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The Therapeutic Value of Valacyclovir Combined with Thymosin Therapy for Esophageal Cancer Complicated with Postherpetic Neuralgia

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Abstract: *Objective:* To evaluate the therapeutic effect of valacyclovir combined with thymosin therapy on patients with esophageal cancer complicated by postherpetic neuralgia (PHN). *Methods:* A total of 76 patients with esophageal cancer complicated by PHN who were admitted for treatment from January 2023 to January 2025 were selected and evenly divided into two groups using a random number table. The observation group received valacyclovir combined with thymosin therapy, while the reference group received valacyclovir monotherapy. The overall response rate, pain scores, serological indicators, and T-lymphocyte subsets were compared between the two groups. *Results:* The overall response rate in the observation group was higher than that in the reference group ($P < 0.05$). After 10 days of treatment, the pain scores in the observation group were lower than those in the reference group, and the serological indicators and T-lymphocyte subsets were superior to those in the reference group ($P < 0.05$). *Conclusion:* Valacyclovir combined with thymosin therapy can improve the clinical efficacy in patients with esophageal cancer complicated by PHN, alleviate pain symptoms, regulate serological indicators, and protect the immune function of patients.

Keywords: Valacyclovir; Thymosin therapy; Esophageal cancer; Postherpetic neuralgia

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1. Introduction

The symptoms of esophageal cancer include dysphagia, ascites, stabbing pain behind the sternum, and weight loss, among others, with squamous cell carcinoma being the predominant type. Surgical intervention combined with radiotherapy and chemotherapy is required to prolong the patient's survival. However, these treatment measures can reduce the patient's immunity, leading to immunosuppressive manifestations due to physiological stress, thereby increasing the risk of viral infections, such as herpes zoster and other viral diseases [1]. Postherpetic neuralgia (PHN) is a common sequelae of herpes zoster, characterized by neuropathic pain persisting for one month or longer after the complete resolution of herpetic skin lesions. It is marked by persistent pain and can coincide with cancer-related pain from esophageal cancer, significantly exacerbating the

patient's physiological discomfort and consequently affecting their treatment compliance. Oral medication is the primary treatment approach for this comorbidity, utilizing antiviral drugs such as valacyclovir and thymosin therapy to alleviate pain symptoms. This approach leverages the synergistic mechanisms between different drugs to exert multi-target therapeutic effects while protecting the patient's immune system and promoting disease recovery. Based on this, the present study selected 76 patients with esophageal cancer complicated by PHN to evaluate the therapeutic effects of valacyclovir combined with thymosin therapy.

2. Materials and methods

2.1. General information

A total of 76 patients with esophageal cancer complicated by PHN who were admitted for treatment between January 2023 and January 2025 were selected and evenly divided into two groups using a random number table. The observation group consisted of 38 patients, including 21 males and 17 females, aged between 24 and 81 years, with a mean age of 44.58 ± 4.91 years. The duration of esophageal cancer ranged from 0.5 to 2 years, with a mean of 1.09 ± 0.49 years, while the duration of PHN ranged from 5 to 10 weeks, with a mean of 7.11 ± 1.53 weeks. The reference group also included 38 patients, with 23 males and 15 females, aged between 22 and 80 years, with a mean age of 44.71 ± 4.85 years. The duration of esophageal cancer ranged from 0.6 to 2 years, with a mean of 1.12 ± 0.46 years, while the duration of PHN ranged from 4 to 11 weeks, with a mean of 7.19 ± 1.46 weeks. There were no significant differences in the data between the two groups ($P > 0.05$).

Inclusion criteria: Diagnosis of esophageal cancer based on esophagoscopy and biopsy pathology; meeting the PHN diagnostic criteria established in the *Chinese Expert Consensus on the Diagnosis and Treatment of Postherpetic Neuralgia* [2]; a Visual Analog Scale (VAS) score of ≥6 points upon admission; stable vital signs; normal communication and cognitive abilities; and informed consent to participate in the study. Exclusion criteria: Use of immunomodulators or antiviral drugs within the past 2 weeks; allergy to the study drugs; abnormal heart, liver, or kidney function; distant metastasis of esophageal cancer; coagulopathy; presence of psychiatric disorders; and withdrawal from the study midway.

2.2. Methods

The reference group received monotherapy with valacyclovir: oral administration of valacyclovir hydrochloride tablets (Kunming Yuanrui Pharmaceutical Co., Ltd., National Medical Products Administration Approval Number H20103021, specification: 0.15 g; tablet form) at a dose of 0.15 g each time, twice daily, for 10 consecutive days. The observation group received a combination therapy of valacyclovir and thymopeptides, with the valacyclovir treatment method being the same as above. Thymopeptides for injection (Furen Pharmaceutical Group Co., Ltd., National Medical Products Administration Approval Number H20074234, specification: 10 mg; injection form) were administered intravenously at a dose of 30 mg each time, once daily, for 10 consecutive days.

