

# Autologous platelet-rich plasma eye drop versus artificial tear eye drop for symptomatic dry eye disease: A prospective comparative interventional study

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**Purpose:** To evaluate and compare the efficacy of autologous platelet-rich plasma (aPRP) eye drop and artificial tear (AT) eye drop in moderate to severe symptomatic dry eye disease (DED). **Methods:** This prospective interventional study included 121 eyes of 61 patients of moderate to severe DED. Patients were divided into aPRP (31 patients) and AT (30 patients) group. Ocular Surface Disease Index (OSDI) score, tear film breakup time (TBUT) (s), corneal fluorescein staining (CFS) score, and Schirmer test score (mm) of both the groups were evaluated and compared pre-treatment and post-treatment at the end of 3 months. **Results:** The mean age of the aPRP group and AT group was  $52.8 \pm 12.8$  years and  $55.5 \pm 13.4$  years, respectively. At the end of 3 months, OSDI score reduced more in the aPRP group as compared to AT group, and the mean difference ( $-22.7$ ) was statistically significant ( $P < 0.001$ ). There was no significant difference in post-treatment Schirmer test score between the two groups ( $P = 0.44$ ). Post-treatment improvement in TBUT and CFS score in the aPRP group was significantly higher in the aPRP group as compared to that in the AT group ( $P < 0.05$ ). Bruising at the site of blood withdrawal was noted in two patients in the aPRP group. **Conclusion:** aPRP is safe and more effective than AT in treating patients with moderate to severe symptomatic DED.

**Key words:** Artificial tear, autologous platelet-rich plasma, dry eye disease, OSDI

Dry eye disease (DED) is a multifactorial disease of the ocular surface with tear film instability, hyperosmolarity, and ocular surface inflammation.<sup>[1]</sup> Tear film plays an important role in maintaining the health of the ocular surface.<sup>[2]</sup> Tear film contains various essential components, including epidermal growth factors, vitamin A, hepatocyte growth factor, fibronectin, and neurotrophic growth factor. These growth factors are associated with the regulation of proliferation, differentiation, and maturation of ocular surface epithelium.<sup>[3,4]</sup> Imbalance in these growth factors may be responsible for the pathogenesis of DED.<sup>[5]</sup>

Detection and treatment of dry eye is important as patients are very prone to potentially blinding infections, such as bacterial keratitis,<sup>[5]</sup> and are at an increased risk of complications following common procedures such as laser refractive surgery. Various treatment modalities are available for the treatment of DED, including artificial tear substitutes, anti-inflammatory agents, immune-suppressants, and punctal plugs. Autologous blood derivatives are newer modalities of dry eye treatment.

The initial reports of the efficacy of autologous serum for the treatment of dry eye promoted interest in the search for an ideal tear substitute.<sup>[6]</sup> The ensuing research not only corroborated the efficacy of autologous serum for the treatment of a variety of pathologies of the ocular surface<sup>[7-9]</sup> but also stimulated newer applications of blood derivatives in ophthalmology. In recent

years, further progress has been made by including the factors derived from platelets in the composition of a novel blood derivative, that is, plasma rich in growth factors (PRGF).<sup>[10]</sup> This product is being successfully applied in various medical areas, such as maxillofacial surgery, traumatology, dermatology, orthopedics, and gynecology.<sup>[11,12]</sup> More recently, its application in ophthalmology for the treatment of persistent epithelial defects has been reported.<sup>[13,14]</sup>

PRP is a newer treatment modality with abundant growth factors, bacteriostatic nature, anti-apoptotic, and anti-collagenase property. It is seen to be very effective in treating dry eye not amenable to treatment by other means. It can be autologous or heterologous. Autologous PRP has added benefits of preventing occurrence of allergy or immunological reactions that may occur in cases of heterologous donation.

## Methods

The present study was conducted on 121 eyes (61 patients) of symptomatic moderate to severe dry eye in a tertiary care center of central India from March 2021 to August 2021. The study protocol was approved by the ethical review committee, and the study was performed in accordance to the tenets of Declaration

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of Helsinki. The study has been registered in Clinical Trial Registry-India (CTRI/2021/03/031887). A written informed voluntary consent was taken from all the study subjects after explaining the nature and possible consequences of the trial. All patients underwent standard ocular examination protocol. Patients were divided into two groups: aPRP (autologous platelets rich plasma) group and AT (artificial tear) group. The aPRP group was treated with 20% autologous PRP eye drops 4–6 times a day for 3 months. The AT group was treated with 0.5% carboxymethyl cellulose eye drops 4–6 times a day for 3 months. Follow-up was done at 1 week, 2 weeks, 1 month, and 3 months. On each follow-up visit, the Ocular Surface Disease Index (OSDI) score, tear film breakup time (TBUT), corneal fluorescein staining (CFS) score, and Schirmer test score were noted. At the last follow-up, the abovementioned parameters in both groups were compared.

