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Evaluation of vitreous cellular activity following per-operative Povidone-iodine alone and combined per-operative Povidone-iodine with topical antibiotic after Intravitreal injection of anti-vascular endothelial growth factor Bevacizumab for retinal pathologies

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Running title: Vitreous cellular activity following per-operative after Intravitreal injection of anti-vascular endothelial growth factor Bevacizumab for retinal pathologies

Abstract:

Purpose: To assess the efficacy of per-operative 5% Povidone-iodine alone or in combination with post injection topical antibiotics for reducing vitreous activity in patients undergoing Intravitreal injection of anti-vascular endothelial growth factors.

Methods: Total of 114 enrolled patients with retinal medical pathologies requiring Intravitreal anti vascular growth factors were randomized to study group A (5% Povidone-iodine per operative on conjunctiva for 3 minutes) and group B (5% Povidone-iodine per-operative on conjunctiva for 3 minutes and post injection topical antibiotics fluroquinolone four times a day for a week) with 57 patients in each group. All Intravitreal injections were performed in operating room in a sterile manner. Vitreous activity assessed using Sun's classification on slit lamp on first day and day 7 post Intravitreal injection of 1.25mg/0.05ml anti VEGF Bevacizumab. Collected data of group A and B was analyzed.

Result: Out of 114 patients, 75 were males and 39 were females. Vitreous activity seen at day one post injection was same in both study groups while at day seven group A had increased vitreous cellular activity as compared to study group B. Both day one and day seven activity within the study groups were insignificant with p=0.244 and p=0.498 respectively.

Conclusions: In both groups A and B, 5% Povidone-iodine (PI) solution shows effective prophylaxis against Endophthalmitis in Intravitreal anti VEGF injections. Post injection topical antibiotics should be avoided following Intravitreal injections of anti VEGF as it can increase microorganism resistance, virulence and add additional cost for the patients.

Keywords: Povidone-iodine (PI), topical antibiotic, Intravitreal injection (IVI), anti-vascular endothelial growth factor (anti VEGF), Bevacizumab, vitreous activity.

Introduction:

Intravitreal injections (IVI) of anti VEGF have revolutionized management of posterior segment pathologies like age related macular degeneration (AMD), diabetic retinopathy (DR), retinal vascular occlusion (RVO) and more[1,2]. Functional and anatomical improvement is

documented with anti VEGF injections such as Bevacizumab, Ranibizumab and Aflibercept in above mentioned pathologies [3]. Anti VEGF, in one way or another, inhibit VEGF-A, reducing macular edema and neo-vessel formation. Selected anti-VEGF is usually administered initially at monthly interval and then according to protocol selected for a period of several months or years, making it the most common performed procedure in USA, Canada and United Kingdom[4,5,6].

IVI being invasive procedure comes with risk of complications with post-injection Endophthalmitis as most devastating, often leading to blindness. A rise in number of IVI has led to the increase in Endophthalmitis[7,8].

Endophthalmitis is defined as intraocular inflammation response to bacterial or fungal infection that commence either in aqueous humor, vitreous humor or both [4,9]. Clinical features may include red eye, ocular pain of varying intensity, decrease vision, anterior chamber inflammation and vitritis[10].

Although incidence of Endophthalmitis is low after IVI of anti VEGF[4,10], the risk increases with repeated injections. Prompt diagnosis and intervention can save vision and the eye.

In terms of prophylaxis, topical application of antibiotics before and after IVI injection is being used. Several studies showed no beneficial results [11,12,13,14] in prevention of and surprisingly it may increase the risk of post injection Endophthalmitis [15,16]. This could be related to alteration of ocular flora and developing microorganism resistance to repeated exposure of topical antibiotics in anti VEGF injections[16,17].

Current evidence shows topical application of PI as most effective prophylaxis measure in reducing post injection bacterial infection. Levinson et al demonstrated that using PI after placement of lid speculum result in reduced contact between eye lid and site of injection, decreasing incidence of Endophthalmitis. However, PI antisepsis does not reduce risk of Endophthalmitis to nil after Intravitreal injection of anti VEGF[18].

