Clinical study on the effect of preloaded punctal plug in the treatment of aqueous-deficient dry eye

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OBJECTIVE: *To evaluate the effect of OASIS preloaded punctal plug versus Smart Plug punctal plug Retrospectively registered in the treatment of aqueous-deficient dry eye.*
METHODS: *47 patients were randomly divided into a control group and an experimental group. The control group was treated with Smart Plug punctal plug treatment, and the experimental group was treated with OASIS preloaded punctal plug treatment. The ocular surface disease index (OSDI) questionnaire score, Schirmer I test and break-up time (BUT) results before and after treatment, and the incidences of postoperative complications were compared between the two groups.*
RESULTS: *This study showed that compared with before treatment, the OSDI scores of patients were significantly improved at six months after treatment in both the experimental group and control group. After treatment, there was no significant difference in OSDI score, Schirmer I test, and BUT level between the two groups. In addition, the Smart Plug punctal plug treatment group had a significant improvement in BUT at three months after operation compared with before treatment.*
CONCLUSION: *The OASIS preloaded punctal plug and the Smart Plug punctal plug can significantly improve dry eye symptoms. Furthermore, the OASIS preloaded punctal plug can facilitate intraoperative procedures, and the abnormal implantation due to the expansion of the embolic volume can be reduced.*

KEY WORDS: OSDI questionaire, Dry eye, Embolisation implantation, Preloaded punctal plug, Smart Plug punctal plug

Introduction

Dry eye is a chronic ocular surface disease caused by multiple factors. It is caused by the instability of the tear film or the imbalance of the ocular surface microenvironment caused by the abnormal quality, quantity and dynamics of the tear fluid. It can be accompanied by ocular surface inflammation, tissue damage and neurological abnormalities, causing various ocular discomforts and visual dysfunction [1,2]. The incidence of dry eye in China is similar to that of other Asian countries and is higher than that of the United States and Europe. Its incidence is about 21%-52.4% [3,4]. Dry eyes are divided into aqueous-deficient, evaporative dry eye and mixed.[5] Among them, aqueous-deficient dry eye can be divided into Sjögren dry eye and without Sjögren dry eye [5,6].
Currently, the therapeutic options for dry eye include artificial tears, lid hygiene, collagen or silicone plugs, anti-inflammatory treatment with corticosteroids or cyclosporine A eye drops, orally administered tetracycline derivatives and omega-3 or omega-6 fatty acids, and submandibular gland transplantation [7-9]. In recent years, the Smart Plug punctal plug has become more frequently

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used to treat aqueous-deficient dry eye by blocking the tear dots of patients to prevent the discharge of tears. The normal secretion of tears is retained in the eyes, thereby improving symptoms and achieving a good curative effect [10-12]. However, the complications of lacrimal duct plugs, especially those of long-term follow-up, have not yet attracted enough attention [13,14].

The OASIS preloaded punctal plug is a new type of lacrimal duct plug that has attracted significant interest. However, there are few clinical studies comparing the OASIS preloaded punctal plug and Smart Plug punctal plug for dry eye. Therefore, in this study, patients with aqueous-deficient dry eye treated in our hospital from January 2018 to January 2020 are the main research subjects. We intend to explore the clinical efficacy of OASIS preloaded punctal plugs in the treatment of aqueous-deficient dry eye.

Materials and Methods

Research Subjects

A randomised, controlled, prospective study was performed. The main research subjects were 47 patients with aqueous-deficient dry eye at our hospital from January 2018 to January 2020. The included patients were randomly divided into a control group and an experimental group in the form of randomised cards (24 in the experimental group, 23 in the control group).

Patients in the control group were treated with a Smart Plug punctal plug, and patients in the experimental group were treated with an OASIS preloaded punctal plug. This study complies with the 'Declaration of Helsinki of the World Medical Association' and has been approved by the ethics committee of our hospital. All patients signed an informed consent form.