### Study design

Prospective interventional comparative study.

### Inclusion criteria

All patients with symptomatic dry eye since last 3 months with an OSDI score of  $>40$ , a TBUT score of  $<10$  s (5  $\mu$ L of fluorescein sodium 2% eye drops was used for each measurement by using a pipette for standardization and the mean value of three readings per eye was taken), positive CFS score ( $\geq$  grade 1 according to the Van Bijsterveld score), Schirmer test score  $<10$  in 5 min (without topical anesthesia), able to acknowledge and give informed written consent, and able to cooperate with the investigation and treatment plans were taken.

### Exclusion criteria

Patients who were unwilling or unable to give consent, refused to accept randomization or follow-up plans, involved in other clinical trial, uncooperative patients, under 18 years of age, pregnant females or expecting to become pregnant during the study, contact lens user, patients with active ocular infection, and patients using other eye drops example anti-glaucoma medications.

### Autologous PRP preparation and storage

Autologous PRP was prepared according to the protocol described by Alio *et al.* in 2012.<sup>[15]</sup> The patient's blood was extracted into 10-mL sterile tubes containing 1 mL sodium citrate acting as an anticoagulant. Centrifugation of total blood at optimal condition was done to achieve enrichment of platelets in plasma fraction [Fig. 1]. Next, 3–4 mL of platelet-rich plasma (PRP) was aspirated (one part of PRP was mixed with four parts of BSS to make 20% concentration of autologous PRP (aPRP)) and kept in a sterile amber glass bottles with eye drop applicators under laminar flow cabin. Patients were instructed to wash their hands before the application of eye drop. The bottle in use was given to the patient and instructed to be kept at 2°C–8°C for 1 week, and the remaining bottles were kept in blood bank of our hospital at -20°C.

### Statistical analysis

Mean and standard deviation of all the parameters were calculated using SPSS Statistics 22, and a comparison of the pre-treatment versus post-treatment parameters in both aPRP group and AT group was done using the paired student's *t* test to determine the degree of statistical significance. Comparison of post-treatment parameters in both aPRP group and AT group



**Figure 1:** Centrifuged blood sample containing PRP

was done using unpaired student's *t* test to determine the statistical significance.  $P < 0.05$  was considered as statistically significant.

### Results

The present prospective comparative interventional study was conducted on 121 eyes (61 patients) of symptomatic moderate to severe dry eye. The mean age of the patients in the aPRP group was  $52.8 \pm 12.8$  years, while the mean age of patients in

the AT group was  $55.5 \pm 13.4$  years. There was preponderance of female over male in both groups. Demographic data of both the groups is given in Table 1.

The common underlying causes of DED were primary lacrimal gland deficiency (age-related dry eye) and dry eye associated with connective tissue disorders. The whole sample completed the follow-up period, and there were no changes in group assignment.

Tables 2 and 3 show the changes in the OSDI score, TBUT, CFS score, and Schirmer test score at 3 months of follow-up in the aPRP group and AT group, respectively. OSDI score reduced and CFS score improved significantly in both aPRP and AT groups, whereas TBUT (s) increased significantly only in the aPRP group. Schirmer test scores also improved in both aPRP and AT groups, but the improvement was statistically nonsignificant in both groups.

In the aPRP group, the mean OSDI score reduced from  $77.3 \pm 17.1$  to  $43.9 \pm 24.3$  ( $P < 0.0001$ ), the mean TBUT (s) increased from  $2.45 \pm 2.26$  to  $4.91 \pm 2.46$  ( $P < 0.001$ ), the mean CFS score reduced from  $2.63 \pm 0.54$  to  $1.13 \pm 0.97$  ( $P < 0.001$ ), and the mean Schirmer test score (mm) increased from  $4.14 \pm 2.50$  to  $4.19 \pm 2.48$  ( $P = 0.083$ ) at 3-month follow-up.

