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Original Article

Ki-67, CyclinD1 and P53 as expected new targets for pterygium treatment in clinical practice

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Abstract: Objective: To investigate the expression and study the clinical correlation of Ki-67, cyclin D1 (CyclinD1) and p53 in pterygium. Methods: Forty-six patients with pterygium admitted to our hospital were selected as study subjects. Another 46 patients with concurrent physical examination were selected as the control subjects. All the patients in the study group were treated with pterygium excision and autologous conjunctival flap transplantation after diagnosis. Four mL of fasting venous blood was taken before operation (T0), 2 hours after surgery (T1), 3 days after surgery (T2), and 7 days after surgery (T3). The serum concentration of Ki-67, Cyclin D1, and p53 was detected by enzyme-linked immunosorbent assay (ELISA). The serum concentrations of Ki-67, CyclinD1 and p53 in the two groups were observed. The changes of Ki-67, CyclinD1 and P53 during the treatment and the correlation of treatment time in the study group were also observed. The concentration changes of Ki-67, CyclinD1 and P53 in different pathological features were observed. Results: Serum Ki-67, Cyclin D1 and p53 in the study group were higher than that in the control group (P<0.001). The concentration changes of Ki-67, CyclinD1 and P53 in the study group were statistically significant (P<0.001). The serum concentration of Ki-67, CyclinD1 and P53 in the study group was the highest at T0 (P<0.001). The value at T1 was lower than that at T0 (P<0.001). The value at T2 was lower than that at T1 (P<0.001), and the value was the lowest at T3 (P<0.001). According to the correlation coefficient of Spearman, Ki-67, CyclinD1 and p53 were negatively correlated with treatment time (r=-0.784, -0.692, -0.692, P<0.001). Among different cases of pterygium, the distance from the farthest pterygium to the scleral spur, course of disease, pterygium grade and pterygium size, there were significant differences in Ki-67, CyclinD1, and p53 concentration (P<0.001). Conclusion: The serum concentration of Ki-67, CyclinD1 and p53 in patients with pterygium was higher than that in normal subjects. It suggested that Ki-67, CyclinD1 and P53 are expected to be new targets for pterygium treatment in future clinical practice.

Keywords: Ki-67, CyclinD1, P53, pterygium

Introduction

Pterygium is a very common high-risk disease in ophthalmology, it is a chronic inflammatory disease caused by external stimuli [1]. At present, the pathogenesis of pterygium is not completely clear. Studies have shown that environmental factors and personal factors may induce the occurrence of pterygium [2, 3]. At present, the incidence of pterygium varies from region to region. The incidence rate in Australia is as high as 1.9%, while it is only 0.05% in Europe [4]. In recent years, it has been found that the prevalence rate of pterygium is increasing over the years. The challenges of treatment are becoming increasingly severe in clinical practice [5]. Pterygium can cause irregular astigmatism and pupil obstruction due to the growth of the corneal facet. Patient's vision will decrease and blur, which has a great impact on the daily life of the patient [6]. At present, the main treatment for pterygium is surgery (or combined tissue transplantation). However, during the operation, it may cause damage to the corneal epithelium, and increase the recurrence and infection risk of pterygium patients after surgery [7]. Data show that the recurrence rate of pterygium patients after resection can reach 20% to 60% [8]. Therefore, researchers are working hard to find a new method to diagnose and treat pterygium. With the deepening of research in recent years, more and more scholars have

proposed that the treatment objective should focus on the molecular pathology of pterygium [9, 10].

Ki-67 is a non-nuclear protein. It has been shown to be closely related to the proliferative capacity of cells. It is often located in the nucleus and has a short half-life. It is often used to evaluate the proliferative state of cells [11]. Previous studies have confirmed that Ki-67 can be used as a marker of breast cancer proliferation [12]. CyclinD1 is an important regulatory protein of cell cycle. Excessive CyclinD1 can accelerate cell cycle progression and promote cell dysplasia [13]. Lange et al. [14] showed that overexpression of CyclinD1 in neural stem cells can promote the formation and expansion of basal progenitor cells. P53 is one of the most commonly damaged genes in oxidative stress injury, and it also has strong regulatory ability in cell proliferation [15]. Wang et al. [16] believed that cytoskeletal regulation can results in increased tumor survival and drug resistance by attenuating p53-dependent apoptosis. At present, studies on Ki-67, CyclinD1, and p53 are all closely related to the biological behavior of cells; pterygium is considered as a proliferative disease, and cell proliferation and apoptosis are the key factors in inducing disease [17]. Therefore, we suspect that Ki-67, CyclinD1, and p53 may closely regulate the occurrence and development of pterygium. There are still few studies on Ki-67, CyclinD1 and P53 in pterygium, and it is still unknown to understand the relationship between them. Therefore, this study provides a new reference and guidance for pterygium diagnosis and treatment by studying the relationship between Ki-67, CyclinD1, P53 and pterygium.