2.3. Observation indicators

(1) Pain score: The McGill Pain Questionnaire (MPQ) was used, which includes the Present Pain Intensity (PPI, ranging from 0 to 12 points), Sensory Pain Rating Index (PRI, ranging from 0 to 33 points), and Visual Analog Scale (VAS, ranging from 0 to 10 points). Pain severity was positively correlated with the score.

(2) Serological indicators: Before treatment and after 10 days of treatment, venous blood (10 ml) was collected in a fasting state, centrifuged for 10 minutes at a speed of 3,000 r/min and a radius of 10 cm, and the serum was extracted. Enzyme-linked immunosorbent assay was used to evaluate the levels of serum substance P (SP), neuropeptide Y (NPY), and β-endorphin (β-EP).

(3) T-lymphocyte subsets: Fasting venous blood (5 ml) was collected at the same time points, and density gradient centrifugation was used for cell processing. Flow cytometry was used to evaluate the levels of $CD3^+$, $CD4^+$, and $CD8^+$.

2.4. Efficacy evaluation criteria

The overall response rate was evaluated using the efficacy index (difference in VAS scores before and after treatment ÷ VAS score before treatment × 100%). A cure was defined as an efficacy index of 100%; a significant response as an efficacy index between 60 and 99%; a preliminary response as an efficacy index between 30 and 59%; and no response as an efficacy index of <30%.

2.5. Statistical analysis

Data were processed using SPSS 28.0 software. Count data were expressed as [*n* (%)] and compared using the chi-square test. Measurement data were tested for normal distribution using the Kolmogorov-Smirnov (K-S) test and expressed as mean ± standard deviation (SD). Independent samples *t*-tests were used for comparisons between groups, and paired *t*-tests were used for comparisons within groups. A statistically significant difference was defined as $P < 0.05$.

3. Results

3.1. Comparison of overall efficacy rates

Between the two groups, the overall efficacy rate in the observation group was higher than that in the reference group ($P < 0.05$). See **Table 1**.

Table 1. Comparison of overall efficacy rates between the two groups [*n* (%)]

Group	Number of cases	Disease cure	Significant efficacy	Initial efficacy	No efficacy	Total effective rate
Observation group	38	17	10	9	2	94.74% (36/38)
Reference group	38	13	10	7	8	78.95% (30/38)
χ^2						4.146
P						0.042

3.2. Comparison of pain scores

Before treatment, there was no significant difference in pain scores between the two groups ($P > 0.05$). After 10 days of treatment, the pain score in the observation group was lower than that in the reference group ($P < 0.05$). See **Table 2**.

Table 2. Comparison of pain scores between the two groups (mean ± SD, points)

Group	Number of cases	PPI		PRI		VAS	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	38	7.16 ± 1.53	4.02 ± 1.06	18.95 ± 2.34	8.11 ± 1.59	6.75 ± 1.48	3.11 ± 0.68
Reference group	38	7.19 ± 1.55	4.98 ± 1.09	19.02 ± 2.31	10.73 ± 1.65	6.71 ± 1.46	3.92 ± 0.73
t		0.085	3.892	0.131	7.048	0.119	5.005
P		0.933	0.000	0.896	0.000	0.906	0.000

3.3. Comparison of serological indicators

Before treatment, there were no significant differences in serological indicators between the two groups ($P > 0.05$). After 10 days of treatment, the levels of SP and NPY in the observation group were lower than those in the reference group, while the level of β-EP was higher than that in the reference group ($P < 0.05$). See **Table 3**.

Table 3. Comparison of serological indicators between the two groups (mean ± SD, ng/L)

Group	Number of cases	SP		NPY		β-EP	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	38	172.65 ± 25.41	105.16 ± 12.74	301.59 ± 28.76	237.65 ± 15.84	16.54 ± 2.35	25.64 ± 3.11
Reference group	38	171.19 ± 25.33	123.65 ± 12.81	301.44 ± 29.02	258.44 ± 16.49	16.57 ± 2.38	21.05 ± 3.06
t		0.251	6.309	0.023	5.605	0.055	6.485
P		0.803	0.000	0.982	0.000	0.956	0.000

3.4. Comparison of T-lymphocyte subsets

Before treatment, there were no significant differences in T-lymphocyte subsets between the two groups ($P > 0.05$). After 10 days of treatment, the levels of $CD3^+$ and $CD4^+$ in the observation group were higher than those in the reference group, while the level of $CD8^+$ was lower than that in the reference group ($P < 0.05$). See **Table 4**.