Inclusion and Inclusion Criteria:

1. *Patients aged between 10 and 70 years.*
2. *The lacrimal duct is unobstructed.*
3. *Patient has at least one of the subjective symptoms such as dryness, foreign body sensation, burning sensation, fatigue, discomfort, vision fluctuations and meets one of the following criteria:*
   A. BUT ≤ 5s or 2 mm/5 min ≤ Schirmer I test ≤ 5 mm/5 min;
   B. 5s < BUT ≤ 10s or 5 mm/5 min < Schirmer I test ≤ 10/5 min, at the same time corneal fluorescein staining is positive.
4. *All patients have signed informed consent.*

Exclusion criteria: 1. Patients with lacrimal duct disease; 2. Patients with abnormal ocular surface structure; 3. Patients with active ocular surface inflammation.

Research Methods

The experimental group used the 6303 preloaded punctal plug produced by OASIS Medical (Glendora, California, USA) (Fig. 1), and the control group used the Smart Plug punctal plug. Before the operation, the two groups of patients flushed the lacrimal duct, applied Alkain surface anaesthesia under the microscope, lightly pressed the eyelid to expose the punctum (if the punctum is too small, it can be expanded), and placed the brown tip of the implanter at the punctum and squeezed the implanter so that the preloaded punctal plug entered the lacrimal canaliculus from the tip of the implanter. The top edge of the plug should be below the punctum. If necessary, the punctal plug was pushed further with micro tweezers to reach the level of the canaliculus. One drop of levofloxacin eye drops was applied after the operation. Ofloxacin eye drops were applied to the eyes for three days. Smart Plug punctal plug in operation method: the lacrimal duct was washed without obstructing the lacrimal duct. Proparacaine hydrochloride eye drops were applied for ocular surface anaesthesia, and the lower eyelid was pulled apart to expose the lacrimal punctum. Depending on the size of the lower lacrimal punctum, it was expanded with the punctum dilator. The other hand-held embedded tweezers along the tooth groove clamped the Smart Plug punctal plug. The other end was quickly inserted vertically along the lacrimal duct about two-thirds of the length of the plug. The embedded tweezers were released, and the remaining plug was observed retracting completely into the lacrimal site. Ofloxacin eye drops were applied to the eyes for three days. Patients were followed up for six months.

Main Observation Indicators And Methods

Before the lacrimal canalicular embolisation and one week, one month, three months, and six months after the embolisation, the treated patients were successively surveyed with OSDI scores. Eye examinations included visual acuity examination, intraocular pressure, slit-lamp

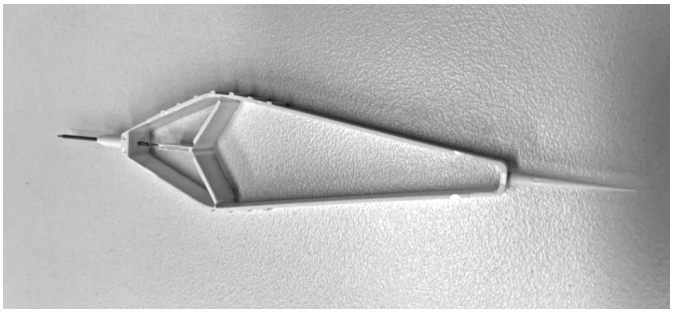

Fig. 1: Model 6303 preloaded punctal plug produced by OASIS Medical, USA.

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examination, and corneal fluorescein staining, lissamine green staining of conjunctiva, BUT and Schirmer I test (without surface anaesthesia). The corneal fluorescein staining score was scored using a 0–12-point system to record the staining results. The cornea was divided into four quadrants, and each quadrant was divided into 0 to 3 points according to the degree of staining and the staining area. All tested patients were examined by the same doctor in the same examination room, and the result was the average of three repeated examinations.

Statistical Methods

In this study, SAS 9.4 statistical software was used for data processing, and the measurement data were expressed as mean ± standard deviation (x±s). Counting data were expressed as percentages (%). The comparison between the experimental group and the control group of each index used a mixed-effect linear model, and $p < 0.05$ was considered to be statistically significant. The experimental group and the control group of each index were compared with a mixed-effect linear model at different time points. A Chi-square test was used for counting data. As it involved many comparisons and corrections of test level, $p < 0.005$ was considered to be statistically significant.