Materials and methods

From Feb 2017 to Feb 2019, 46 patients with pterygium admitted to our hospital were randomly selected as study subjects. There were 28 males and 18 females. The age was 34-68 years, with an average age of (48.2±11.5) years. There were 16 cases of grade I pterygium, 24 cases of grade II pterygium, and 6 cases of grade III pterygium (grade I pterygium: atrophic, the episcleral blood vessel under the pterygium was unobstructed and clearly distinguished; Grade II pterygium: fleshy, the episcleral blood vessel was completely blocked; Grade III pterygium: all pterygium apart from Grade I or Grade III, see [18]). Another 46 patients with concurrent physical examination were selected as the control subjects. There were 30 males and 16 females, aged 32-70 years, with a mean value of (49.1±12.1) years. This experiment has been approved by the Ethics Committee of our hospital, and all the above subjects have signed an informed consent.

Inclusion and exclusion criteria

Inclusion criteria: patients aging from 18 to 75 years old; patients with clinical manifestations of pterygium (foreign body sensation, photophobia, itching, eye pain, dry eyes, a sense of heaviness, blurred vision, discomfort, eye discharge, tears, etc.) [19] and with the size of the primary pterygium ≥2 mm; patients treated with pterygium excision and autologous conjunctival flap transplantation after diagnosis; patients willing to cooperate with the work arrangements of our medical staff.

Exclusion criteria: patients with following conditions, bilateral pterygium; refractive error; ocular pathological changes; history of ophthalmic surgery or trauma; stenotic atresia angle; high intraocular pressure; patients with history of physiological or glaucomatous optic nerve disease; patients with SC cupping; family history of glaucoma long-term wearing of contact lenses; eye infections; nystagmus; corneal epithelial lesions and paralytic keratitis; and combined mental illness.

Operation plan

The patients in the study group were treated by senior ophthalmologists of our hospital. Every day, levofloxacin eye drops were given 3 days before surgery (manufactured by SANTEN Pharmaceutical Co., Ltd., packed by China SANTEN Pharmaceutical Co., Ltd., GYZZ J20-150106), with 5 g/L and 4 times/d. The operation plan was as follows: 1-2 mL of 2% lidocaine was used for subconjunctival anesthesia. Blepharostat was used to separate corneal limbus and remove pterygium. Conjunctival pterygium tissue was sharply dissected. Pterygium tissue in the neck was cut off. Conjunctival pterygium tissue was removed completely. The corneal tissue of corneal surface was reversely torn apart from the neck. The residual pterygium tissue of corneal surface was scraped off with a screw cutting tool to keep the cornea smooth and flat. From the upside of temporo, the conjunctival flap of the limbal stem cells which was

equal to the size of the exposed scleral surface was taken. Subsequently, it was placed on the exposed scleral surface of the excised pterygium tissue. The four corners of the conjunctival flap were sutured with the surrounding conjunctiva by a 10-0 nylon thread. The non-corneal limbus was sutured with 1-2 needles. The knot was not buried. Blepharostat was removed. Antibiotic eye ointment was used in the conjunctival sac to prevent infection. The eye was bandaged for 1 day. After removing the gauze, levofloxacin eye drops (5 g/L) was used, 4 times/d. The ocular surface was improved by HYCOSAN 4 times/day. Prednisolone acetate anti-inflammatory was used 4 times/day. The dose should be gradually decreased for a total of 4 weeks. The conjunctival suture was removed in 7 to 10 days. Four mL of fasting venous blood was taken before operation (T0), 2 hours after surgery (T1), 3 days after surgery (T2), and 7 days after surgery (T3). It was placed at room temperature for 30 min, and then centrifuged for 10 min (4000 rpm/min). The upper serum was obtained and was stored at -80°C to be measured.