In the AT group, the mean OSDI score reduced from  $74.7 \pm 16.1$  to  $66.6 \pm 19$  ( $P < 0.001$ ), the mean TBUT (s) increased from  $2.91 \pm 1.48$  to  $3.03 \pm 1.5$  ( $P = 0.058$ ), the mean CFS score reduced from  $2.41 \pm 0.59$  to  $2.01 \pm 0.7$  ( $P < 0.005$ ), and the mean Schirmer test score (mm) increased from  $4.26 \pm 1.91$  to  $4.30 \pm 1.90$  ( $P = 0.159$ ) at 3-month follow-up.

The pre-treatment parameters (OSDI score, TBUT, CFS score, and Schirmer test score) in both groups were comparable ( $P > 0.05$ ). Table 4 compares the mean values in both groups at 3-month follow-up. The OSDI score reduced

in both groups, but the reduction was more in the aPRP group as compared to AT group, and the mean difference (MD:  $-22.7$ ) was statistically significant ( $P < 0.0001$ ). Improvement in TBUT and CFS score was significantly more in the aPRP group as compared to that in the AT group ( $P < 0.001$  and  $P < 0.0001$ , respectively). There was no significant difference in the mean Schirmer test score between both groups ( $P = 0.44$ ). Although at last follow-up, the mean Schirmer test score (mm) was more in the AT group ( $4.30 \pm 1.90$ ) as compared to aPRP group ( $4.19 \pm 2.48$ ), the improvement in the mean Schirmer test score was more in the aPRP group ( $0.05$  mm) as compared to the AT group ( $0.04$  mm). Bruising at the site of blood withdrawal was noted in two patients in the aPRP group.

### Discussion

Blood derivatives such as autologous serum and aPRP are the newer modalities for the treatment of dry eye. Fox *et al.*<sup>[6]</sup> first described the benefits of AS for the treatment of dry eyes in patients with Sjogren’s syndrome and later described by Tsubota *et al.*<sup>[7]</sup> Blood derivatives have added advantages over artificial tears as being preservative-free and present a greater similarity to the natural healthy tear film in terms of pH, osmolarity, and biomechanical properties.<sup>[16]</sup> AS contains vitamins and fibronectin, which have epitheliotropic effects and help to maintain ocular surface integrity. However, AS is very poor in growth factors because platelets are eliminated in the process of its production.<sup>[17]</sup> As a new alternative, aPRP is a hemoderivative product, different from AS, and has been proposed for the treatment of DED.<sup>[18]</sup>

The theoretical background of using PRP is the supplementation of important tear components that may be lacking in dry eyes and cannot be supplemented by artificial tear substitutes. PRP becomes more effective when presenting higher indexes of growth factors such as epithelial growth factor (EGF), vitamin A, neural growth factor (NGF), insulin type I growth factor,<sup>[19]</sup> and platelet factor IV.<sup>[20]</sup> PRP is a preservative-free biological product from the patient’s own blood having a platelet concentration above baseline. The main advantage of PRP over other products is the presence of the platelets and the prolonged release of growth factors that are involved in the wound-healing process of the cornea and conjunctival surface.<sup>[21,22]</sup> PRP can be stored at  $-20^{\circ}\text{C}$  for up

**Table 1: Demographic data**

	aPRP group	AT group	Total
No. of Patients	31	30	61
Eyes	61	60	121
Male	11	12	23
Female	20	18	38
Mean age (years)	$52.8 \pm 12.8$	$55.5 \pm 13.4$	

**Table 2: Pre- and post-treatment mean scores of parameters in the aPRP group**

aPRP group	Mean±SD Pre-treatment	Mean±SD Post-treatment (at 3 months)	Mean difference	P
OSDI score	$77.3 \pm 17.1$	$43.9 \pm 24.3$	33.4	<0.0001
TBUT (s)	$2.45 \pm 2.26$	$4.91 \pm 2.46$	2.46	<0.001
CFS score	$2.63 \pm 0.54$	$1.13 \pm 0.97$	1.5	<0.001
Schirmer test score (mm)	$4.14 \pm 2.50$	$4.19 \pm 2.48$	0.05	0.083

**Table 3: Pre- and post-treatment mean scores of parameters in the AT group**

AT group	Mean±SD Pre-treatment	Mean±SD Post-treatment (3 months)	Mean difference	P
OSDI score	$74.7 \pm 16.1$	$66.6 \pm 19$	8.1	<0.001
TBUT (s)	$2.91 \pm 1.48$	$3.03 \pm 1.5$	0.12	0.058
CFS score	$2.41 \pm 0.59$	$2.01 \pm 0.7$	0.4	<0.005
Schirmer test score (mm)	$4.26 \pm 1.94$	$4.30 \pm 1.9$	0.04	0.159