Results

General Information

A total of 47 patients with water-deficiency dry eye were included in this study, including six males (six eyes) and 41 females (41 eyes), aged 26 to 70 years. The average age of the experimental group was 48.4 ± 9.6 years, and that of the control group was 42.8 ± 8.1 years ($p = 0.10$). The duration of the disease was 6–36 months. The clinical follow-up time was six months.

Comparison of Osdi Scores Between The Two Groups

After six months of treatment, there was no significant difference in OSDI scores between the experimental group and the control group ($p = 0.53$). The OSDI scores of the two groups at each time point after treatment were lower than those before treatment, and the difference was statistically significant (Fig. 2).

Comparison of the results of the Schirmer I test between the two groups

In the OASIS preloaded punctal plug treatment group, the results of the Schirmer I test were not statistically different at each time point. In the Smart Plug punctal plug treatment group, there was a statistical difference between Schirmer I and Schirmer 4, and there was no statistical difference between the other time points. There was no statistical difference between the experimental group and the control group in the Schirmer I test six months after treatment ($p = 0.41$) (Fig. 3).

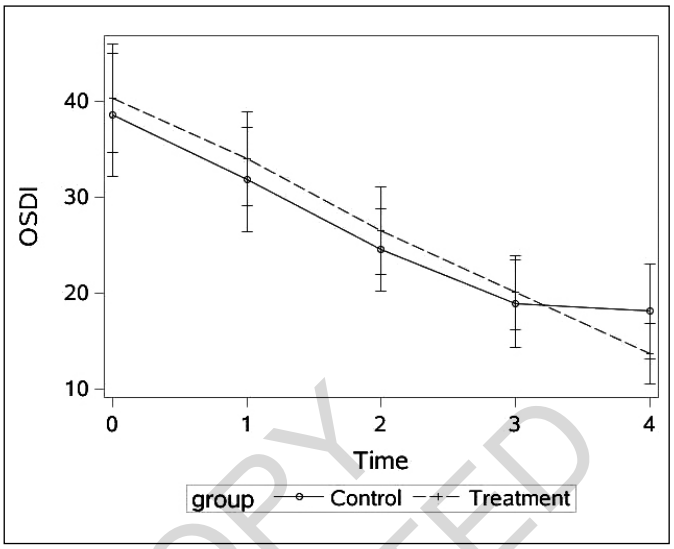

Fig. 2: Comparison of OSDI scores between the two groups. x-axis: Before the lacrimal canalicular embolization and 1 week, 1 month, 3 months, and 6 months after the embolization. There was no statistically significant difference in OSDI scores between the experimental group and the control group at 6 months after treatment (p=0.53).

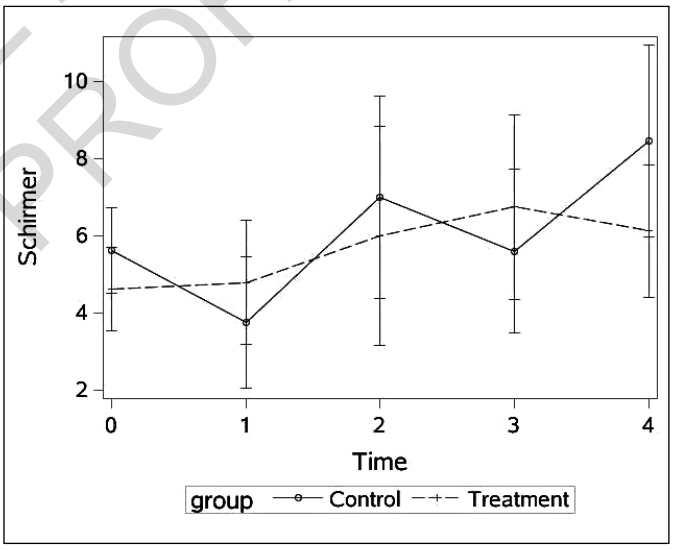

Fig. 3: Comparison of the results of the Schirmer test between the two groups. x-axis: Before the lacrimal canalicular embolization and 1 week, 1 month, 3 months, and 6 months after the embolization. There was no statistical difference between the experimental group and the control group in the Schirmer test 6 months after treatment (p=0.41).