Outcome measures

The serum concentration of Ki-67, CyclinD1 and P53 in the two groups was detected by enzyme-linked immunosorbent assay (ELISA). The Ki-67 kit, CSB-E16294h was purchased from Xiamen Yanke Biotechnology Co., Ltd. The CyclinD1, QC14015-A kit was purchased from Shanghai Qincheng Biotechnology Co., Ltd. The p53 kit, HD40411 was purchased from Shanghai Hengdu Biotechnology Co., Ltd. The procedure was carried out strictly conforming to the kit instructions in a sterile environment.

The changes of Ki-67, CyclinD1 and P53 during the treatment and the correlation of treatment time in the study group was measured with the concentration changes of Ki-67, CyclinD1 and P53 in different pathological features.

Statistical methods

All the experimental results were statistically calculated using SPSS 24.0 statistical software (Beijing Strong-vinda Information Technology Co., Ltd.). All the graphs were drawn using Graphpad8 (Shenzhen Tianruiqi Software Technology Co., Ltd.) software and a secondary checking calculation was conducted. The enumeration data, such as patient gender, diseased eye, etc. were expressed in the form of (rate). The chi-square test was performed between groups. The measurement data, such as Ki-67, CyclinD1, and P53 concentration were expressed in the form of (mean ± standard deviation). T test was performed between groups. One-way analysis of variance and LSD back testing were used for comparison between groups. Comparisons among multiple time points were performed by variance analysis of repeated measures and Bonferroni back testing; correlation analysis was performed by Spearman correlation coefficient analysis. $P<0.050$ was considered statistically significant.

Results

Comparison of general data

There was no remarkable difference in the age, the distance from the farthest pterygium to scleral spur, BMI, operative time, course of disease, gender, family disease history, outdoor occupation, diseased eye, marital status, education level, and smoking habits of the two groups ($P>0.050$), which indicated that the two groups of patients were comparable (**Table 1**).

Comparison of Ki-67, CyclinD1 and p53 concentration

The serum Ki-67, CyclinD1 and p53 concentration at T0 in the study group was higher than that in the control group, $P<0.001$ (**Table 2**).

Changes of Ki-67, CyclinD1, and p53 of the study group during treatment

There was statistical significance in the concentration changes of Ki-67, CyclinD1 and P53 of the study group over time ($P<0.001$). The serum concentration of Ki-67, CyclinD1 and P53 in the study group was the highest at T0 ($P<0.001$). The value at T1 and T2 was lower than that at T0 and T1, respectively ($P<0.001$), and the value was the lowest at T3 ($P<0.001$) (**Figures 1-3**).

Correlation analysis between Ki-67, CyclinD1, p53 and treatment time

According to the Spearman correlation coefficient analysis, Ki-67 was negatively correlated with treatment time ($r=-0.784$, $P<0.001$). CyclinD1 and p53 were also negatively correlated

Table 1. General data in the two groups [n (%)]

	Study group (n=46)	Control group (n=46)	t or χ^2	*P*
Age (year)	48.2±11.5	49.1±12.1	0.366	0.716
The distance from the farthest pterygium to scleral spur (mm)			0.214	0.831
BMI (KG/cm^2)	4.12±0.87	4.08±0.92	0.379	0.706
	21.83±4.08	22.16±4.27		
Operative time (min)	52.12±8.69	53.48±9.05	.735	0.464
Course of disease (week)	2.21±0.49	2.12±0.54	0.837	0.405
Gender			0.187	0.666
Male	28 (60.87)	30 (65.22)		
Female	18 (39.13)	16 (34.78)		
Family disease history			0.239	0.625
Yes	12 (26.09)	10 (21.74)		
No	34 (73.91)	36 (78.26)		
Outdoor occupation			1.903	0.168
Yes	42 (91.30)	45 (97.83)		
No	4 (8.70)	1 (2.17)		
Diseased eye			0.697	0.835
Left eye	24 (52.17)	20 (43.48)		
Right eye	22 (47.83)	26 (56.52)		
Marital status			0407	0.524
Yes	29 (63.04)	26 (56.52)		
No	17 (36.96)	20 (43.48)		
Education level			0.697	0.404
<High school	26 (56.52)	22 (47.83)		
≥High school	20 (43.48)	24 (52.17)		
Smoking habits			0.449	0.503
Yes	42 (91.30)	40 (86.96)		
No	4 (8.70)	6 (13.04)		