The aim of the comparative, prospective and interventional study is to assess efficacy of per-operative 5% topical PI and combined 5% PI and topical antibiotic (Fluroquinolone 0.3%) post injection of anti VEGF in prevention of Endophthalmitis. The study is sought to evaluate vitreous activity which help predict prophylaxis regime useful for prevention of post-injection endopthalmitis.

Materials and method:

After getting approval from the ethical review board of Sir Ganga Ram hospital/ Fatima Jinnah Medical University (certificate attached), a total of 114 patients with macular edema due to various retinal pathologies, documented clinically and diagnostically with Topcon-3D OCT-2000 were inducted in the study. Consent was taken from each patient for study purpose. Patients allocated in either group using randomized controlled trial with restricted block sample technique. Sample size came out to be 57 eyes in each group with 38% population proportion. Inclusion criteria included macular edema due to retinal pathology, above 20 years, clear cornea and no anterior chamber or vitreous activity. Exclusion criteria included presence of eye with any ocular infection, corneal opacity, any anterior chamber and vitreous activity, vitreous hemorrhage and dense cataract that obscure view of posterior segment assessing vitreous activity. Baseline data included best corrected visual activity (BCVA), anterior segment examination with slit lamp, posterior segment examination using 78D non-contact lens for vitreous activity and retina. OCT was done to document macular edema. Grading of vitreous activity with slit lamp beam of 1x2mm using Sun classification group [19] was used for post injection assessment of vitreous activity.

Group A (57patients) were treated with conjunctival instillation of 5% PI for three minutes while group B (57patients) received both 5% PI for three minutes and post injection topical antibiotics (flouroquinolone, 0.3%) four times a day for five days.

All cases were treated in eye operation theatre by single surgeon. Theatre specimens and swabs are regularly sent for microbiological testing and culture to keep it contaminated free. All patients followed same treatment regime wearing

disposable gown, surgical masks and head caps. Surgeon protocol included face mask, surgical scrubbing, wearing sterile gown and gloves. Following topical application of 1% proparacaine, periorbital skin, eyebrows, eyelids and eyelashes was disinfected with 5% PI for 5 minutes. Sterile eye drape and eye speculum applied. 5% PI in sterile syringe is instilled on conjunctival sac for three minutes. Under operating microscope, freshly prepared prefilled, sealed injection of 1.25mg/0.05ml Bevacizumab (Avastin) in 30 gauge insulin syringe, obtained from pharmacist for every patient, was opened and IVI in mid-vitreous cavity through supero-temporal quadrant in right eye and superonasal quadrant in left eye, 3.5mm from limbus in pseudophakic eyes and 4 mm in phakic eyes. Following injection, needle was pulled away from injection site, conjunctiva gently massaged and eye pad applied for 4 hours.

Avastin injection is prepared in well reputed hospital pharmacy in highly sterile area. It is dispensed and prepared under laminar air flow (LAF) in control environment by air handling unit (AHU) (HVAC system) i.e temperature, air pressure, air changes etc. After withdrawal of the dose, Avastin syringe recapped carefully to avoid unnecessary exposure to minimize contamination or mishandling. Then dispensing dose is stored in air tight packaging, highly sterile refrigerator at 2-6 degree centigrade. The area is sterilized by UV light after every 2 hours and packaging is sterilized by UV and isopropyl alcohol (IPA).

In group A, after completion of procedure (5% PI alone), patient discharged and follow up done on first post-injection day using slit lamp and Sun classification for assessment and grading of vitreous activity. Second follow up was done on day 7 post injection using same clinical examination parameters.

In group B, on completion of above mentioned procedure with 5% topical PI and IVI of Avastin, post injection topical antibiotic (flouroquinolone 0.3%) advised four times a day for five days. follow up protocol was same as group A.

Using slit lamp beam 1x2 mm, vitreous activity was graded according to Sun classification as:

Grade	Number of cells
0	0
0.5+	1-5
1+	6-10
2+	11-20
3+	21-50
4+	> 50

Results:

Out of 114 patients, 75 were males and 39 females. 57 were included in group A whereas 57 in group B. In group A, 42 males (56%) and 15 females (38.5%) while in group B, 33 (57.9%) males and 24 (42.1%) females were seen. Looking at study group, males dominated in both groups

Age ranged between 20-65 years with mean of 54.47±9.68SD. In group A, 21 (44.7%) patients age was ≤ 55years and 36 (53.7%) patients were > 55 years. In group B, 26 patients (55.3%) aged ≤ 55 years while 31 patients (46.3%) were aged > 55 years.