**Table 4: Comparison of various parameters in both groups at the end of 3 months**

Parameters	Mean Score (aPRP group)	Mean Score (AT group)	Mean difference	P
OSDI score	43.9±24.3	66.6±19.8	-22.7	<0.0001
TBUT (s)	4.91±2.46	3.03±1.56	1.8	<0.001
CFS score	1.13±0.97	2.01±0.72	-0.92	<0.0001
Schirmer test score (mm)	4.19±2.48	4.30±1.90	-0.11	0.44

to 3 months maintaining constant or slight variations in the concentration of the most important growth factors.<sup>[23]</sup>

We reported a significant reduction in the mean OSDI score in the aPRP group ( $P < 0.0001$ ). Similar results were obtained by Alio *et al.* (2017),<sup>[24]</sup> Sanchez-Avila *et al.* (2017),<sup>[25]</sup> and Merayo-Llives *et al.* (2016).<sup>[26]</sup> In the present study, the OSDI score reduced in both the groups, but the reduction was more in the aPRP group (43.2%) as compared to the AT group (10.8%), with a mean difference of -22.7, which was statistically significant ( $P < 0.0001$ ). Our results correlated with the results of Celebi *et al.*,<sup>[27]</sup> who noted a 55.18% reduction in the OSDI score in AS versus a 19.50% reduction in the preservative-free artificial tears (PFAT) treatment group ( $P < 0.001$ ). Yilmaz *et al.*<sup>[28]</sup> compared autologous serum versus PFAT in patients with dry eyes due to systemic isotretinoin therapy and found that the OSDI score reduced significantly in both groups, but OSDI score reduction was more significant in the AS group as compared to the PFAT group ( $P < 0.0001$ ). Wang *et al.* (2020)<sup>[29]</sup> studied autologous serum eye drops versus artificial tear drops for DED and concluded that the OSDI after AS treatment was lower than that after the AT treatment.

The present study showed a significant improvement in the mean TBUT (s) at 3-month follow-up in the aPRP group ( $P < 0.001$ ), whereas after AT treatment, the improvement was nonsignificant ( $P = 0.058$ ). At the final follow-up, the difference between both groups was statistically significant ( $P < 0.001$ ). In the aPRP group, an improvement of >2 s was seen in 42.6% (26 eyes) of the cases, while the remaining 57.4% (35 eyes) of the cases showed an improvement of 1–2 s. Worsening of TBUT was not seen in any of the patients. Takashi *et al.* (2005)<sup>[9]</sup> also noted a significant improvement in the mean TBUT in patients treated with autologous serum eye drop as compared with subjects treated with PFAT after 2 weeks of treatment. Similar results were noted by Celebi *et al.* (2014),<sup>[27]</sup> Noda-Tsuruya *et al.* (2006),<sup>[30]</sup> Yilmaz (2017),<sup>[28]</sup> and Wang *et al.*<sup>[29]</sup> Alio *et al.*<sup>[31]</sup> noted an improvement of >2 s in the TBUT in 46% of the cases after treatment with PRP.

We noted a significant reduction in the CFS score in both aPRP and AT groups ( $P < 0.001$  and  $P < 0.005$ , respectively) at the last follow-up. However, the reduction in the CFS score was much lower in the aPRP group as compared to that in the AT group, and this difference between both groups was significant ( $P < 0.0001$ ). Similar results were obtained in a study done by Takashi Kojima *et al.* (2005),<sup>[9]</sup> which showed a significant improvement in the CFS score in the patients assigned to autologous serum eye drops compared with subjects assigned to PFAT after 2 weeks of treatment. Alio *et al.* (2017)<sup>[24]</sup> and Natanael *et al.* (2019)<sup>[32]</sup> also showed that after the use of autologous PRP in severe dry eye, the Oxford scale score of CFS decreased significantly ( $P < 0.05$ ). In contrast to the present study, Wang *et al.* (2020)<sup>[29]</sup> and Noda-Tsuruya

*et al.* (2006)<sup>[30]</sup> noted no significant difference in the CFS scores between patients using autologous serum eye drops and patients using artificial tears.

