

Effect of Pingxiao capsule on thyroid nodules and its influence on serum TGF- β 1 and IGF-1 levels

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Abstract: To investigate the effect of Pingxiao capsule on the treatment of thyroid nodules and its effect on the levels of serum transforming growth factor- β 1 (TGF- β 1) and insulin-like growth factor 1 (IGF-1). Eighty-six patients with thyroid nodules admitted to the First Hospital Affiliated to Heilongjiang University of Traditional Chinese Medicine were selected and divided into 2 groups according to the random number table method. In the study, the control group received sodiumlevothyroxine treatment, while the observation group received a combination of Pingxiao capsule and sodiumlevothyroxine. A comparative analysis was conducted between the two groups, assessing Chinese medicine symptom scores, clinical effectiveness, thyroid nodule size, thyroid function indices, serum levels of TGF- β 1 and IGF-1, as well as adverse reactions. **RESULTS:** Post-treatment, both groups exhibited decreased scores in patients with palpable neck nodules, laryngeal obstruction, depression, Shantaixi, and dizziness ($P < 0.05$). Notably, the observation group demonstrated lower scores than the control group ($P < 0.05$). The observation group exhibited a higher total effective rate compared to the control group ($P < 0.05$). Reductions in thyroid nodule sizes and serum thyrotropin (TSH) levels were observed in both groups after treatment ($P < 0.05$), with the observation group displaying lower values than the control group ($P < 0.05$). Additionally, serum free tri-iodothyronine (FT₃) and free tetra-iodothyronine (FT₄) levels increased in both groups ($P < 0.05$), with the observation group showing higher levels ($P < 0.05$). Post-treatment, serum TGF- β 1 levels increased in both groups ($P < 0.05$), with the observation group exhibiting higher levels ($P < 0.05$). Moreover, serum IGF-1 levels decreased in both groups ($P < 0.05$), and the observation group displayed lower levels than the control group ($P < 0.05$). Importantly, there was no statistically significant difference in the incidence rate of adverse reactions between the two groups ($P > 0.05$). Pingxia capsule used in the treatment of patients with thyroid nodules can reduce clinical symptoms, improve the therapeutic effect, and at the same time can promote the recovery of thyroid function and regulate the serum TGF- β 1, IGF-1 levels.

1. Introduction

Thyroid nodules represent a prevalent thyroid condition in clinical practice, with a high incidence rate of 20.43% in China, particularly affecting women, the elderly, those with iodine deficiency, and individuals exposed to radiation. Among these nodules, approximately 5% to 10% are identified as malignant, posing significant health risks to patients [1-2].

Thyroid nodules are caused by the disruption of the homeostasis between proliferation and apoptosis of thyroid cells and abnormal proliferation. Surgical resection and medication are mostly used to treat thyroid nodules in clinical practice, but surgical resection is prone to damage normal thyroid glands, and sodiumlevothyroxine is a commonly used medication for the treatment of thyroid nodules, which is able to alleviate the clinical symptoms and reduce the size of the thyroid gland, but the overall efficacy of simple western medication is less than satisfactory [3-4].

In the realm of Chinese medicine, thyroid nodules are categorized as "gall tumors" based on their symptoms and signs. The underlying pathogenesis involves phlegm condensation, Qi stagnation, and blood stasis. The majority of cases are diagnosed with Qi stagnation and blood stasis. Clinical intervention aligns with the principles of activating blood circulation, eliminating blood stasis, regulating Qi, dredging the liver, and dispersing nodules while addressing phlegm [5]. Pingxiao capsule, a traditional Chinese medicine compound preparation, combines Xianhecao, alum, yujin, nitrate, strychnine powder, and gluten-fried Citrus aurantium, exhibiting functions such as dispersing knots, removing blood stasis, regulating Qi, alleviating depression, and resolving phlegm, effectively addressing thyroid nodules [6]. Animal experiments showed that Pingxiao capsule could inhibit thyroid enlargement in rats with nodular goiter and induce apoptosis of thyroid tumour cells. However, the effect of Pingxiao capsule on the treatment of thyroid nodules and its effect on serum TGF- β 1 and IGF-1 levels are still unclear, so this study

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selected 86 patients with thyroid nodules admitted to the First Hospital of Heilongjiang University of Traditional Chinese Medicine to investigate the specific therapeutic effect of Pingxiao capsule and its effect on serum TGF- β 1 and IGF-1 levels.