Table 1: Socio-Demographic Characteristics of the Study Groups

Variables		Study Group A n=57	Study Group B n=57	Total	p-value
Age (Years) 54.47±9.68*	≤ 55	21 (44.7%)	26 (55.3%)	47	0.341
	> 55	36 (53.7%)	31 (46.3%)	67	
Sex	Male	42 (56.0%)	33 (44.0%)	75	0.076
	Female	15 (38.5%)	24 (61.5%)	39	

*Mean±SD

Out of 114 patients, 76 patients (66.7%) were diagnosed with diabetic macular edema, 27 patients (23.7%) with age related macular detachment, and 11 patients (9.6%) with branch retinal vein occlusion with macular edema.

Patients examined and graded for vitreous activity on day 1 post IVI Avastin on slit lamp using sun classification. In group A 54 (94.7%) showed no cellular activity with vitreous graded as 0. Grade 1 comprising of 6-10 cells was observed in 2 patients (3.5% %) and grade 2 (11-20 cells) were observed in 1

patient (1.8%). In Group B, 53 (93%) showed no vitreous cellular activity graded as grade 0. Vitreous activity of grade 0.5 was observed in 2 patients (3.5%). grade 1 was seen in 2 (3.5%). Thus, there was higher vitreous activity at day 1 seen in the study group B than study group A.

Day seven post injection follow up for group A was insignificant showing previous picture; However, in group B, 2 patients improved further and showed grade 0 vitreous activity increasing the number from 53 (93%) to 55 (96.5%). Those 2 patients that were previously graded as 0.5 were the ones improving to grade 0. Rest was insignificant with 2 patients as grade 1 and none in grade 2. Those patients with persistent vitreous activity on second follow-up in group A (grade 1 in 2 patients and grade 2 in 1 patient) and group B (grade 1 in 2 patients) were kept under daily follow up. Vitreous activity settled within a week requiring no intervention of any kind. Though the vitreous activity at day seven was higher in study group A than patients in group B; However, all of the attributes were insignificant statistically. (Table 2)

Table 2: Grades of Vitreous Activity within the Study Groups

Variables		Study Group A n=57	Study Group B n=57	Total	p-value
Grades (Day1)	0	54 (94.7%)	53 (93%)	107	0.244*
	0.5+	00	02 (3.5%)	2	
	1+	02 (3.5%)	02 (3.5%)	4	
	2+	01 (1.8%)	00	1	
Grades (Day7)	0	54 (94.7%)	55 (96.5%)	109	0.498*
	1+	02 (3.5%)	02 (3.5%)	4	
	2+	01 (1.8%)	00	1	
Total		57 (100%)	57 (100%)	114	

