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RETINAL DISORDERS

Minimizing the endophthalmitis rate following intravitreal injections using 0.25 % povidone–iodine irrigation and surgical mask

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Abstract
Background To examine the efficacy of complying with an infection control manual for intravitreal injection of anti-vascular endothelial growth factor (VEGF) preparations in reducing the rate of endophthalmitis.
Methods We retrospectively reviewed intravitreal anti-VEGF injections conducted by vitreoretinal specialists at the outpatient injection room of a single university hospital between July 2009 and July 2012. The injections were conducted following an infection control manual established by our department. Doctors and nurses wore surgical masks, and disinfected the patient's eyelid skin with 10 % povidone–iodine and then the conjunctiva with 0.25 % povidone–iodine. After putting a drape on the patient's face, a lid speculum was placed. The conjunctival surface was again washed with 5 ml of 0.25 % povidone–iodine. After waiting at least 30 seconds, intravitreal injection was performed through povidone–iodine. Following injection, the injection site was again washed with 5 ml of 0.25 % povidone–iodine. Patients were treated with topical levofloxacin 4 times a day for 3 days before and after the injection.
Results A total of 15,144 injections comprising 548 injections of pegaptanib sodium, 846 injections of bevacizumab, and 13,750 injections of ranibizumab were performed. During this period, no case of suspected or proven infectious endophthalmitis occurred. The endophthalmitis rate was 0 per 15,144 injections, (95 % confidence interval, 0.0–0.0 %).
Conclusion The results suggest that endophthalmitis can be reduced to a minimum by preventing normal flora of the conjunctiva and bacteria in the oral cavity from entering the vitreous. For this purpose, an infection control manual that requires nurses and doctors to wear surgical mask and drape the patient's face, irrigate the conjunctiva with 0.25 % povidone–iodine and wait at least 30 seconds before performing intravitreal injection is useful.

Keywords Bevacizumab · Conjunctival flora · Endophthalmitis · Eye drape · Eyelid speculum · Face mask · Intravitreal injection · Oral flora · Pegaptanib · Povidone–iodine · Ranibizumab · Vascular endothelial growth factor

Introduction

Topical antibiotics and povidone–iodine are widely used for reducing the ocular surface bacterial load during intravitreal injections. However, Moss et al. [1] showed that although topical gatifloxacin use is effective in reducing the frequency of conjunctival bacterial growth, antibiotic use confers no additional benefit in combination with povidone–iodine than eyes receiving povidone–iodine alone. Therefore povidone–iodine is a more effective agent than antibiotics for infection prophylaxis in intravitreal injections. In a prospective multicenter study reported by Stewart et al. [2] in 2011, culture of the needles that had been used to perform intravitreal injection after povidone–iodine disinfection yielded bacteria from 18 % of the needles. This result suggests that disinfection with povidone–iodine by conventional methods cannot effectively kill the bacterial flora that inhabit the complicated structures of the conjunctiva.

To obtain transient sterilization of the conjunctiva, it is essential to use a volume of povidone–iodine that infiltrates the complicated structure [3], wait for the bactericidal effect to take place [4], and inject through the povidone–iodine used

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in washing. Since a 22-gauge needle is used for intravitreal injection [5], the povidone–iodine that enters the vitreous via the needle has important clinical implications with respect to ocular toxicity. Therefore, repeated washing with a concentration of povidone–iodine that is safe for ocular tissues is essential [6, 7]. We reported that in 25-gauge vitrectomy, irrigating the surgical field with 0.25 % povidone–iodine after placing the lid speculum and waiting for at least 30 seconds before creating three sclerotomies with trocars reduced bacterial contamination of the vitreous to 0 % (0/103 eyes) [7].

In operating rooms, doctors and nurses wear surgical masks; therefore, deposition of oral flora onto the operative field is probably adequately prevented.

Face masks are not generally used in preparation and administration of intravitreal injections [8]. Hence, deposition of oral bacterial flora on the injection site or the needle tip may be a potential cause of endophthalmitis. A meta-analysis of endophthalmitis following intravitreal injection of anti-VEGF agents reported by McCannel [9] in 2011 shows that *Streptococcus* species are isolated approximately three times more frequently after intravitreal anti-VEGF injection than after intraocular surgery. It is speculated that the *Streptococcus* species originate from the respiratory tract. An experimental study has proven that use of a surgical mask or silence effectively decreases the oral flora contamination of intravitreal injections, and that application of 5 % povidone–iodine prevents bacterial growth even when bacteria have deposited on the injection site [10].

With this background, we prepared an infection control manual for anti-VEGF intravitreal injection, which requires nurses and doctors to wear surgical masks, drape the patient's face as a substitute for a mask, irrigate the conjunctiva with 5 ml of 0.25 % povidone–iodine, and wait at least 30 seconds before performing intravitreal injection. We report here that by complying with the infection control manual, we have achieved an extremely low endophthalmitis rate of 0/15,144 intravitreal injections performed by vitreoretinal specialists in an outpatient office setting.