1.1. Clinical date

From June 2022 to June 2023, the First Hospital Affiliated to Heilongjiang University of Traditional Chinese Medicine admitted eighty-six patients with thyroid nodules. These patients were randomly assigned to either the observation group or the control group using a random number table. The basic demographic data of both groups were comparable, as indicated in Table 1 ($P > 0.05$). Approval for this study was obtained from the Ethics Committee of the hospital.

Inclusion criteria: all met the diagnostic criteria of thyroid nodules [7], and all were diagnosed by puncture sampling; Chinese medicine diagnosis of qi stagnation and blood stasis [8]; age 25-66 years old; informed consent.

Exclusion criteria: comorbidity with other thyroid disorders; haematological disorders; immune system disorders; malignant tumours; abnormalities of cardiac, hepatic and renal functions; women during lactation or pregnancy.

Table 1 Comparison of basic information between two groups

Group	n	Gender (Example)	Age (Year)	Disease duration (Month)
		Male/Female		
Observation group	43	15/28	44.58 \pm 7.02	8.79 \pm 2.15
Control group	43	13/30	45.81 \pm 7.38	8.95 \pm 2.32
t/χ^2	-	0.212	0.792	0.332
P	-	0.645	0.431	0.741

1.2. Method

All three groups lived with iodine-containing foods such as non-iodised salt contraindicated seafood. The control group was treated with sodiumlevothyroxine (China National Drug Standard J20160065, Merckel Pharmaceutical Co., Ltd.), 25 μ g/time, 1 time/d, orally, and the observation group was treated with pingxiao capsules (China National Drug Standard Z61021330, Xi'an Zhengda Pharmaceutical Co., Ltd.) combined with sodiumlevothyroxine, and sodiumlevothyroxine usage was the same as that of the control group, and pingxiao capsules were 4-8 capsules (adjusted according to the condition), 1 time/d, orally. The 2 groups of patients continued to use the drug for 3 months.

1.3. Observation indications

1) Evaluations of traditional Chinese medicine (TCM) symptom scores were conducted both prior to and post-treatment. These assessments focused on symptoms such as palpable nodules in the neck, sensations of laryngeal obstruction, emotional depression, shantaixi, and symptoms of dizziness. Each symptom was assigned a severity rating of 0, 2, 4, or 6, with higher scores corresponding to increased symptom severity [9].

2) The clinical effectiveness was evaluated three months into the treatment. Notably, a significant effect was defined by the disappearance of traditional Chinese medicine (TCM) symptoms, accompanied by a reduction of over 70% in symptom scores. Cases categorized as effective exhibited a substantial decrease in TCM symptoms, with scores reduced between 30% and 70%. Ineffective outcomes were identified when TCM symptom scores experienced a reduction of less than 30%. The overall statistical effective rate was determined based on these criteria [10].

3) Prior to and post-treatment, ultrasonic diagnostic instruments (Beckman, USA) were employed to measure both the size of thyroid nodules and thyroid function indexes. The determination of thyroid nodule size was conducted through ultrasonic assessments. Simultaneously, electrochemiluminescence immunoassay was utilized to assess the levels of serum thyrotropin (TSH), free tri-iodothyronine (FT₃), and free tetra-iodothyronine (FT₄) before and after the treatment.

4) Serum TGF- β 1 and IGF-1 levels were measured by double antibody ELISA before and after treatment, respectively (The kits were purchased from Shanghai Novartis Biotechnology Co).

1.4. Statistical analysis

Statistical analysis was performed using SPSS 22.0. Measurement data, following a normal distribution, were presented as " $\bar{x} \pm s$ " and analyzed using the t-test. Count data were represented as percentages (%) and analyzed using the χ^2 test. A p-value < 0.05 was considered indicative of a statistically significant difference.

2. Result

2.1. Comparison of Traditional Chinese Medicine Symptom Scores between Two Groups of Patients

After treatment, the scores of patients in the 2 groups were reduced in neck touching nodules, feeling of obstruction between the larynx, emotional depression, good tai chi, dizziness and dizziness ($P < 0.05$), and the observation group was lower than the control group ($P < 0.05$), as shown in Table 2.