*Fisher Exact Test

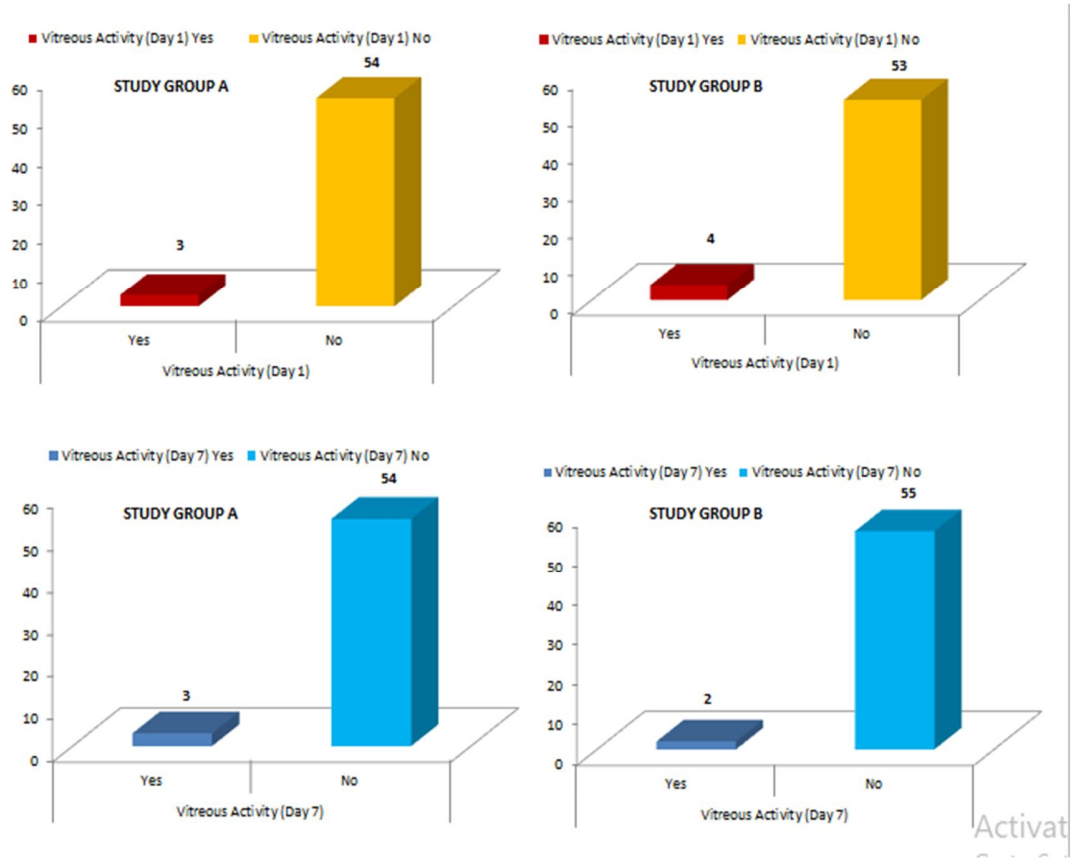

Figure I: Vitreous activity at day 1 and day 7 within the study groups.

There was slightly more vitreous cellular activity seen at day one in group B (4 patients) than group A (3 patients) on first post injection day. On day seven post injection the study group A had persistent vitreous activity in 3 patients (two in

grade 1 and one in grade 2) as compared to study group B where only 2 patients showed vitreous cells in grade 1. Both day one and day seven post injection activities within the study groups were insignificant with p=0.244 and p=0.498 respectively. (Figure 1)

Discussion

Worldwide, retinal specialists have incorporated intravitreal injections into their armamentarium for treatment of various retinal pathologies [20,21,22]. Of these, anti VEGF top the list due to its relative efficacy, resulting in millions of these injections administered annually. IVI of Avastin, which is the drug used for our study purpose is routinely compounded by authorized hospital pharmacy into prefilled ready to use syringe following strict aseptic measures. Alternatively, a single manufacturer vial may be used.

Risk of intraocular inflammation in the form of either sterile endophthalmitis or more grave visually blinding endophthalmitis is a cause of concern with intravitreal injections. Controversies exist regarding patient's pathology, type of injection, protocols of application and its frequency[20,21,22]. Though clinical trials have provided safety protocols of intravitreal injection, still concerns regarding injection application and intraocular inflammation may not be fully answered.

Our study protocol was based on pre-injection topical PI 5% use for three minutes as protective prophylactic measure in both groups A and B with 57 patients each. In addition, Group B was given topical antibiotics (flouroquinolone 0.3%) post injection four times a day for five days. Rest of injection protocol was identical for both groups in terms of operation theatre, pupil dilatation; sterile gowns wear by patient and surgeon, masks, gloves, sterile draping and lid speculum with Intravitreal injection of 1.25mg/0.05ml Avastin under microscope. Our study showed minimal vitreous activity on first op day with 54 patients (94.7%) showing grade 0 in group A (PI only) and 53 patients (93%) in group B (PI and topical fluroquinolone). On first week follow up further improvement was seen in group B with 55 patients (96.5%) showing grade 0. Group A remained the same. No intervention of any kind was needed and patient remained visually and anatomically stable. Both day one and first week vitreous activities within the study groups A and B were insignificant with p=0.244 and p=0.498 respectively. No intravitreal injection related endophthalmitis was seen in our study groups. Several studies have reported clusters of sterile endophthalmitis following intravitreal injection of Bevacizumab.

