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Prevalence of Endophthalmitis after Intravitreal Injection of Avastin (Bevacizumab) in Patients Wearing Masks

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ABSTRACT

Background and Objective: Although the likelihood of endophthalmitis after intravitreal injection is low, one of the side effects of this injection is blindness. With the prevalence of the COVID-19 pandemic and the necessity of mask use in patients and physicians, mask use has increased. Previous studies have reported a high risk of endophthalmitis after intravitreal injection in patients who wore masks. The present study was conducted to investigate the pattern of endophthalmitis after intravitreal injection of Avastin (Bevacizumab) in patients wearing masks.

Methods: This prospective cohort study was conducted on 3938 patients who underwent intravitreal injection from March 2021 to March 2022 at the eye surgery center. Bevacizumab injection was performed after local anesthesia in the operating room and under sterile conditions. Local antibiotic drops (chloramphenicol) were then used. It should be noted that patients' masks were not removed at any of the stages mentioned. Patients were followed up one week after discharge to be examined for infection.

Findings: A total of 3938 patients were included in the study, 56.6% of whom were male and 43.4% were female. The mean age of the patients was 39.61±16.10 years. Moreover, no significant difference was observed between men and women. The highest frequency of injection was related to diabetic macular edema (27.8%) and the lowest frequency was related to neovascular glaucoma (0.5%). Only one patient was diagnosed with endophthalmitis after intravitreal injection. In addition, no significant relationship was found between age, gender, and the occurrence of endophthalmitis.

Conclusion: According to the results of this study, the incidence of endophthalmitis after intravitreal injection is very low, and the use of a face mask in patients has no effect on the occurrence of endophthalmitis.

Keywords: *Endophthalmitis, COVID-19, Bevacizumab.*

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Introduction

In recent years, invasive methods have saved human lives on the one hand, but have resulted in many fatal consequences due to resistant and severe hospital infections. Despite the progress made in ophthalmology in the last two decades, infection control remains a highly serious issue (1). One of the main concerns of ophthalmologists after eye surgery is post-intravitreal injection endophthalmitis, which can lead to serious complications such as blindness (2) Nowadays, intravitreal administration of drugs has become a common method for the treatment of various eye diseases, especially the posterior part of the eye (3).

Intravitreal injection is one of the most common standard procedures performed worldwide in the treatment of many common retinal diseases, including diabetic macular edema (DME), retinal vein occlusion (RVO), and age-related macular degeneration (AMD) (4). The medicinal agents used in this intervention include vascular endothelial growth factors (VEGF) inhibitors, triamcinolone acetonide, dexamethasone, antibiotics, Bevacizumab (Avastin), and antivirals (5). Bevacizumab is a humanized monoclonal antibody against anti-vascular endothelial growth factor (anti-VEGF) (6), which was used in 2004 for the treatment of colon cancers. Then, it became popular among specialists, including ophthalmologists, for the treatment of various eye diseases such as proliferative diabetic retinopathy, DME, endophthalmitis, neovascularization of the iris, and neovascular glaucoma and edema (7).

Endophthalmitis is an intraocular inflammation with a severe vision threat, which is diagnosed based on clinical signs and symptoms. Its usual symptoms include pain, decreased visual acuity, conjunctivitis, anterior chamber reaction, hypopyon, and vitritis (8, 9). Endophthalmitis is considered acute if it occurs in the first 6 weeks after surgery. Clinical findings in acute endophthalmitis include eye redness, swelling of the eyelids, reduced vision, swollen eyelid, corneal infiltration, fibrin reaction in the anterior chamber, vitreous inflammation, retinitis and retinal peri-phlebitis (10).

Different risk factors are involved in the occurrence of acute endophthalmitis. Endophthalmitis usually occurs due to transmission of the infectious agent following surgery or trauma (11). Evidence shows that topical betadine 5% is effective in reducing the rate of infection after injection and eye interventions, but topical antibiotics before and after interventions do not have a definite effect on reducing the incidence of eye infections (12, 13).

COVID-19 was declared a public health emergency of international concern by the WHO on January 30, 2020, which has posed significant challenges to more than 200 countries and regions worldwide (14). Due to the difficulties caused by this pandemic, the NHS has ordered selective and on-demand services to be suspended to minimize the use of hospital resources, minimize transmission of the virus and increase capacity to deal with the increase in COVID-19 infections, minimizing virus transmission and increasing the capacity to deal with COVID-19. Accordingly, on 28 March 2020, the Royal College of Ophthalmologists (RCOphth) advised eye units to postpone all elective eye operations and non-urgent outpatient clinic (15). In the meantime, there may be a need to prioritize for people who seem to be at the highest risk of vision problems (16). All people visiting hospitals, including patients, use masks to prevent coronavirus disease.