Table 2 Comparison of Traditional Chinese Medicine Symptom Scores between Two Groups of Patients.

Group	n	Neck palpable nodules (points)		Throat obstruction (points)		Emotional depression (points)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	43	3.51±0.87	1.21±0.41 ^a	3.09±0.77	0.93±0.33 ^a	2.74±0.72	0.88±0.32 ^a
Control group	43	3.37±0.86	1.58±0.49 ^a	3.33±0.83	1.26±0.44 ^a	2.60±0.69	1.05±0.30 ^a
<i>t</i>	-	0.750	3.798	1.390	3.934	0.921	2.541
<i>P</i>	-	0.455	<0.001	0.168	<0.001	0.360	0.013

Continued

Group	n	Shantaixi (points)		Dizziness and dizziness (points)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	43	1.93±0.50	0.81±0.39 ^a	1.84±0.43	0.72±0.45 ^a
Control group	43	1.81±0.44	0.98±0.34 ^a	1.88±0.44	0.93±0.45 ^a
<i>t</i>	-	1.181	2.155	0.426	2.164
<i>P</i>	-	0.241	0.034	0.671	0.033

Note: Compared with before treatment, ^a*P*<0.05.

2.2. Comparison of clinical efficacy between two groups

Table 3 illustrates that the observation group achieved a significantly higher total effective rate than the control group (*P*<0.05).

Table 3 Comparison of clinical efficacy between two groups of patients (n/%)

Group	n	significant	effectiveness	ineffective	total effectiveness
Observation group	43	26 (60.47)	14 (32.56)	3 (6.98)	40 (93.02)
Control group	43	15 (34.88)	18 (41.86)	10 (23.26)	33 (76.74)
χ^2	-				4.440
<i>P</i>	-				0.035

2.3. Comparison of thyroid nodule size and thyroid function indicators between two groups of patients

After treatment, the size of thyroid nodules and serum TSH levels were reduced in both groups (*P*<0.05) and

lower in the observation group (*P*<0.05), and serum FT₃ and FT₄ levels were increased in both groups (*P*<0.05) and higher in the observation group (*P*<0.05), see Table 4.

Table 4 Comparison of thyroid nodule size and thyroid function indicators between two groups of patients

Group	n	Maximum diameter of thyroid nodules (mm)		TSH (mIU/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	43	10.58±1.85	7.30±1.25 ^a	2.75±0.63	1.18±0.42 ^a
Control group	43	11.02±1.91	8.67±1.57 ^a	2.81±0.68	1.49±0.51 ^a
<i>t</i>	-	1.085	4.477	0.424	3.077
<i>P</i>	-	0.281	<0.001	0.672	0.003

Continued

Group	n	FT ₃ (nmol/L)		FT ₄ (nmol/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	43	4.37±0.76	4.79±0.90 ^a	14.08±2.24	16.52±2.66 ^a
Control group	43	4.55±0.80	5.22±0.98 ^a	14.63±2.44	18.95±2.80 ^a
<i>t</i>	-	1.070	2.119	1.089	4.126
<i>P</i>	-	0.288	0.037	0.279	<0.001

Note: Compared to before treatment, ^a*P*<0.05

2.4. Comparison of serum TGF between two groups of patients-β1. IGF-1 level

After treatment, serum TGF-β1 levels were increased in

both groups ($P < 0.05$) and higher in the observation group ($P < 0.05$), and serum IGF-1 levels were decreased in both groups ($P < 0.05$) and lower in the observation group ($P < 0.05$), as shown in Table 5.

Table 5 Comparison of serum TGF between two groups of patients- β1. IGF-1 level

Group	n	TGF-β1 (pg/mL)		IGF-1 (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	43	198.53±26.12	231.94±32.89 ^a	42.57±7.55	36.79±6.00 ^a
Control group	43	205.48±28.52	268.62±35.43 ^a	41.83±7.16	32.55±6.63 ^a
<i>t</i>	-	1.178	4.975	0.466	3.109
<i>P</i>	-	0.242	<0.001	0.642	0.003

Note: Compared to before treatment, ^a $P < 0.05$

2.5. Comparison of adverse reactions between two groups of patients

There was one case of nausea and one case of diarrhoea in the observation group, and one case of dry mouth in the control group, and the difference in the incidence of adverse reactions between the two groups was not statistically significant ($P > 0.05$).