In our study, the mean Schirmer test score at the final follow-up increased in both groups, but the increment was nonsignificant as compared to the pre-treatment value. The mean difference between both groups at the final follow-up was also statistically nonsignificant ( $P = 0.44$ ). Noda-Tsuruya *et al.* (2006)<sup>[30]</sup> and Wang *et al.* (2020)<sup>[29]</sup> compared autologous serum with artificial tears for dry eyes and obtained similar results. In contrast to the present study, Celebi *et al.* (2014),<sup>[27]</sup> Jirsova *et al.*,<sup>[33]</sup> Hussain,<sup>[17]</sup> and Garcia-Conca *et al.* (2018)<sup>[34]</sup> reported a significant increase in the Schirmer test score with the use of autologous serum/PRP as compared to artificial tear in patients of DED.

## Conclusion

Autologous PRP treatment provides a greater improvement in signs and symptoms of DED patients as compared to AT treatment. It is a safe therapy without any serious adverse effects, with the added benefit of being preservative free. aPRP can be given safely up to 10–12 weeks with a significant improvement in moderate to severe DED. Thus, we conclude that aPRP is safe and more effective than AT in treating patients with symptomatic moderate to severe DED.

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## Conflicts of interest

There are no conflicts of interest.

## References

- Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo C-K, *et al.* TFOS DEWS II definition and classification report. *Ocul Surf* 2017;15:276–83.
- Yoon KC, Im SK, Park YG, Jung YD, Yang SY, Choi J. Application of umbilical cord serum eyedrops for the treatment of dry eye syndrome. *Cornea* 2006;25:268–72.
- Bradley JC, Bradley RH, McCartney DL, Mannis MJ. Serum growth factor analysis in dry eye syndrome. *Clin Exp Ophthalmol* 2008;36:717–20.
- Poon AC, Geerling G, Dart JK, Fraenkel GE, Daniels JT. Autologous serum eyedrops for dry eyes and epithelial defects: clinical and *in vitro* toxicity studies. *Br J Ophthalmol* 2001;85:1188–97.
- Ohashi Y, Ishida R, Kojima T, Goto E, Matsumoto Y, Watanabe K, *et al.* Abnormal protein profiles in tears with dry eye syndrome. *Am J Ophthalmol* 2003;136:291–9.
- Fox RI, Chan R, Michelson JB, Belmont JB, Michelson PE. Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. *Arthritis Rheum* 1984;27:459–61.
- Tsubota K, Goto E, Fujita H, Masafumi O, Hiroko I, Ichiro S, *et al.*