Table 2. Ki-67, CyclinD1 and p53 concentration

	Study group (n=46)	Study group (n=46)	t or χ^2	*P*
Ki-67 (ng/mL)	46.24±6.24	12.83±2.64	33.442	<0.001
CyclinD1 (ng/mL)	4.23±0.54	0.07±0.02	52.214	<0.001
p53 (pg/mL)	194.51±34.64	86.66±12.57	19.853	<0.001

with treatment time (r=-0.692, r=-0.692, all P<0.001) (**Figures 4**-**6**; **Table 3**).

Concentration changes of Ki-67, CyclinD1 and p53 in different pathological features

There were no dramatic differences in the serum concentrations of Ki-67, CyclinD1 and p53 among patients with different ages, genders and diseased eyes (P>0.050). However, among different pterygium, for the farthest to the scleral spur, course of disease, pterygium grade and pterygium size, there were significant differences in Ki-67, CyclinD1, and p53 concentrations (P<0.001) (**Tables 4**-**6**).

Discussions

As a common chronic proliferative eye disease in ophthalmology, it is believed that pterygium is often caused by degeneration of conjunctival tissue. As the research progresses, people tend to believe that pterygium is induced by cell proliferation disorders [20]. Study of Shimmura et al. [21] showed that the pathological changes of pterygium are mainly caused by the proliferation of fibrous tissue and neovascularization. Reisman et al. [22] showed that the occurrence of pterygium is a benign lesion of retinal tumors. At present, pterygium treatment in clinical practice is mainly based on resection. With the development of the disease, more and more

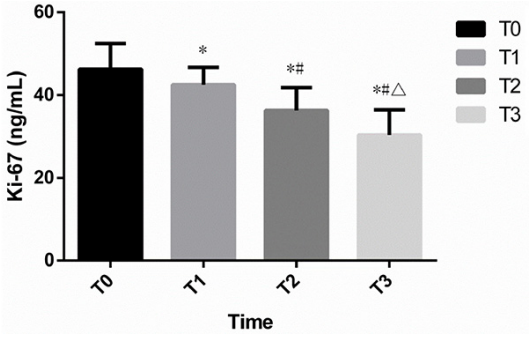

Figure 1. Concentration changes of Ki-67 in the study group during treatment. *represents a comparison with the serum Ki-67 concentration at T0, P<0.001; #represents a comparison with the serum Ki-67 concentration at T1, P<0.001; ∆represents a comparison with the serum Ki-67 concentration at T2, P<0.001. CyclinD1.

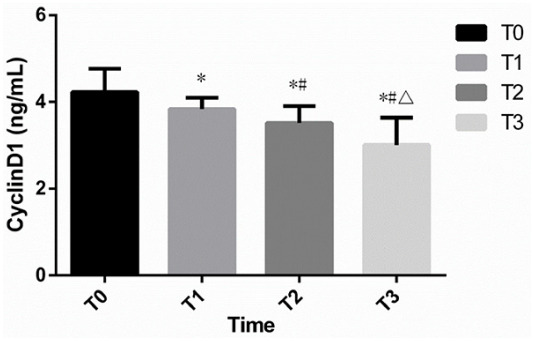

Figure 2. Concentration changes of CyclinD1 in the study group during treatment. *represents a comparison with the serum CyclinD1 concentration at T0, P<0.001; #represents a comparison with the serum CyclinD1 concentration at T1, P<0.001; ∆represents a comparison with the serum CyclinD1 concentration at T2, P<0.001.

