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Prolidase Enzyme Activity in Conjunctiva and Pterygium Tissues

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: The aim of this study was to determine prolidase activity in conjunctival tissue and its relationship with pterygium.

Material/Methods: Prolidase activity was measured in 23 pterygium and 25 healthy conjunctival tissues and the 2 groups were compared.

Results: Prolidase enzyme activity could not be measured in either the healthy conjunctival or in pterygium tissues. The mean serum prolidase levels of the control and pterygium groups were 967.46±353.64 and 858.29±301.83, respectively. Statistically, there was no significant difference between the groups with regard to serum prolidase levels ($p>0.05$).

Conclusions: In conclusion, absence of prolidase activity in pterygium tissue indicates that there is no collagen turnover in this tissue. We may explain this finding with the elastin-rich structure of the conjunctiva.

MeSH Keywords: Conjunctiva • Prolidase Deficiency • Pterygium

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Background

Prolidase (PR) is a cytosolic enzyme, which hydrolyzes the peptide bonding of imidodipeptides and imidotripeptides, which include proline or hydroxyproline in the carboxyl terminal position [1–3]. This enzyme is present in many tissues in animals and humans and plays an important role in collagen metabolism [4]. Proline and hydroxyproline are formed when collagen is degraded. While proline takes part in collagen synthesis again, hydroxyproline is excreted in urine [5].

The conjunctiva and the underlying tenon cover the sclera and contain elastin-rich connective tissue [6]. Conjunctival fibroblast activity and wound healing are of great importance in pterygium and trabeculectomy operations. Fibrosis, scarring, and rapid proliferation are unwanted conditions. Collagen production occurs in fibrosis and scarring. Detection of prolidase enzyme in conjunctival tissue would create a novel field of debate on the diseases and the operations concerning this tissue, as prolidase enzyme is a rate-limiting enzyme in collagen metabolism. To the best of our knowledge, there are no published studies on the presence of prolidase enzyme activity in the conjunctiva. Therefore, we aimed to investigate the presence of this enzyme activity in conjunctival tissue and its relationship with pterygium, which is a disease of collagen tissue irregularity in the conjunctiva.

Material and Methods

Prolidase enzyme activity was measured in serum and conjunctival tissues of 23 eyes of 23 pterygium patients, who had undergone an operation in our clinic between 2013 and 2015. The control group was composed of 25 patients with similar age and sex distribution, who did not have pterygium, and conjunctival tissues obtained from 25 eyes of 25 patients and their serum samples were used. The study was conducted in accordance to the tenets of the Declaration of Helsinki. Approval for the study was granted by the local ethics committee and informed consent was obtained from all patients.

Prolidase measurement

Prolidase enzyme was measured photometrically at 515 nm using the Chinard method. Prolidase enzyme activation was provided with incubation for 3 h with MgCl2. Afterwards, glycine-proline was used as substrate and the revealed proline was stained with ninhydrin in an acid environment and measurement was made at 515 nm.

Statistical analysis

All analyses were carried out using the Statistical Package for Social Sciences version 13 (SPSS, Inc, Chicago, IL.). The Kolmogorov-Smirnov test was used to evaluate the normality of the distributions. The relationships between parameters were evaluated using the Pearson correlation test.

Results

The demographic findings were similar between the control and the patient groups. Statistically, there were no significant differences between age and sex distribution (Table 1).

Prolidase activity could not be measured in healthy conjunctiva or in pterygium tissues (Table 2 and Figure 1).

Mean serum prolidase level of the control and pterygium groups was 967.46±353.64 and 858.29±301.83, respectively (Figure 2). Statistically, there was no significant difference between serum prolidase levels ($p>0.05$).

Discussion

Prolidase enzyme has an important role in collagen metabolism. This enzyme enables proline to contribute to collagen production again. This enzyme is accepted as the rate-limiting enzyme in collagen metabolism, as 90% of proline used in collagen production is provided from the proline included in the cycle [7].

The association of proline with various diseases has been demonstrated. The reason for the absence of a difference between serum prolidase levels may be pterygium not being a systemic disease.

Prolidase enzyme activity has been demonstrated in various tissues, such as serum, plasma, erythrocytes, leukocytes, amniotic fluid, intestinal mucosa, kidneys, liver, brain, heart, uterus, and the thymus [8]. Prolidase activity is usually determined with photometric methods. In previous studies, prolidase activity was examined in serum or tissues. Proline is excreted with urine because it is not included in the cycle in prolidase deficiency. Skin ulcers, mental retardation, specific facial characteristics, skeletal anomalies, splenomegaly, hematological disorders, and chronic infections are seen in these patients [9]. Prolidase activity is related to the pathogenesis of various disorders. Elevated serum prolidase activity has been associated with oxidative stress and increased collagen formation-degradation [10]. Serum prolidase activity has been found to increase in diabetic nephropathy, metabolic syndrome, Behcet's disease, and chronic hepatitis, whereas it has been found to decrease in keratoconus, systemic sclerosis, joint hypermobility syndrome, and myeloproliferative syndromes [11–17]. In some studies, serum prolidase activity has been shown to alter in

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Table 1. Comperison of demographic findings.