Fiden et al reported multiple cases of sterile endophthalmitis with Bevacizumab with higher levels of endotoxin [23]. Yamashiro et al also reported a cluster of cases of sterile endophthalmitis related to a batch of Bevacizumab that was speculated to be contaminated with endotoxins [24]. Similarly, Wickremasinghe et al documented similar findings of sterile endophthalmitis with bevacizumab, suggested possible speculations of endotoxins, immune sensitization with repeated injections and or compromised storage of drug[25].

Our study group used ready to use preformed compounded Bevacizumab (Avastin) injection due to financial restriction and cost effectiveness. With minimal vitreous activity which settled within a week requiring no intervention proves that handling, collection and application of injection was satisfactory. Goldberg et al have reported outbreak of Bevacizumab related endophthalmitis previously [26].

In United States, Intravitreal injections are predominantly given in office settings while in Europe it's preferred in operating room. In our study, all IVI injections were performed in operating theatre with same procedural guidelines. This might be one of the reasons of grade 0 vitreous cellular activity in majority of our study cases in both groups. Abell et al found that endophthalmitis occurrence was lower in patients injected in operating room than in office based setting [27].

The use of topical antibiotics as prophylaxis does not reduce the risk of endophthalmitis following intravitreal anti VEGF injection, instead documented reports show higher incidence of such events [14,28] and greater antibiotic resistance [29,30]. Our study did not use pre injection topical antibiotics but received post injection topical antibiotics for five days in group B.

Difference in vitreous activity with or without topical antibiotics remained insignificant in our study of p=0.244 and p=0.498 respectively.

The use of topical 5% PI is the most widely used antiseptic and disinfectant for any kind of ocular surgery. Its efficacy in different concentration is tried for Intravitreal injection. Several studies documented better tolerability and lesser corneal damage with lower PI concentration when using 2.5% and absent corneal damage when using 1% and 0.5% [31]. Our study used 5% PI and found favorable results with minimal vitreous cellular activity and no endophthalmitis. However, we did not include tolerability or corneal damage in our study criteria. Michele Reibaldi et al in their study used 0.6% preservative free PI drops as prophylaxis drops instilled three times a day 3 days before and one drop on day of intravitreal injection, along with preinjection 5% PI [32]. They studied the bacterial growth on conjunctival swab and injection needle and found culture conjunctival growth reduction from 74% to 14%. This proved that lower concentration of PI is well tolerated with no safety concerns.

Use of topical antibiotics in conjunction with 5% PI did not have any additional favorable effects in our group B patients. Both groups with and without topical antibiotics had satisfactory (> 90%) vitreous grading 0. Several studies have shown that no apparent beneficial effect of topical antibiotics before or after IVI injection of anti VEGF on rates of endophthalmitis [11,12,13,14]. In fact it may increase the risk of endophthalmitis [15,16] due to multiple exposures to topical antibiotic drops which alters ocular flora, increase virulence and resistance of organisms coming in contact with ocular surface [16,17]. Another important factor to consider is the cost. Using pre or post injection topical antibiotics puts financial burden on patients. Bande MF et al also documented benefit of low cost of treatment without topical antibiotic prophylaxis for Intravitreal injections [15].

Limitation of study

The study sample size was small and only one type of IVI of anti VEGF (Bevacizumab) was studied due to financial restraints. Short follow up is another limitation factor. Study is single centered. Multicenter study is required to have greater impact on the results.

Conclusion

The present study provides evidence of effectiveness of 5% PI as a good prophylactic agent with antiseptic and disinfectant properties in controlling post injection vitreous cellular activity. Post injection topical antibiotics following IVI of anti VEGF should be avoided as it can increase microorganism resistance, virulence and add additional cost for the patients.

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Ethics declarations

Conflict of interest

Huma Kayani Saigol 1, Seemab Akbar, Haroon Tayyab, Shahzad Saeed, Khurram Chuhan, Abdul Rauf, all authors have no conflicts of interest that are directly relevant to the content of this review.