- Treatment of dry eye by autologous serum application in Sjögren's syndrome. *Br J Ophthalmol* 1999;83:390–5.
8. Tananuvat N, Daniell M, Sullivan LJ, McKelvie P, McCarty D, Taylor HR. Controlled study of the use of autologous serum in dry eye patients. *Cornea* 2001;20:802–6.
  9. Kojima T, Ishida R, Dogru M, Goto E, Matsumoto Y, Kaido M, *et al.* The effect of autologous serum eyedrops in the treatment of severe dry eye disease: A prospective randomized case-control study. *Am J Ophthalmol* 2005;139:242–6.
  10. Anitua E. Plasma rich in growth factors: Preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants* 1999;14:529–35.
  11. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of protein for healing and tissue regeneration. *Thromb Haemost* 2004;91:4–15.
  12. Anitua E, Andia I, Sanchez M, Azofra J, Zalduendo M, Fuente M, *et al.* Autologous preparation rich in growth factors promote proliferation and induce VEGF and HGF production by human tendon cells in culture. *J Orthop Res* 2005;23:281–6.
  13. Rocha G, Acera A, Durañ JA. Laser *in situ* keratomileusis flap necrosis after trigeminal nerve palsy. *Arch Ophthalmol* 2007;125:1423–5.
  14. Lopez-Plandolit S, Morales MC, Freire V, Etxebarria J, Duran JA. Plasma rich in growth factors (PRGF) as a therapeutic agent for severe persistent corneal epithelial defects. *Cornea* 2010;29:843–8.
  15. Alio JL, Arnalich-Montiel F, Rodriguez AE. The role of “Eye Platelet Rich Plasma” (E-PRP) for wound healing in ophthalmology. *Curr Pharm Biotechnol* 2012;13:1257–65.
  16. Liu L, Hartwig D, Harloff S, Herminghaus P, Wede IT, Kasper K, *et al.* Corneal epitheliotropic capacity of three different blood-derived preparations. *Invest Ophthalmol Vis Sci* 2006;47:2438–44.
  17. Hussain M, Shtein RM, Sugar A, Soong HK, Woodward MA, DeLoss K, *et al.* Long-term use of autologous serum 50% eye drops for the treatment of dry eye disease. *Cornea* 2014;33:1245–51.
  18. Lopez-Plandolit S, Morales MC, Freire V, Grau AE, Durañ JA. Efficacy of plasma rich in growth factors for the treatment of dry eye. *Cornea* 2011;30:1312–7.
  19. Wu TE, Chen JC, Hu C, Cheng CK. Easy-to-prepare autologous platelet-rich plasma in the treatment of refractory corneal ulcers. *Taiwan J Ophthalmol* 2015;5:132–5.
  20. Ribeiro MV, Barbosa FT, Ribeiro LE, Lacet CM, Lyra JM, Guedes VL, *et al.* Platelet-rich plasma in diabetic dry eye disease. *Rev Bras Oftalmol* 2016;75:308–13.
  21. Alio JL, Rodriguez AE, Wróbel DD. Eye platelet-rich plasma in the treatment of ocular surface disorders. *Curr Opin Ophthalmol* 2015;26:325–32.
  22. Drew VJ, Tseng CL, Seghatchian J, Burnouf T. Reflections on dry eye syndrome treatment: Therapeutic role of blood products. *Front Med (Lausanne)* 2018;5:33.
  23. Anitua E, Muruzabal F, Pino A, Merayo-Llodes J, Orive G. Biological stability of plasma rich in growth factors eye drops after storage of 3 months. *Cornea* 2013;32:1380–6.
  24. Alio JL, Rodriguez AE, Oliveira RF, Dudzińska DW, Abdelghany AA. Autologous platelet-rich plasma in treatment of post-LASIK chronic ocular surface syndrome. *Ophthalmol Ther* 2017;6:285–93.
  25. Sanchez-Avila RM, Lloves JM, Riestra AC, Anitua E, Muruzabal F, Orive G, *et al.* The effect of immunologically safe plasma rich in growth factor eye drops in patients with Sjogren Syndrome. *J Ocul Pharmacol Ther* 2017;33:391–9.
  26. Merayo-Llodes J, Sanchez-Avila RM, Riestra AC, Anitua E, Begoña L, Orive G, *et al.* Safety and efficacy of autologous plasma rich in growth factors eye drops for the treatment of evaporative dry eye. *Ophthalmic Res* 2016;56:68–73.
  27. Celebi AR, Ulusoy C, Mirza GE. The efficacy of autologous serum eye drops for severe dry eye syndrome: A randomized double-blind crossover study. *Graefes Arch Clin Exp Ophthalmol* 2014;52:619–26.
  28. Yılmaz U, Küçük E, Koç Ç, Gökler E. Comparison of autologous serum versus preservative free artificial tear in patients with dry eyes due to systemic isotretinoin therapy. *Curr Eye Res* 2017;42:827–31.
  29. Wang L, Cao K, Wei Z, Baudouin C, Labbé A, Liang Q. Autologous serum eye drops versus artificial tear drops for dry eye disease: A systematic review and meta-analysis of randomized controlled trials. *Ophthalmic Res* 2020;63:443–51.
  30. Noda-Tsuruya T, Asano-Kato N, Toda I, Tsubota K. Autologous serum eye drops for dry eye after LASIK. *J Refract Surg* 2006;22:61–6.
  31. Alio JL, Pastor S, Ruiz-Colecha J, Rodriguez A, Artola A. Treatment of ocular surface syndrome after LASIK with autologous 126 platelet-rich plasma. *J Refract Surg* 2007;23:617–9.
  32. Levy N, Wang Yin GH, Noharet R, Ghazouane R, Grimaud F, Aboudou H, *et al.* A retrospective analysis of characteristic features of responder patients to autologous serum eye drops in routine care. *Ocul Surf* 2019;17:787–92.
  33. Jirsova K, Brejchova K, Krabcova I, Filipec M, Al Fakih A, Palos M, *et al.* The application of autologous serum eye drops in severe dry eye patients; subjective and objective parameters before and after treatment. *Curr Eye Res* 2014;39:21–30.
  34. García-Conca V, Abad-Collado M, Hueso-Abancens JR, Mengual-Verdú E, Piñero DP, Aguirre-Balsalobre F, *et al.* Efficacy and safety of treatment of hyposecretory dry eye with platelet-rich plasma. *Acta Ophthalmol* 2019;97:e170–8.