Parameter	Controls (n=25)	Patients (n=23)	Value of p
Gender (M/F)	19/6	18/5	>0.05
Age (years)	52.34±16.71	51.04±14.63	>0.05

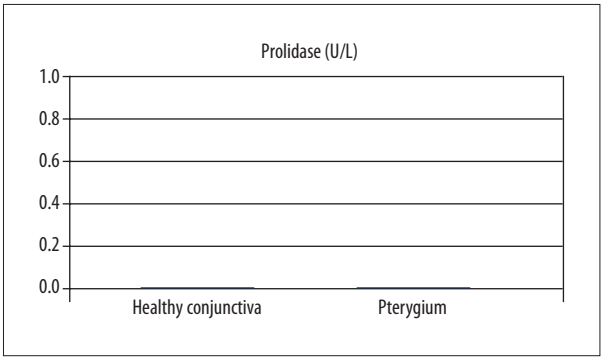

Figure 1. Prolidase activity could not be measured in healthy conjunctiva or in pterygium tissues.

Table 2. Prolidase activity could not be measured in healthy conjunctiva or in pterygium tissues.

Tissue	Prolidase
Helthy conjuctiva	N/A
Prerygium	N/A

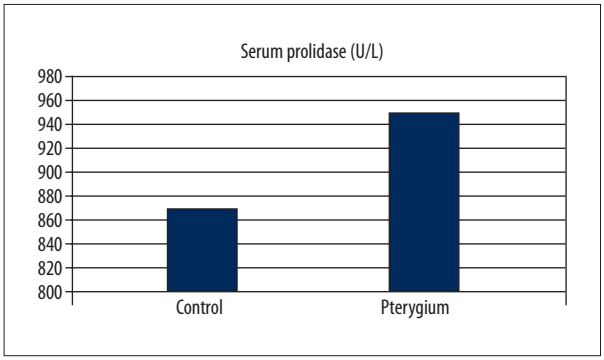

Figure 2. There was no statistically significant difference between serum prolidase levels of control and patient groups (p>0.05).

fibrotic diseases and some cancers [18–21]. Therefore, abnormal prolidase levels may be a useful marker in cancers and fibrosis.

Tissue prolidase levels was shown to be altered in some diseases. A statistically significant elevation has been demonstrated in tissue prolidase activity in nasal polyps, chronic wounds, and keloid tissue [22,23].

Pterygium is a chronic proliferative lesion of the conjunctiva, characterized by inflammation and angiogenesis [24]. The pathogenesis of pterygium is not clearly understood. However, angiogenesis plays an important role in the formation of fibrovascular tissue, especially in recurrent pterygium [25].

Significant prolidase activity was not detected in normal and pterygium conjunctival tissues in our study. This indicates that prolidase activity is absent or scarce in conjunctival tissue. This is not surprising, considering the histological structure of conjunctiva. Conjunctiva is composed of epithelium and substantia propria. The underlying tenon is composed of elastin-rich connective tissue. A low level of prolidase taking part in collagen metabolism is an expected condition because these tissues are not collagen-rich.

Excessive fibrosis developing after trabeculectomy operations impairs the success of the operation. Collagen production occurs in postoperative fibrosis [26]. Mitomycin-C, which is used postoperatively, prevents scarring by hindering fibroblast proliferation and migration [27,28]. While there is no prolidase activity in conjunctiva, there may be fibroblast-derived prolidase activity during scar formation after trabeculectomy. Inhibition of prolidase may prevent scarring because it is a rate-limiting enzyme.

Although the conjunctiva is not collagen-rich, pterygium, which is a pathology of this tissue, is characterized by connective tissue irregularity. A study reported that prolidase activity was increased 4-fold in keloid tissue that accompanies connective tissue irregularity [29]. Although the pathology in pterygium is different, irregularity and hypertrophy are also present in this disease. Therefore, we suggest that prolidase activity could increase in pterygium tissue; however, prolidase activity could not be detected in pterygium tissue. This result suggests that there is no difference in collagen production and destruction in pterygium tissue. Impaired elastin production is known in the pathogenesis of pterygium. Elastin material increases and connective tissue irregularity develops as a result of elastodysplasia and elastodystrophy [30].

Conclusions

Our results indicate that the main problem in the pathogenesis of pterygium is related to abnormality in elastin, and collagen is not included in this process.

Conflicts of interest

None.

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