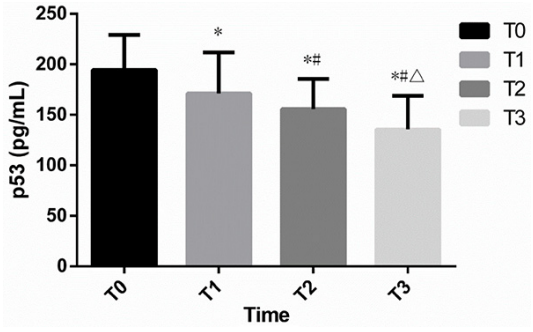

Figure 3. Concentration changes of p53 in the study group during treatment. *represents a comparison with the serum p53 concentration at T0, P<0.001; #represents a comparison with the serum p53 concentration at T1, P<0.001; ∆represents a comparison with the serum p53 concentration at T2, P<0.001.

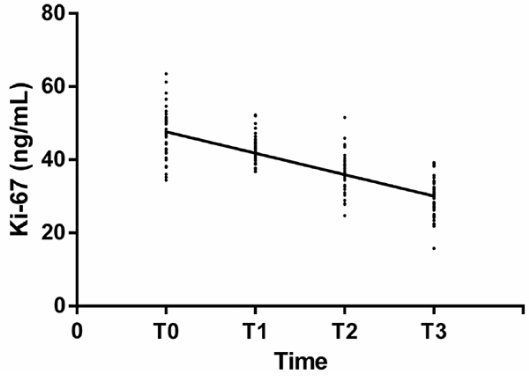

Figure 4. Correlation analysis between serum Ki-67 and treatment time in the study group. According to the Spearman correlation coefficient analysis, Ki-67 was negatively correlated with treatment time (r=-0.784, P<0.001).

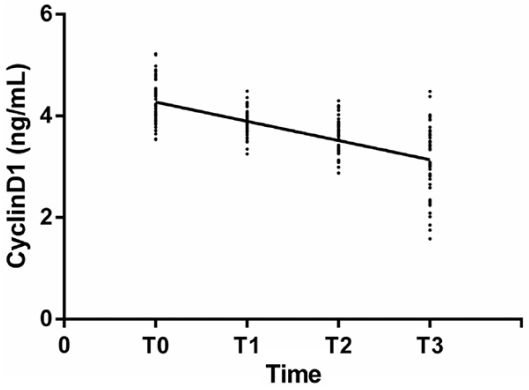

Figure 5. Correlation analysis between serum CyclinD1 and treatment time in the study group. According to the Spearman correlation coefficient analysis, CyclinD1 was negatively correlated with treatment time (r=-0.692, P<0.001).

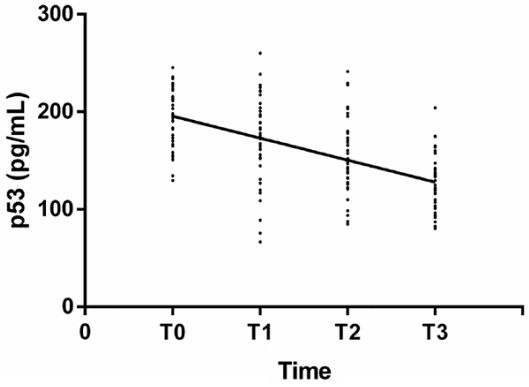

Figure 6. Correlation analysis between serum p53 and treatment time in the study group. According to the Spearman correlation coefficient analysis, p53 was negatively correlated with treatment time (r=-0.692, P<0.001).

Table 3. Changes of Ki-67, CyclinD1, and p53 of the study group during treatment

	Ki-67	CyclinD1	p53
r	-0.784	-0.692	-0.599
95% CI	-0.836~-0.719	-0.763~-0.606	-0.687~-0.494
P	<0.001	<0.001	<0.001

studies have proposed that traditional resection surgery cannot meet the clinical treatment requirements. Postoperative recurrence occurs in an increasing number of patients [23]. Cui et al. [24] have indicated that the regulation of miR-122 in pterygium by targeting Bcl-w can effectively interfere with apoptosis. Liu also have demonstrated that [25] mTOCR1 regulates the proliferation and apoptosis of pterygium cells by targeting autophagy and FGFR3. Although these studies suggest that the pterygium may be cured by treatment of molecular pathology in the future, it is not yet perfected. Moreover, as the mRNA needs to be obtained in the patient's tissues, it is difficult to be detected in clinical practice. Therefore, it is not yet conducive to clinical promotion. In this experiment, it is convenient to detect the serum concentration of Ki-67, CyclinD1, and P53 in patients with pterygium, which can be widely used in clinical practice. What's more, molecular pathology research is also in line with the current research status of pterygium.