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References:

1. Fileta JB, Scott IU, Flynn HW Jr. Meta-analysis of infectious endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. Ophthalmic Surg Lasers Imaging Retina 2014 Mar; 45(2): 143-9.
2. Garg SJ, Dollin M, Hsu J, Vander JF, Storey P. Effect of a strict 'no-talking'policy during intravitreal injection on

post-injection endophthalmitis. Ophthalmic Surgery, Lasers and Imaging Retina. 2015 Nov; 46(10):1028-34.

3. Moshfeghi AA, Rosenfeld PJ, Flynn Jr HW, Schwartz SG, Davis JL, Murray TG, et al. Endophthalmitis after Intravitreal Anti-Vascular Endothelial Growth Factor Antagonists: A Six-Year Experience at a University Referral Center. Retina. 2011 Apr; 31(4):662-8.
4. Durand ML. Endophthalmitis. Clin Microbiol Infect. 2013 Mar; 19:227-34.
5. Campbell RJ, Bronskill SE, Bell CM, Paterson JM, Whitehead M, Gill SS. Rapid expansion of intravitreal drug injection procedures, 2000 to 2008: a population-based analysis. Archives of Ophthalmology. 2010 Mar; 128(3):359-62.
6. Williams GA. IVT injections: health policy implications. Review of Ophthalmology 2014; June. Available at: http://bit.ly/2uo84kl (Accessed September 2, 2020).
7. Shah CP, Garg SJ, Vander JF, Brown GC, Kaiser RS, Haller JA, Team PI. Outcomes and risk factors associated with endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. Ophthalmology. 2011 Oct; 118(10):2028-34.
8. Mccannel CA. Meta-analysis of endophthalmitis after intravitreal injection of antivascular endothelial growth factor agents: causative organisms and possible prevention strategies. Retina. 2011 Apr; 31(4):654-61.
9. O'Callaghan RJ. The pathogenesis of Staphylococcus aureus eye infections. Pathogens. 2018 Mar; 7(1):9.
10. Gregori NZ, Flynn HW, Schwartz SG, Rosenfeld PJ, Vaziri K, Moshfeghi AA, et al. Current infectious endophthalmitis rates after intravitreal injections of anti-vascular endothelial growth factor agents and outcomes of treatment. Ophthalmic Surgery, Lasers and Imaging Retina. 2015 Jun; 46(6):643-8.
11. Doshi RR, Leng T, Fung AE. Povidone-iodine before lidocaine gel anesthesia achieves surface antisepsis. Ophthalmic Surgery, Lasers and Imaging Retina. 2011 Jul; 42(4):346-9.
12. Bhavsar AR, Stockdale CR, Ferris FL, Brucker AJ, Bressler NM, Glassman AR. Diabetic Retinopathy Clinical Research Network. Update on risk of endophthalmitis after intravitreal drug injections and potential impact of elimination of topical antibiotics. Archives of ophthalmology. 2012 Jun; 130(6):809-10.
13. Bhavsar AR, Googe JM, Stockdale CR, Bressler NM, Brucker AJ, Elman MJ, et al. Risk of endophthalmitis after intravitreal drug injection when topical antibiotics are not required: the diabetic retinopathy clinical research network laser-ranibizumab-triamcinolone clinical trials. Archives of ophthalmology. 2009 Dec; 127(12):1581-3.
14. Cheung CS, Wong AW, Lui A, Kertes PJ, Devenyi RG, Lam WC. Incidence of endophthalmitis and use of antibiotic prophylaxis after intravitreal injections. Ophthalmology. 2012 Aug; 119(8):1609-14.
15. Bande MF, Mansilla R, Pata MP, Fernández M, Blanco-Teijeiro MJ, Piñeiro A, et al. Intravitreal injections of anti-VEGF agents and antibiotic prophylaxis for endophthalmitis: a systematic review and meta-analysis. Scientific reports. 2017 Dec; 7(1):1-6.
16. Menchini F, Toneatto G, Miele A, Donati S, Lanzetta P, Virgili G. Antibiotic prophylaxis for preventing endophthalmitis after intravitreal injection: a systematic review. Eye. 2018 Sep; 32(9):1423-31.
17. Yin VT, Weisbrod DJ, Eng KT, Schwartz C, Kohly R, Mandelcorn E, et al. Antibiotic resistance of ocular surface flora with repeated use of a topical antibiotic after intravitreal injection. JAMA ophthalmology. 2013 Apr; 131(4):456-61.
18. Levinson JD, Garfinkel RA, Berinstein DM, Flory M, Spellman FA. Timing of povidone–iodine application to reduce the risk of endophthalmitis after intravitreal injections. Ophthalmology Retina. 2018 Jul; 2(7):654-8.
19. Cantor LB, Rapuano CJ, Cioffi GA. Intraocular Inflammation and Uveitis. 9th rev. ed. San Francisco: American Academy of Opthalmology; 2016-17. 96 p.

