of traditional Chinese medicine, has been demonstrated to have a positive therapeutic effect on improving efficacy, alleviating symptoms, reducing the size of nodules, delaying the progression of the disease, eliminating nodules, and reducing the recurrence rate. These findings have significant practical value.

Thyroid nodules are classified as goiters in traditional Chinese medicine. The *Sanyin Ji Yi Bingzheng Fang Lun* (*Treatise on Three Categories of Pathogenic Factors*) states that there are five types of goiter, each with a distinct appearance and etiology. The first is stony goiter, which is characterized by hardness and immobility. The second is fleshy goiter, which is defined by a lack of change in skin color. The third is sinew goiter, which is distinguished by the exposure of tendons and veins. The fourth is blood goiter, which is marked by the presence of red veins. Finally, the fifth type is pneumatocele goiter, which is associated with a sense of sadness. *Jisheng Fang* (*Prescriptions for Succouring the Sick*) postulates that the initiating factor of goiter disease is the internal injury of emotion[9], resulting from physical factors, diet, labor, and emotional disorders. These factors lead to an abnormal rise and fall of qi, which in turn causes gas stagnation and blood stasis, gas stagnation and phlegm stagnation, phlegm stagnation, and blood stasis, each of which exerts a detrimental effect on the neck and ultimately results in goiter[10].

Rhizoma Sparganii, Thunberg Fritillary Bulb, and Laminaria Thallus in the Xiaoying patch have been demonstrated to have the following effects: dissolution of phlegm and softening of hardness, activation of blood and dispersion of knots. Collectively, these effects are considered to be the monarch drug in the prescription. Thunberg Fritillary Bulb is a unique pharmaceutical agent for the treatment of goiter tumors, which is frequently combined with Laminaria Thallus and seaweed, as documented in *Medical Innermost Words. The Collection of Clinical Experiences for Shi Jinmo's Prescription of Medicine* states that Rhizoma Sparganii enters the liver, spleen, and blood, and is a blood qi medicine. It is longer than the qi in the blood and is used to break through the blood and promote meridians. Fructus Aurantii Immaturus and Pericarpium Citri Reticulatae Viride are hepatoprotective and regulate qi, facilitating the dispersion of phlegm-dampness and blood stasis. Collectively, these drugs are considered ministerial drugs. *Medical Origins* notes that Pericarpium Citri Reticulatae Viride is effective in breaking up hard lumps, dispersing stagnant qi, removing all dampness in the lower energizer, and there is pneumatosis in the left flank. Spica Prunellae and Semen Brassicae are known to play a role in reducing phlegm and resolving masses. *Jingyue Complete Works* records that Spica Prunellae is beneficial in dissolving liver qi, nourishing liver blood, and thus dispersing knots and opening depressions. This is particularly useful in the treatment of scrofula, tuberculous fistula, porrigo, and other conditions. Flos Carthami and Chuanxiong Rhizoma are employed as adjuvants to resolve blood stasis and disperse knots. The aforementioned drugs act in concert to regulate qi and resolve phlegm, eliminate goitres and knots, and activate blood circulation and detoxification, thus demonstrating significant therapeutic effects on TN[11]. Modern pharmacological analysis has demonstrated that the application of the patch externally has a therapeutic effect on TN by inhibiting inflammation, anti-tumorigenic activity, regulating immunity, regulating microcirculation, and other pharmacological activities[12-13].

The Sanying capsule is manufactured through the addition and subtraction of Chaihu Shugan Powder. In the formula, Bupleuri Radix is the most important medicine for treating yang-deficient liver disease, with an aromatic odor that is beneficial for dispersing liver qi and relieving depression; Fructus Aurantii, with a bitter and pungent flavor, is matched, as it is effective in destroying qi and eliminating stagnation, and resolving phlegm and removing lumps; the pungent Pericarpium Citri Reticulatae Viride is combined to facilitate the dispersal and warming, and descending of bitter discharge. The simultaneous administration of three pharmaceutical agents serves to facilitate the cleansing of the liver and the regulation of the flow of qi, the dissolution of nodules, and the alleviation of discomfort. The formula contains Rhizoma Curcumae and Rhizoma Curcumae Longae, which are blood-activating medicines with strong medicinal properties. These can not only break blood stasis, but also move qi and relieve pain. Modern pharmacological studies have demonstrated that Radix Scrophulariae possesses anti-inflammatory, antipyretic, and antioxidant properties[14]. It is frequently combined with Spica Prunellae, which primarily enters into the liver meridian to dispel knots and relieve heat, thereby achieving the desired effect of dispersing stagnant knots and clearing liver fire. The *Sheng Nong's Herbal Classic* indicates that Spica Prunellae is employed primarily for the treatment of cold and heat, miasmatic carbuncles, the dispersal of goitres, and the accumulation of qi. Modern pharmacological studies have demonstrated that Spica Prunellae possesses anti-inflammatory, antihypertensive, and immunomodulatory effects[15-16]. Its aqueous decoction exerts an inhibitory effect on *Bacillus*, while its water decoction and alcohol precipitation solution demonstrates an inhibitory effect on swelling. Additionally, it protects thyroid cells and exerts a superior tonic effect on TN[17]. The liver, a visceral organ, can be tonified by Radix Angelicae Sinensis, a sweet, warm, and moist substance. This tonic can address blood deficiency and liver dryness. When the liver insults the spleen, Poria is employed to fortify the spleen and tonify the middle, exuding dampness and resolving phlegm. The simultaneous administration of all the aforementioned drugs has the potential to facilitate the movement of qi and the resolution of phlegm, the elimination of edema, and the dispersion of knots.