The results of this experiment show that patients with pterygium are mainly engaged in outdoor work. This also conforms to the incidence of pterygium because pterygium may be related to long-term chronic stimulation such as wind, sun and smoke. By observing the family history of genetic disease, it was found that there were not many patients with a history of genetic disease in this study. It suggested that the family inheritance of pterygium was not the main pathogenic factor. However, it is not excluded that there is a certain ambiguity in the statistical results due to limited case load. The serum concentration of Ki-67, CyclinD1 and p53 was compared between patients with pterygium and patients with normal physical examination. The serum concentration of Ki-67, CyclinD1 and p53 in the study group was higher than that in the control group. It indicated that the Ki-67, CyclinD1, P53 may be participating in the occurrence and development of pterygium. This is also consistent with the results of Wu [26], Feng [27], etc. The concentration changes of Ki-67, CyclinD1, and P53 in the study group during the treatment were further analyzed, and the results were Ki-67, CyclinD1 and P53 decreased gradually with the treatment time. This also indicates that Ki-67, CyclinD1, and P53 have changed during the rehabilitation process of pterygium, which is closely related to the patient's condition. In order to confirm this, the concentration changes of Ki-67, CyclinD1, and P53 under different clinical characteristics were analyzed. It was found that among different pterygium, distance to the scleral spur, course of disease, pterygium grade and pterygium size, there were significant differences in Ki-67, CyclinD1, and p53 concentration. This indicates that Ki-67, CyclinD1 and P53 are expected to be new molecular markers for the diagnosis and treatment of pterygium. Ki-67 is a nuclear antigen associated with proliferative cells. It is usually located in the nucleus. Studies have shown that Ki-67's ability to affect cell proliferation is mainly achieved by chromatin and mitosis [28]. In addition, the concentration of pterygium is increased. The reason may be that as a neoplastic tissue on the bulbar conjunctiva and cornea of the palpebral fissure, the pterygium is gradually enlarged by invading the cornea. This tissue is made up with collagen fibrosis splitting in the conjunctival epithelium and the new vessels in the lamina propria [29, 30]. Therefore, for patients with more severe conditions, the Ki-67 test results increased dramatically. During the treatment process, with the disintegration of the neoplastic tissue, patient's retina gradually returned to normal. Then Ki-67 also gradually decreased.

Transient expression exists for CyclinD1 only at the early stages of DNA synthesis. Once CyclinD1 is over-expressed, it can accelerate the DNA transformation process from early synthesis to late stage [31]. On the other hand, pterygium produces an extracellular matrix by transforming limbal stem cells. Extracellular matrix is a secretable macromolecular substance that promotes cell proliferation [32]. It has been speculated that the concentration of CyclinD1 in pterygium is increased due to the large formation of extracellular matrix, which accelerates the proliferation of cells. The activity of various molecules and DNA among cells has accelerated. Therefore, the expression of CyclinD1and is increased.

Table 4. Concentration changes of Ki-67 in different pathological features (ng/mL)

	Ki-67	t or F	P
Age (year)		0.542	0.590
<48 (27)	45.27±5.84		
≥48 (19)	46.24±6.16		
The distance from the farthest pterygium to scleral spur (mm)		0.133	0.895
<4 (30)	46.12±6.05		
≥4 (16)	45.87±6.15		
Course of disease (week)		4.743	<0.001
<2 (22)	40.52±7.25		
≥2 (24)	49.62±5.73		
Gender		0.707	0.484
Male (28)	46.05±6.12		
Female (18)	47.34±5.92		
Diseased eye		0.332	0.741
Left eye (24)	45.37±6.84		
Right eye (22)	46.05±7.03		
Pterygium grade		8.349	<0.001
Grade I (16)	38.65±8.22		
Grade II (24)	42.53±5.84*		
Grade III (6)	51.96±6.24*,#		
Pterygium size		3.400	0.001
<2 mm (15)	40.59±5.15		
≥2 mm (31)	48.34±8.04		

Note: *represents a comparison with grade I pterygium, P<0.001; #represents a comparison with grade II pterygium, P<0.001.