20. Aiello LP, Brucker AJ, Chang S, Emmett T Cunningham Jr, D'amico Dj, Harry W Flynn Jr, et al. Evolving guidelines for intravitreous injections. Retina. 2004 Oct; 24(5):S3-19.
21. Jager RD, Aiello LP, Patel Sc, Cunningham Jr ET. Risks of intravitreous injection: a comprehensive review. Retina. 2004 Oct; 24(5):676-98.
22. TA CN. Minimizing the risk of endophthalmitis following intravitreous injections. Retina. 2004 Oct; 24(5):699-705.
23. Fielden M, Nelson B, Kherani A. Acute intraocular inflammation following intravitreal injection of bevacizumab–a large cluster of cases. Acta ophthalmologica. 2011 Dec; 89(8):e664-5.
24. Yamashiro K, Tsujikawa A, Miyamoto K, Oh H, Otani A, Tamuara H, et al. Sterile endophthalmitis after intravitreal injection of bevacizumab obtained from a single batch. Retina. 2010 Mar; 30(3):485-90.
25. Wickremasinghe SS, Michalova K, Gilhotra J, Guymer RH, Harper CA, Wong TY, Qureshi S. Acute intraocular inflammation after intravitreous injections of bevacizumab for treatment of neovascular age-related macular degeneration. Ophthalmology. 2008 Nov; 115(11):1911-5.
26. Goldberg RA, Flynn Jr HW, Isom RF, Miller D, Gonzalez S. An outbreak of streptococcus endophthalmitis after intravitreal injection of bevacizumab. American journal of ophthalmology. 2012 Feb; 153(2):204-8.
27. Abell RG, Kerr NM, Allen P, Vote BJ. Intravitreal injections: is there benefit for a theatre setting? British J ophthalmology. 2012 Dec; 96(12):1474-8.
28. Storey P, Dollin M, Pitcher J, Reddy S, Vojtko J, Vander J, et al. Post-Injection Endophthalmitis Study Team. The role of topical antibiotic prophylaxis to prevent endophthalmitis after intravitreal injection. Ophthalmology. 2014 Jan; 121(1):283-9.
29. Milder E, Vander J, Shah C, Garg S. Changes in antibiotic resistance patterns of conjunctival flora due to repeated use of topical antibiotics after intravitreal injection. Ophthalmology. 2012 Jul; 119(7):1420-4.
30. Reibaldi M, Pulvirenti A, Avitabile T, Bonfiglio V, Russo A, Mariotti C, et al. Pooled estimates of incidence of endophthalmitis after intravitreal injection of anti–vascular endothelial growth factor agents with and without topical antibiotic prophylaxis. Retina. 2018 Jan; 38(1):01-11.
31. Jiang J, Wu M, Shen T. The toxic effect of different concentrations of povidone iodine on the rabbit's cornea. Cutaneous and ocular toxicology. 2009 Jan; 28(3):119-24.
32. Reibaldi M, Avitabile T, Bandello F, Longo A, Bonfiglio V, Russo A, et al. The effectiveness of 0.6% povidone iodine eye drops in reducing the conjunctival bacterial load and needle contamination in patients undergoing anti-vegf intravitreal injection: a prospective, randomized study. Journal of clinical medicine. 2019 Jul; 8(7):1031.