3. Discussion

Belonging to the spectrum of endocrine system diseases, thyroid nodules manifest as single or multiple nodular masses within the thyroid gland. Conditions such as focal thyroiditis, parathyroid cysts, cystic lesions of the thyroid, and thyroid cancer can present as thyroid nodules. The etiology of thyroid nodules is intricate, and despite ongoing research, a comprehensive understanding of its pathogenesis remains elusive [11].

Thyroid nodules in the motherland medicine are called "gall tumour", "Gall Tumour Treatment" pointed out that the disease and emotional upset, qi stagnation related to emotional upset caused by liver stagnation, phlegm and turbidity [12]. As delineated in the "Surgery Zhengzong-Gall Tumour Treatise," the primary pathology of this ailment involves the accumulation of gas, stasis of blood, and condensation of phlegm [13]. Chinese medicine research posits that the underlying pathology of gall tumor is associated with liver qi stagnation, with phlegm and blood stasis identified as key pathological factors. The liver's inability to disperse stagnant qi over time results in its transformation into fire. Simultaneously, irregularities in the spleen's transportation and transformation of phlegm contribute to the mutual condensation of stagnant qi and phlegm, giving rise to gall formations in the anterior neck region [14]. Therefore, the treatment should resolve phlegm and eliminate galls, and move qi to relieve depression as the treatment principle. Pingxiao capsule, a traditional Chinese medicine (TCM) prescription included in the Chinese Pharmacopoeia (2010 edition), is renowned for its efficacy in promoting blood circulation, reducing swelling, boosting immunity, and alleviating pain. The components of Pingxiao capsule include Yujin (Radix Curcumae Wenyujin), Xianhecao (Herba Agrimoniae),

Wulingzhi (Faeces Trogopteri), Baifan (Alumen), Xiaoshi (Nitrum), Ganqi (Resina Toxicodendri), Fuchaozhiqiao (Stir-frying Fructus Aurantii Submaturus in Bran), and Maqianzi (Semen Strychni). The diverse herbal composition of Pingxiao capsule contributes to its multifaceted therapeutic effects. This prescription has a solid foundation in traditional Chinese medicine and has been acknowledged for its role in clinical applications [15]. Pingxiao capsule utilizes Mangxiao and Baifan to address blood stasis, while Zhiqiao and Yujin work on promoting Qi flow and regulating its widening. Ganqi eliminates accumulation and breaks blood stasis. Xianhecao and Wulingzhi astringe, stop bleeding, and promote blood circulation. Together, these components aim to soothe the liver, relieve stagnation, disperse knots, reduce swelling, and enhance the body's resilience. Clinical studies suggest significant anti-tumor effects, making Pingxiao capsule a valuable option for various malignant tumors [16].

4. Conclusion

The study results reveal that post-treatment, patients in the observation group exhibited lower Chinese medicine symptom scores compared to the control group. Additionally, the overall effective rate in the observation group surpassed that in the control group. These findings suggest that the use of Pingfan capsule in treating thyroid nodules contributes to alleviating clinical symptoms and enhancing therapeutic outcomes. Comprising various Chinese medicinal ingredients, Pingxiao capsule incorporates tulip gold for blood circulation and stasis removal, cactus for heart nourishment, alum for phlegm elimination and heat resolution, saltpeter for breaking up accumulation, strychnine for knot dispersion and swelling reduction, and stir-fried Citrus sinensis for spleen strengthening and phlegm elimination. The holistic formula operates to eliminate swellings, disperse knots, activate blood circulation, remove blood stasis, and facilitate qi movement, thereby relieving depression [17]. Recent pharmacological investigations have identified flavonoids and flavonoid glycosides as the primary constituents of tulip gold. These compounds exhibit various pharmacological effects, including anti-inflammatory, antioxidant, and immunomodulatory