Table 5. Concentration changes of CyclinD1 in different pathological features (ng/mL)

	CyclinD1	t or F	P
Age (year)		0.272	0.787
<48 (27)	4.20±0.63		
≥48 (19)	4.15±0.59		
The distance from the farthest pterygium to scleral spur (mm)		5.712	<0.001
<4 (30)	3.57±0.84		
≥4 (16)	4.89±0.52		
Course of disease (week)		6.247	<0.001
<2 (22)	3.25±0.62		
≥2 (24)	4.72±0.93		
Gender		0.295	0.770
Male (28)	4.35±0.70		
Female (18)	4.29±0.68		
Diseased eye		0.227	0.821
Left eye (24)	4.42±0.62		
Right eye (22)	4.38±0.57		
Pterygium grade		24.632	<0.001
Grade I (16)	3.04±0.36		
Grade II (24)	3.84±0.72*		
Grade III (6)	4.92±0.29*,#		
Pterygium size		8.290	<0.001

<2 mm (15)	3.66±0.59
≥2 mm (31)	4.67±0.24

Note: *represents a comparison with grade I pterygium, P<0.001; #represents a comparison with grade II pterygium, P<0.001.

Table 6. Concentration changes of p53 in different pathological features (ng/mL)

	p53	t or F	P
Age (year)		0.155	0.877
<48 (27)	190.85±35.22		
≥48 (19)	192.42±31.62		
The distance from the farthest pterygium to scleral spur (mm)		1.593	0.118
<4 (30)	167.21±42.21		
≥4 (16)	186.54±32.55		
Course of disease (week)		2.314	0.025
<2 (22)	157.62±38.62		
≥2 (24)	184.57±40.21		
Gender		0.266	0.792
Male (28)	189.54±36.21		
Female (18)	192.34±32.72		
Diseased eye		0.527	0.601
Left eye (24)	194.24±28.64		
Right eye (22)	189.64±30.57		
Pterygium grade		5.389	0.008
Grade I (16)	157.62±30.57		
Grade II (24)	175.32±31.84*		
Grade III (6)	204.64±21.18*,#		
Pterygium size		3.318	0.002
<2 mm (15)	162.54±24.87		
≥2 mm (31)	192.75±30.67		

Note: *represents a comparison with grade I pterygium, P<0.001; #represents a comparison with grade II pterygium, P<0.001.

P53 is a currently recognized tumor suppressor gene. Studies have shown that p53 protein expression is remarkably high in outdoor workers, indicating it may be associated with ultraviolet radiation [33]. It also conforms to the basic situation of pterygium patients in this experiment. It indicates that p53 may be one of the pathogenic factors of pterygium. P53 can inhibit the transformation and growth of oncogenes and a series of cells. If gene mutation occurs in p53, mutant p53 can not only inhibit the activity of normal p53 gene, but also promote the malignant transformation process of disease [34], which is similar to the process of pterygium. Neoplastic tissue is developed by the deterioration, expansion and thickening of the bulbar conjunctiva and fibrocytes. Therefore, it is speculated that the occurrence of pterygium may be related to p53 gene mutation, but the exact mechanism needs to be verified by further experiments. In the study of Ni et al. [35], anti-metabolite drugs have successfully reduced the postoperative recurrence rate in patients with pterygium. This also reflects that for the future treatment of pterygium, inhibition of cell proliferative capacity is a new direction.

This study aimed to evaluate the significance of Ki-67, CyclinD1, p53 in patients with pterygium. Nevertheless, there were still some defects due to the ineffective experimental conditions. Patients with pseudopterygium and pinguecula were not included as control subjects in this test because of limited case load. The mechanism of Ki-67, CyclinD1, and P53 on pterygium also requires verification by more in-depth experiments. Related targeted drugs of Ki-67, CyclinD1, and p53 were not used to treat

patients with pterygium in this study. The clinical treatment value has not been confirmed. Some scholars may improve this in the future. A long-term follow-up on the subjects of this experiment will be performed and the sample size of the study will be expanded as soon as possible to obtain the best experimental results.

In summary, the serum concentration of Ki-67, CyclinD1 and p53 in patients with pterygium was higher than that in normal subjects. It suggested that Ki-67, CyclinD1 and P53 were expected to be a new target for pterygium treatment in future clinical practice.

Disclosure of conflict of interest

None.

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