In conclusion, TN is currently highly prevalent and has numerous treatment options. Surgical treatment may result in irreversible damage to patients and lead to compensatory hyperplasia and recurrence of TN. TCM treatment does not cause permanent damage to thyroid function and is a treatment worthy of further investigation.

References

[1] Endocrinology Division of Chinese Medical Association, Endocrinology Group of Surgery Division of Chinese Medical Association, Head and Neck Tumour Committee of Chinese Anti-cancer Association, *et al.* Guidelines for the diagnosis and management of thyroid nodules and differentiated thyroid cancer[J]. Chinese Journal of Nuclear Medicine and Molecular Imaging, 2013, 33(2): 96 – 115. (in Chinese).

[2] LIU CX, XIE XR, ZHANG T, *et al.* Clinical efficacy of abdominal acupuncture combined with encircling needling in the treatment of benign thyroid nodules[J]. Journal of Changchun University of Chinese Medicine, 2022, 38(1): 84 – 87. (in Chinese).

[3] GHARIB H, PAPINI E, PASCHKE R, *et al.* American association of clinical endocrinologists, associazione medici endocrinologi, and european thyroid association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: Executive summary of recommendations[J]. Journal of Endocrinological Investigation, 2010, 33(5): 287 – 291.

[4] WANG JB, LI YX, WANG CC, *et al.* Clinical efficacy and safety of Yingliu Sanjie Formula for benign thyroid nodules[J]. Hebei Journal of Traditional Chinese Medicine, 2022, 44(3): 393 – 396. (in Chinese).

[5] State Administration of Traditional Chinese Medicine. Diagnostic and therapeutic efficacy standards of Chinese medicine[S]. Nanjing: Nanjing University Press, 1994: 42. (in Chinese).

[6] CAI YM. Modern clinical endocrinology of Chinese and western medicine [M]. Beijing: China Press of Traditional Chinese Medicine, 2001: 204 – 210. (in Chinese).

[7] ZHENG XY. Guiding principles for clinical research of new Chinese medicines (for Trial Implementation) [M]. Beijing: China Medical Science and Technology Press, 2002: 462 – 463. (in Chinese).

[8] YANG P, WANG HJ, WANG SL, *et al.* Meta-analysis of the clinical efficacy of Chinese medicine in the treatment of benign simple thyroid nodules[J]. Hubei Journal of Traditional Chinese Medicine, 2022, 44(3): 56 – 63. (in Chinese).

[9] LI R, REN JP, FAN HJ. Application value of Bazhen decoction after thyroid nodule needle puncture[J]. Shaanxi Journal of Traditional Chinese Medicine, 2019, 40(6): 777 – 780. (in Chinese).

[10] TIAN WH, HU XJ. Treatment of 120 cases of thyroid nodules with Sanying prescription[J]. Shaanxi Journal of Traditional Chinese Medicine, 2012, 33(11): 1526 – 1527. (in Chinese).

[11] XIAO Y, QIN Y, HU XJ. Treatment of 120 cases of thyroid nodules by external application of Xiaoying Paste[J]. Shaanxi Journal of Traditional Chinese Medicine, 2015, 36(11): 1496 – 1497. (in Chinese).

[12] BIAN DZ, XU K, HUANG F, *et al.* Experimental effect and related mechanism of diosgenin in the treatment of Graves' disease rats[J]. Journal of Clinical and Experimental Medicine, 2018, 17(18): 1908 – 1911. (in Chinese).

[13] MEI WT, HUANG F. Clinical efficacy of external application of Jiajiexiao paste in the treatment of benign thyroid nodules[J]. Inner Mongolia Journal of Traditional Chinese Medicine, 2022, 41(12): 90 – 92. (in Chinese).

[14] GUO LZ, LU X, HUANG YL, *et al.* Observation of clinical curative effect of Flavored Bupleurum and Cinnamon Twig Decoction on thyroid nodules[J]. Henan Traditional Chinese Medicine, 2018, 38(12): 1799 – 1801. (in Chinese).

[15] DOU JY, YU JS. Research progress of pharmacological effects and clinical application of Xia Gu Cao[J]. Journal of Modern Medicine & Health, 2013, 29(7): 1039 – 1041. (in Chinese).

[16] JIA CL, LU JD, ZHI ZJ. Clinical efficacy observation on treating thyroid nodules with the formula of dredging liver and activating blood, resolving phlegm and dispersing nodules[J]. Journal of Hebei North University: Natural Science Edition, 2022, 38(10): 29 – 31. (in Chinese).

[17] DONG Z, ZHAO XD. Clinical effect of Jianpi Huazhuosanjie Xiaoying Decoction on thyroid nodule[J]. Guide of China Medicine, 2015, 13(11): 204 – 205. (in Chinese).