



# Serum Vascular Endothelial Growth Factor, Insulin-Like Growth Factor-1 and Aflibercept Levels in Retinopathy of Prematurity

Utku Furuncuoglu\*

Department of Ophthalmology, Kastamonu Research and Training Hospital, Kastamonu, Turkey

## DESCRIPTION

The primary goal in the treatment of Retinopathy of Prematurity (ROP) is to ablate the avascular retina to eliminate the hypoxic retina and to reduce the release of vasoproliferative substances such as Vascular Endothelial Growth Factor (VEGF). However, it is aimed to regress the retinal neovascularization with the least complication and to maintain the neurosensory structure and function at the highest level. VEGF levels have gained importance in preterm infants due to their role in neurodevelopment. In recent studies, the importance of VEGF has been understood in the pathogenesis of ROP [1]. In order to prevent retinal neovascularization, the focus on reducing the level of intravitreal VEGF.

Intravitreal agents are commonly used in the treatment of ROP. Aflibercept, bevacizumab, and ranibizumab are anti-VEGF agents used intravitreally in proliferative eye diseases. Aflibercept is the newest agent. It is a recombinant fusion protein that binds VEGF-A and VEGF-B with high affinity. It also inhibits Placental Growth Factor (PGF) [2]. Aflibercept has a higher binding capacity for VEGF than other agents and acts longer in the eye [3]. Bevacizumab was first introduced, so there is more information about it in the literature. Then, ranibizumab and aflibercept were used. Aflibercept and ranibizumab are ophthalmological agents specifically developed for intravitreal administration. Although the efficacy, long-term clinical results and side effects of drugs have been investigated with many studies, there is no consensus on the ideal drug and dosage.

VEGF is an important neurodevelopmental growth factor in the early neonatal period. Since anti-VEGF agents can have systemic transmission, it is important to know their safety in the early neonatal period. The goal of anti-VEGF treatment for ROP is optimum intravitreal concentration and minimal transmission to the systemic circulation. At this point, it becomes important how long the agent remains in the systemic circulation and how long it suppresses VEGF. Recent investigations show that VEGF inhibitors administered intravitreally suppress systemic VEGF levels for at least 2 weeks [4-6]. This study shows that serum VEGF levels are suppressed for at least 8 weeks.

Although there are studies in adults regarding the systemic transmission of intravitreal administered aflibercept, this is the first study to evaluate serum aflibercept levels in infants with ROP. This study shows that aflibercept reached high levels in the systemic circulation at the first day after injection, and then decreased. Aflibercept could be detected in the systemic circulation 4 weeks after injection. These informations are important and will lead to new studies.

Albeit anti-VEGF agents have known systemic side effects and tolerability, further information is needed on the potential effects of decreased systemic VEGF levels in early neonatal period. Anti-VEGF agents are administered at half the adult dose, the effective dose has not yet been determined in treatment of ROP. At the same time, the development of premature infants continues; both VEGF and IGF-1 play an important role in this development. Therefore, further and long term clinical studies are needed. In the future, new agents will probably become available for treatment, efficacy and safety will be discussed in different ways.

The primary goal in the treatment of Retinopathy of Prematurity (ROP) is to ablate the avascular retina to eliminate the hypoxic retina and to reduce the release of vasoproliferative substances such as Vascular Endothelial Growth Factor (VEGF). However, it is aimed to regress the retinal neovascularization with the least complication and to maintain the neurosensory structure and function at the highest level. VEGF levels have gained importance in preterm infants due to their role in neurodevelopment. In recent studies, the importance of VEGF has been understood in the pathogenesis of ROP [1]. In order to prevent retinal neovascularization, the focus on reducing the level of intravitreal VEGF.