A study by Mason et al. (17) on acute onset of endophthalmitis in patients undergoing intravitreal Bevacizumab (Avastin) (IVB) injection, showed the overall incidence rate of 0.019% (1 in 5233 injections), which has been considered rare. In another study by Hadayer et al. (18), 10 healthy volunteers were requested to put on three distinct surgical face masks designed for professionals, while the amount of air escaping around their eyes was observed. They found that in 81% of the cases, air flow was detected coming from the upper edges of the masks and directed towards the eyes.

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A study by Naguib et al. (19) evaluated the rates of post-intravitreal injection–related endophthalmitis during the COVID-19 pandemic. 41 cases of acute endophthalmitis were observed in the pre-COVID group (0.04%, or one in 2,500 injections), while the post-COVID group had 7 cases (0.03%, or one in 3,333 injections).

Given the increase of using face mask during pandemic and lack of the current evidence in our country, this study aims to evaluate the prevalence of endophthalmitis after intravitreal injection of Avastin (Bevacizumab) in patients using face mask in an eye surgery center.

Methods

After being approved by the ethics committee of Islamic Azad University, Ardabil branch with the code IR.IAU.ARDABIL.REC.1401.099, this prospective cohort study was conducted on 3938 patients who underwent intravitreal injection at the eye surgery center from March 2021 to March 2022. Patients who underwent intravitreal injection of Avastin while wearing a mask during the years 2021-2022 were included in the study. Patients who did not use masks and had incomplete data were excluded from the study. A written letter of introduction was obtained from the officials of the university and selected centers. The objective of the research was explained to all research units and written consent was obtained from them.

The injection was performed in the operating room under sterile conditions and all patients kept their face masks through the entire operation. At first, tetracaine drops were poured into the patient's eyes for local anesthesia 3 times at 5-minute intervals to make them completely numb, then the patients were placed in a lying position on the operating room. Then the eyelids and the skin around the eyes were washed with 5% Betadine (Prep). A sterile surgical drape was used and then an eyelid speculum was placed to open the eyelids. Then the phrenic was washed with 5% Betadine (Povidone-iodine) and then a distance of about 4 mm was measured using a caliper. In the next step, Avastin (1.25 mg) was injected into the eye with a 30-gauge insulin needle syringe. Then chloramphenicol topical drops were used. After that, eyelid speculum was removed and the area around the eyes was dried. The patients were discharged without prescribing medication. They were asked to avoid water contact with their eyes for one day. It should be noted that the masks of the patients were not removed in any of the mentioned steps.

Follow-up of the patients was done one week after discharge to control infection and patients were assessed for endophthalmitis. The diagnosis of endophthalmitis was made based on the patient's symptoms such as eye pain, vision loss and clinical examination of corneal tail, anterior chamber inflammation, presence of hypopyon, reduction of red reflex and vitreous opacity, retinitis and retinal periphlebitis.

Descriptive statistics (frequency, percentage, mean and standard deviation) were used for data analysis and the results were presented in tables and graphs. The data recorded in the checklists were subjected to statistical analysis using SPSS version 25 and chi-square test, and $p < 0.05$ was considered statistically significant.

Results

A total of 3938 patients were included in the study. Of these, 1684 patients (42.8%) were related to 2021 and 2254 patients (57.2%) were related to 2022, consisting of 2229 (56.6%) men and 1709 (43.4%) women. The mean age of male and female patients was 12.36±61.51 and 9.79±61.08, respectively, which did not show a significant difference. The prevalence of endophthalmitis in the study patients was investigated and the results showed that one patient (0.03%) had endophthalmitis. According to the results, the highest

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frequency of intravitreal injection indication was Diabetic Macular Edema (DME) (27.8%) and the lowest frequency was found to be neovascular glaucoma (0.5%) (Table 1). In total, 53.5% of the causes of injection were related to eye complications of diabetes.