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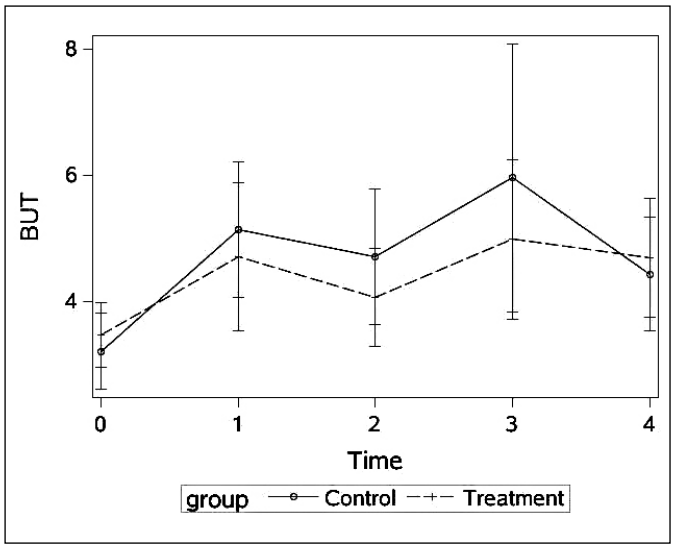

Fig. 4: Comparison of BUT results between the two group. x-axis: Before the lacrimal canalicular embolization and 1 week, 1 month, 3 months, and 6 months after the embolization. There was no statistically significant difference in BUT levels between the experimental group and the control group 6 months after treatment (p=0.35).

Comparison of BUT results between the two groups

There was no statistically significant difference in BUT levels among patients in the OASIS preloaded punctal plug treatment group. In the Smart Plug treatment group, there was a statistical difference between BUT0 and BUT3, and there was no statistical difference at other time points. There was no significant difference in BUT levels between the experimental group and the control group six months after treatment (p = 0.35) (Fig. 4).

Comparison of postoperative complications between the two groups

One patient in the OASIS preloaded punctal plug treatment group developed conjunctivitis on the second day after implantation and recovered after four days of drug treatment. There were no abnormal complications in the Smart Plug punctal plug treatment group.

The Intraoperative and Postoperative Complications

The Intraoperative And Postoperative Complications Are Shown in Table I. All symptoms were relieved after symptomatic treatment.

Discussion

A total of 47 patients with aqueous-deficient dry eye were included in this study. The results of the study showed that compared with before treatment, the OSDI scores of patients in the OASIS preloaded punctal plug treatment group and Smart Plug punctal plug treatment group were significantly improved six months after treatment. After treatment, the two groups of patients were similar in OSDI score, Schirmer I test, and BUT levels, and there was no significant difference.

In recent years, with the ageing of the population, the use of electronic devices, and environmental factors, the number of patients with dry eye has been on the rise.[15-18] At present, there are various ways to treat dry eye, mainly including the elimination of incentives, artificial tear replacement therapy, preservation of own tears, promotion of tear secretion, further combining anti-inflammatory and immunosuppression, and surgical treatments [19-21]. However, general incentives are difficult to eliminate. Although there are various artificial tears for different tear film components, they still cannot completely replace natural tears due to the complex composition of human tears. The side effects of immunosuppressive agents are many and expensive.[22] Moreover, the preservatives in long-term topical medication can easily cause damage to the ocular surface. If patients with dry eye need to use artificial tears frequently, such as more than 4–6 times a day, if the application of artificial tears has