Intravitreal agents are commonly used in the treatment of ROP. Aflibercept, bevacizumab, and ranibizumab are anti-VEGF agents used intravitreally in proliferative eye diseases. Aflibercept is the newest agent. It is a recombinant fusion protein that binds VEGF-A and VEGF-B with high affinity. It also inhibits Placental Growth Factor (PGF) [2]. Aflibercept has a higher binding capacity for VEGF than other agents and acts longer in the eye [3]. Bevacizumab was first introduced, so there is more information

**Correspondence to:** Utku Furuncuoglu, Department of Ophthalmology, Kastamonu Research and Training Hospital, Kastamonu, Turkey, E-mail: utkufuruncuoglu@gmail.com

**Received:** 07-Apr-2022, Manuscript No. JVMS-22-16028; **Editor assigned:** 11-Apr-2022, PreQC No. JVMS-22-16028 (PQ); **Reviewed:** 25-Apr-2022, QC No. JVMS-22-16028; **Revised:** 28-Apr-2022, Manuscript No. JVMS-22-16028 (R); **Published:** 07-May-2022, DOI: 10.35841/2329-6925.22.10.447.

**Citation:** Furuncuoglu U (2022) Serum Vascular Endothelial Growth Factor, Insulin-Like Growth Factor-1 and Aflibercept Levels in Retinopathy of Prematurity. J Vasc Surg. 10:447.

**Copyright:** © 2022 Furuncuoglu U. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

about it in the literature. Then, ranibizumab and aflibercept were used. Aflibercept and ranibizumab are ophthalmological agents specifically developed for intravitreal administration. Although the efficacy, long-term clinical results and side effects of drugs have been investigated with many studies, there is no consensus on the ideal drug and dosage.

VEGF is an important neurodevelopmental growth factor in the early neonatal period. Since anti-VEGF agents can have systemic transmission, it is important to know their safety in the early neonatal period. The goal of anti-VEGF treatment for ROP is optimum intravitreal concentration and minimal transmission to the systemic circulation. At this point, it becomes important how long the agent remains in the systemic circulation and how long it suppresses VEGF. Recent investigations show that VEGF inhibitors administered intravitreally suppress systemic VEGF levels for at least 2 weeks [4-6]. This study shows that serum VEGF levels are suppressed for at least 8 weeks.

## CONCLUSION

Although there are studies in adults regarding the systemic transmission of intravitreal administered aflibercept, this is the first study to evaluate serum aflibercept levels in infants with ROP. This study shows that aflibercept reached high levels in the systemic circulation at the first day after injection, and then decreased. Aflibercept could be detected in the systemic circulation 4 weeks after injection. These informations are important and will lead to new studies.

Albeit anti-VEGF agents have known systemic side effects and tolerability, further information is needed on the potential effects

of decreased systemic VEGF levels in early neonatal period. Anti-VEGF agents are administered at half the adult dose, the effective dose has not yet been determined in treatment of ROP. At the same time, the development of premature infants continues; both VEGF and IGF-1 play an important role in this development. Therefore, further and long term clinical studies are needed. In the future, new agents will probably become available for treatment, efficacy and safety will be discussed in different ways.

## REFERENCES

1. Sato T, Kusaka S, Shimojo H, Fujikado T. Simultaneous analyses of vitreous levels of 27 cytokines in eyes with retinopathy of prematurity. *Ophthalmology*. 2009;116(11):2165-2169.
2. Stewart MW. Aflibercept (VEGF Trap-eye): The newest anti-VEGF drug. *Br J Ophthalmol*. 2012;96(9):1157-1158.
3. Papadopoulos N, Martin J, Ruan Q, Rafique A, Rosconi M, Shi E, et al. Binding and neutralization of vascular endothelial growth factor (VEGF) and related ligands by VEGF Trap, ranibizumab and bevacizumab. *Angiogenesis*. 2012;15(2):171-185.
4. Sato T, Wada K, Arahori H. Serum concentrations of bevacizumab (avastin) and vascular endothelial growth factor in infants with retinopathy of prematurity. *Am J Ophthalmol* 2012;153(2):327-333.
5. Wu WC, Lien R, Liao PJ. Serum levels of vascular endothelial growth factor and related factors after intravitreal bevacizumab injection for retinopathy of prematurity. *JAMA Ophthalmol*. 2015;133(4):391-397.
6. Hoerster R, Muether P, Dahlke C, Mehler K, Oberthür A, Kirchhof B, et al. Serum concentrations of vascular endothelial growth factor in an infant treated with ranibizumab for retinopathy of prematurity. *Acta Ophthalmol*. 2013;91:74-75.