Table 4. Comparison of T-lymphocyte subsets between the two groups (mean ± SD, %)

Group	Number of cases	$CD3^+$		$CD4^+$		$CD8^+$	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	38	55.46 ± 5.19	67.18 ± 7.20	29.44 ± 3.51	40.21 ± 4.85	32.38 ± 3.64	25.77 ± 2.58
Reference group	38	55.50 ± 5.23	61.49 ± 7.15	29.48 ± 3.56	34.91 ± 4.77	32.41 ± 3.69	28.43 ± 2.60
t		0.033	3.457	0.049	4.803	0.036	4.477
P		0.973	0.001	0.961	0.000	0.972	0.000

4. Discussion

Esophageal cancer is a highly prevalent type of malignant tumor that significantly depletes the body's nutritional reserves, weakens cellular immune function, and activates latent viruses within the body, leading to complications such as herpes zoster. Furthermore, treatments such as esophageal cancer resection and postoperative radiotherapy and chemotherapy can adversely affect the patient's immune system, reducing their disease resistance and thereby increasing the risk of herpes zoster [2]. While systemic treatment can significantly alleviate herpes zoster, it often results in persistent neuropathic pain after skin lesion healing, with a prolonged duration that is detrimental to disease prognosis.

Valacyclovir is a commonly used medication for treating patients with esophageal cancer complicated by PHN. It exhibits potent antiviral activity against the herpes zoster virus and serves as a prodrug of acyclovir, offering 2 to 4 times greater efficacy than acyclovir without inducing toxicity in human cells, ensuring high treatment safety. After oral administration, valacyclovir accumulates in large quantities within infected cells, forming acyclovir triphosphate, a biologically active substance that competitively binds to DNA polymerase, thereby blocking viral replication and inhibiting proliferation [3,4]. Thymopeptides, extracted from calf thymus, are rich in active peptides and possess antiviral protein gene activation properties within target cells, inhibiting viral proliferation. Additionally, thymopeptides strongly stimulate lymphocytes or mononuclear macrophages, regulating the immune system and providing immune protection.

The results showed that the overall response rate in the observation group was higher than that in the reference group, and the pain score after 10 days of treatment was lower in the observation group ($P < 0.05$). The reasons are as follows: Valacyclovir demonstrates excellent antiviral effects, with good water solubility, rapid absorption after oral administration, and high bioavailability, effectively clearing the varicella-zoster virus and improving treatment efficacy [5,6]. Thymopeptides, as immunomodulators, enhance mitogen activity after intravenous infusion, promoting peripheral lymphocyte maturation, accelerating the secretion of T-cell lymphokines by various antigens, and increasing lymphokine receptor content, effectively resisting varicella-zoster virus invasion and controlling the disease.

After 10 days of treatment, the serological indicators in the observation group were superior to those in the reference group ($P < 0.05$). Among them, SP participates in the inflammatory response process, activates immune cell agents, and affects pain signal transmission [7]. NPY reflects the degree of nerve injury, with increased synthesis and elevated levels due to sensory neuron and sympathetic nerve proliferation. β-EP binds to endogenous opioid receptors and opioid peptides, producing a sense of pleasure and effectively exerting analgesic mechanisms, showing a negative correlation with the patient's pain level [8]. Valacyclovir treatment can alleviate nerve injury, inhibit the release of pain substances, and suppress the pathological remodeling process of NPY, thereby blocking pain signal transmission and improving pain-related serological indicators. Thymopeptides reduce the overall release of pro-inflammatory factors, continuously exerting anti-inflammatory mechanisms, thereby assisting in downregulating SP and NPY levels [9,10]. Additionally, thymopeptides activate the body's analgesic system, increasing β-EP release from the pituitary gland and immune cells, thereby providing long-lasting analgesia.

After 10 days of treatment, the T-lymphocyte subsets in the observation group were superior to those in the reference group ($P < 0.05$). T-lymphocyte subsets such as $CD3^+$ and $CD4^+$ objectively reflect the patient's immune function. The thymus contains α, γ, and β hormones that promote T-cell differentiation and accelerate their maturation. Thymosin α1, the most abundant active component in thymopeptides, contains 28 amino

acids and exhibits strong biological activity, inducing T-cell differentiation, increasing cytokine synthesis, and enhancing B-cell antibody response capabilities, thereby regulating the immune system and enhancing disease resistance. Additionally, thymopeptides increase the secretion of inflammatory factors such as interleukin-2, indirectly enhancing B-cell activity, thereby improving immune system function and the levels of the above indicators [11].

5. Conclusion

In conclusion, combined treatment with valacyclovir and thymopeptides for patients with esophageal cancer complicated by PHN yields favorable results, reducing pain levels, regulating pain-related serological indicators, improving T-lymphocyte subset levels, protecting the patient's immune function, and maximizing physiological comfort. This combination therapy demonstrates significant advantages.

Disclosure statement

The author declares no conflict of interest.

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