Table I - *The intraoperative and postoperative complications of two groups.*

Group	Intraoperative	Postoperative
The control group (n=23)	(1) Overexpansion occurred in 2 cases with lower lacrimal punctum laceration (2) In 2 cases, the plug was not implanted for the first time due to the rapid expansion of punctal plug, and the new plug was implanted again (3) In 1 case, the plug was lost because the embedded tweezers were not aligned with the end of the plug, and a new plug was re-implanted	(1) 2 cases had redness and swelling of lower lacrimal punctum one day after operation (2) 1 case had epiphora one week after operation (withdrawal from clinical)
The experimental group (n=24)	–	(1) 2 cases had redness and swelling of lower lacrimal punctum one day after operation (2) 1 patient presented lower lacrimal punctum redness and swelling accompanied by conjunctival congestion (withdrawal from clinical)

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side effects or patients cannot tolerate or do not accept long-term drug treatment, or if the drug treatment effect is poor or the symptoms cannot be completely solved by using artificial tears alone, lacrimal embolisation can be adopted.

The first lacrimal plug used is a degradable punctum plug for the treatment of severe dry eye. Nowadays, the lacrimal plug has developed a variety of shapes and materials, and its application is becoming more and more extensive. Lacrimal embolism can be divided into punctal plug and canaliculus embolism according to its location, and the time of their placement is divided into temporary and permanent embolism. Embolism is made of different materials, and current reports include collagen, silica gel, hydrogel, polydioxanone, and acrylic acid [23]. Generally speaking, when local lubrication cannot be improved, these small plugs improve the signs and symptoms of moderate dry eye. Permanent plugs have a longer residence time, so their impact is usually greater than that of temporary degradable plugs. Punctal plugs are well tolerated, only about 10% need to be removed due to irritation. The literature shows that compared with the lacrimal canalicular plug, the lacrimal punctum plug has a higher probability of lacrimal overflow and plug body loss. Permanent punctal plugs are more prone to side effects such as lacrimal canaliculitis and pyogenic granuloma. For a small number of patients, more invasive treatments are needed to remove them, such as lacrimal canalitomy and dacryocystorhinostomy.

Smart Plug punctal plugs have been used for many years and are effective in treating aqueous-deficient dry eye.[11,24] The results of this study support the fact that Smart Plug punctal plug significantly improved subjective symptoms in patients with dry eye and prolonged BUT after surgery. However, Schirmer did not show significant improvement, presumably because punctal plugs do not increase the secretion of the main and accessory lacrimal glands, thus increasing tear production. Instead, the symptoms of dry eye can be improved by reducing the limited tear drainage and increasing tear film stability. The OASIS preloaded punctal plug is a new type of lacrimal duct plug, but high-quality clinical research articles are few. Our current study showed that the OASIS preloaded punctal plug is comparable with the Smart Plug punctal plug for treating aqueous-deficient dry eye, and both can significantly improve dry eye symptoms. The OASIS preloaded punctal plug uses the device's own punctum dilator, is a better match for the implant and reduces the risk of intraoperative overdilation of the lacrimal duct. Furthermore, it simplifies the surgical procedure. Lacrimal punctum expansion and plug implantation can be completed in one step, and the loss of embolisation before implantation and the abnormal implantation due to the expansion of the embolic volume can be reduced. This minimises the risk of intraoperative complications. Therefore, it is worthy of clinical promotion.

Although the two kinds of lacrimal duct plugs had different degrees of postoperative complications, they were relieved by simple treatment, and no serious irreversible complications occurred. Perhaps due to the short observation time, no canaliculus granuloma or canaliculitis requiring surgical treatment were observed. Whether there are serious complications in the later stage still needs further observations.

This research has the following shortcomings. First, although this study is a randomised controlled experiment, it is not blinded. Second, this study is a single-centre clinical study, and the sample size included is relatively small. It is still necessary to increase the sample size and conduct multi-centre clinical research. Finally, the clinical follow-up time of this study is relatively short, and long-term clinical follow-up observation is still needed.

Conclusion

The OASIS preloaded punctal plug can achieve similar therapeutic effects as the Smart Plug punctal plug. Because of the simple operation procedure of the preloaded punctal plug, it can complete the dilation and embolisation of the lacrimal punctum in one step and can reduce the loss of the embolisation before the implantation and the abnormal implantation due to the expansion of the embolisation volume, which is worthy of clinical application.

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