Table 1. Evaluation of patients' diagnosis

Variable	Number(%)
Diabetic Macular Edema	1094(27.8)
Diabetic Vitreous Hemorrhage	959(24.4)
Choroidal Neovascularization	1048(26.6)
Central Retinal Vein Occlusion	352(8.9)
Branch Retinal Vein Occlusion	435(11.1)
Neovascular Glaucoma	20(0.5)
Diabetic Tractional Retinal Detachment	30(0.8)

Discussion

In the present study, among people undergoing intravitreal Avastin injection, only one case (0.03%) had severe endophthalmitis during a two-year period. Petel et al. (16) reported that, 85 among 294514 (0.02%) cases of presumed endophthalmitis were found in the "no face mask" group, and 45 among 211454 (0.02%) cases were found in the "universal face mask" group. Their findings were consistent with the present study. Reyes-Capo et al. investigated 71 cases regarding incidence and clinical features of infectious endophthalmitis after intravitreal (IV) injection of Anti-VEGF Agent, of which 15 (0.02%) had endophthalmitis (20).

In a study by Mirghorbani et al., it was found that referrals for intravitreal injection decreased by 41.4% with the emergence of the COVID-19 epidemic (21). In the COVID-19 era, symptoms related to DM remained the most common cause of post-intravitreal injection endophthalmitis, with RVO being the second most common symptom. In the current study, the most common reason for referral was related to diabetic patients, which was similar to the above study (2083 people, 52.9% of all patients). In this study, the second rank was given to Choroidal Neovascularization and RVO was ranked third.

Mirghorbani et al. (21) did not find a significant change in the rate of post-intravitreal injection endophthalmitis (0.02% before the pandemic and 0.036% during the COVID-19 pandemic). This finding was exactly consistent with the results of the present study. However, it is not possible to compare the results with this variable due to the lack of a similar study before the COVID-19 pandemic. By examining similar domestic and foreign studies, it can be said that there was no significant change in the incidence of endophthalmitis before and during the COVID-19 pandemic, and perhaps the use of masks has helped reduce the incidence of such a complication in some studies. Naguib et al. reported the incidence of post-intravitreal injection endophthalmitis to be 0.04% before the pandemic and 0.03% during the pandemic (19), which is exactly in line with the results of the present study. This finding is consistent with previous studies that reported an incidence of 0 to 0.03% in different settings (22, 23).

Published reports are not in the same direction regarding face masks. In some studies, no difference was observed between the use of a mask by the physician and the strategy of not talking about the incidence of endophthalmitis after intravitreal injection (21). The effect of patient facial masks is a relatively new issue that is closely related to the coronavirus epidemic (24). Initially, it was suggested that patient facial masks may be associated with an increased rate of endophthalmitis. There was the concern that the patient facial masks might facilitate the transfer of oral flow to the eye surface and increase the possibility of infection

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after intravitreal injection. Some studies suggested that the border strip above the mask might reduce this concern (25). Raevis et al. showed that worn masks direct more bacteria toward the eye surface, where CFU mask or surgical masks with taped superior edge were found to have the least bacterial dispersion during simulation (25). At the beginning of the COVID-19 pandemic, there were little data on COVID-19 transmission and effective protections. Gradually, it became clear that wearing a face mask is an effective protective measure (26). In this study, no one (i.e., doctors, staff and patients) wore face masks in the pre-COVID-19 era, but doctors used CFU mask during COVID-19 era, and staff and patients used standard surgical masks. The authors found no difference in the rate of endophthalmitis between the pre-COVID-19 (41 of 111,679; 0.04%) and post-COVID-19 (7 of 22,418; 0.03%) groups.

According to a retrospective study, implementing a strict "no talking" policy during the intravitreal injection procedure for a period of two years led to a decreased rate of post-injection endophthalmitis, as well as a reduction in Streptococcus-related endophthalmitis from 0.015% to 0.002% (27). In another study, using a face mask and avoiding talking resulted in a significant reduction in the spread of respiratory flora during intravitreal injections. However, a microbiological study that simulated an injection environment found that even without a face mask or silence, the use of povidone-iodine was associated with the least bacterial growth, highlighting the importance of conjunctival antisepsis in the procedure (24). These findings have been widely adopted, as evidenced by the use of sterile adhesive eye drapes by 82% of 125 ophthalmologists in the UK (28).

According to the results of this study, the incidence of endophthalmitis after intravitreal injection was rare and the face mask of the patients was not associated with the incidence of endophthalmitis after intravitreal injection. Therefore, it is recommended to use a mask to prevent the transmission of diseases such as COVID-19 during surgery.

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