properties. Specifically, flavonoids in mustard flavonoid can impede the activation of the inflammatory signaling pathway, reduce the release of local inflammatory factors, and stimulate immune cell proliferation, thereby enhancing overall immune function [18]. Strychnine powder, containing a diverse array of alkaloids, demonstrates robust analgesic and expectorant effects [19]. Alum, classified as mineral herbal medicine, primarily contains alkaline aluminum potassium sulfate. This component facilitates the reduction of tissue edema and exerts a broad-spectrum antimicrobial effect [20]. Following the treatment in this study, patients in the observation group exhibited a reduction in thyroid nodule size and lower serum TSH levels compared to the control group. Additionally, serum FT₃ and FT₄ levels were higher in the observation group. Clinical studies underscore the role of TSH in promoting the proliferation of thyroid cells, with its elevated levels being a crucial factor in thyroid nodules. FT₃ and FT₄ serve as vital indicators for assessing thyroid gland function, commonly employed in the diagnosis of thyroid dysfunction and monitoring thyroid disease conditions [21-22]. In a study conducted by Wang Chan et al [23], 100 patients diagnosed with benign thyroid nodules through fine-needle aspiration cytological pathology underwent randomization. The participants were divided into groups, with the treatment group receiving Pingxiao capsule and the observation group remaining untreated. Additionally, a control group was included. Notably, findings revealed that, over a span of 6 months, the treatment group experienced a reduction in thyroid nodule diameter and regulation of thyroid-related hormones following the administration of Pingxiao capsule. This implies the potential effectiveness of Pingxiao capsule in treating benign thyroid nodules. In a separate study by Zhiqian Liu [24], 50 patients with nodular goiter were selected. They were evenly divided into a treatment group (25 individuals treated with Pingbao capsule combined with sodiumlevothyroxine) and a control group (25 individuals treated with sodiumlevothyroxine alone). The study results demonstrated a significantly greater reduction in the internal diameter of thyroid nodules in the treatment group compared to the control group. This suggests that combining Pinnacle Capsules with sodiumlevothyroxine treatment may yield a more pronounced effect for patients with nodular goiter. A study by Si Haiyan et al [25] involved 300 patients with nodular goiter randomly assigned to either a control group or a treatment group. The treatment group received a combination of sodiumlevothyroxine and pingxiao capsule, while the control group received sodiumlevothyroxine alone. The treatment period spanned 3 months, during which clinical efficacy, nodule diameter, as well as serum thyroid hormone and serum factor levels were observed. The results indicated a total effective rate of 94.00% in the treatment group, significantly surpassing that of the control group (87.33%). Following the treatment, the treatment group exhibited a significant reduction in nodule diameter, accompanied by a more pronounced decrease in thyroid-stimulating hormone (TSH) levels. This implies that the combined application of Pingxiao

capsule and sodiumlevothyroxine tablets effectively treats nodular goiter, promoting nodule size reduction and hormone level regulation. These outcomes align with the findings of our study.

In the present research, post-treatment, the observation group displayed a higher serum TGF- β 1 level and a lower serum IGF-1 level compared to the control group. This suggests that Pingxiao capsule has the potential to modulate serum TGF- β 1 and IGF-1 levels. TGF- β 1 and IGF-1 are implicated in thyroid cell proliferation and apoptosis. Specifically, TGF- β 1 can stimulate fibroblast and epithelial cell mitosis, accelerating nodule growth and promoting thyroid nodule progression. Meanwhile, IGF-1 induces thyroid hormones and fosters the proliferation of thyroid epithelial cells [26-27]. The diverse Chinese medicinal ingredients in Pingxiao capsule exert a multi-target, multi-pathway pharmacological effect. When combined with sodium sodiumlevothyroxine, a synergistic effect is achieved, enhancing thyroid gland physiological function and regulating serum TGF- β 1 and IGF-1 levels. Moreover, Pingxiao capsule demonstrate high safety across various Chinese medicine components, with patients experiencing no noticeable adverse drug reactions when following prescribed instructions, ensuring safety and reliability.

In conclusion, Pingxiao capsule used in the treatment of patients with thyroid nodules can reduce clinical symptoms, improve the therapeutic effect, and at the same time can promote the recovery of thyroid function and regulate the serum TGF- β 1, IGF-1 levels. However, only 86 patients with thyroid nodules were included in this study, which is a small sample size and reduces the statistical efficacy. It is still necessary to increase a large number of patients with thyroid nodules, carry out a multicentre study to confirm the specific therapeutic efficacy of Pingxiao capsule, and further investigate the specific mechanism of Pingxiao capsule in the treatment of thyroid nodules through basic experiments.

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