Methods

Between July 2009 and July 2012, vitreoretinal specialists at Surugadai Hospital of Nihon University performed intravitreal injections of anti-VEGF agents in accordance with an infection control manual compiled at the hospital. Intravitreal injections were conducted in an outpatient injection room, which is separated from the outpatient clinic and equipped with two microscopes and a bed. Physicians and nurses working in the injection room wore white coats and sterile caps and surgical masks. The caps and masks were changed twice a day (morning and afternoon). Preoperative antisepsis was conducted by ocular instillation of topical antibiotics (levofloxacin) 4 times a day for 3 days before intravitreal injection. Single-use topical antibiotic was used in each injection.

The patient, wearing his/her own clothes, was instructed to lie on the bed without taking off the shoes. The patient wore a sterile cap but not a mask. A nurse was always present to provide assistance. During injection, the physician and the nurse refrained from talking, coughing, and sneezing. The physician disinfected the eyelid skin with 10 % povidone–iodine (Meiji Seika, Tokyo, Japan) and the conjunctiva with 0.25 % povidone–iodine diluted in physiological saline. Using sterile gloves, a sterile drape was placed on the upper body of the patient, and a sterile adhesive eye drape on the eye. After placing the lid speculum, 4 % xylocaine was instilled. The conjunctiva was irrigated with 5 ml of 0.25 % povidone–iodine. After waiting for at least 30 seconds, with residual 0.25 % povidone–iodine remaining in the conjunctival sac, 2 % xylocaine was injected subconjunctivally into a predetermined site. A caliper was used to determine a site 4 mm from the limbus, and the conjunctiva was displaced with the caliper toward the cornea. With the eye ball immobilized with the caliper, intravitreal injection was performed through povidone–iodine using a 30-gauge needle attached to a syringe. To prevent vitreous reflux, the site of injection was gently compressed with a cotton tip. Then the conjunctiva was again irrigated with 5 ml of 0.25 % povidone–iodine, followed by instillation of topical antibiotics. After injection, no eye patch was worn, and topical antibiotics (levofloxacin) was instilled 4 times a day for 3 days. The patient was educated about the symptoms of endophthalmitis and the need for immediate consultation should the symptoms arise. Appropriate follow-up appointments were scheduled.

Statistical analysis of the data was performed using SPSS software for Windows, version 12 (SPSS, Chicago, IL, USA).

Results

A total of 15,114 injections comprising 548 injections (215 eyes) of pegaptanib sodium, 846 injections (270 eyes) of bevacizumab, and 13,750 injections (2,350 eyes) of ranibizumab were performed. All patients in this study had at least 2 months follow-up after an injection. There was no case of suspected or proven infectious endophthalmitis. The endophthalmitis rate was 0 per 15,114 injections (95 % confidence interval, 0.0–0.0 %).

Discussion

In the present study, by performing office-based intravitreal anti- VEGF injection according to an infection control manual prepared for a single university hospital, we achieved a very low endophthalmitis rate of 0/15,114 injections.

Between 2006 and 2012, 22 papers on infectious endophthalmitis following intravitreal anti-VEGF injections, which each evaluated over 3,000 injections, were published (Table 1) [11–32]. The cumulative average endophthalmitis rate was 141/291,328 or 0.048 %. This rate is similar to the reported frequencies of endophthalmitis after cataract surgery, typically 0.048 % (109 of 225,471 eyes) [33] and 0.052 % (52 of 100,539 eyes) [34]. If one considers that intravitreal injections are often conducted several times in the same eye, there is an urgent need to reduce the infection rate further.

Much progress has been made in research on the risk factors associated with endophthalmitis following intravitreal injections of anti-VEGF agents. The factors that have no significant association with the risk include use of lid speculum, [26] conjunctival displacement, [26] injection site (inferior hemisphere or superior hemisphere), [26] and type of anti-VEGF agent (bevacizumab or ranibizumab) [26].

Reducing bacteria in the operative field is an important factor to prevent endophthalmitis. Use of povidone–iodine [10, 35], use of surgical mask [10, 36], and silence when a surgical mask is not used [10, 36] have been shown to be effective measures to achieve ocular surface antisepsis.

Table 1 Studies of the rate of endophthalmitis following anti VEGF agent injection (more than 3,000 injections in each study)

Study	Suspected or proven endophthalmitis cases	Number of injections	Endophthalmitis rate (%)
Rosenfeld et al. [11] (MARINA)	5	10,443	0.048
Fung et al. [12]	1	7,113	0.014
Singerman et al. [13] (VISION)	12	7,545	0.159
Fintak et al. [14]	6	26,905	0.022
Mason et al. [15]	1	5,233	0.019
Pilli S et al. [16]	3	10,254	0.029
Wu et al. [17]	7	4,303	0.163
Diago et al. [18]	3	3,874	0.077
Artunay et al. [19]	2	3,022	0.066
Klein et al. [20]	15	30,736	0.049
Brown et al. (ANCHOR) [21]	3	5,921	0.096
Lima et al. [22]	3	3,068	0.098
Bhavsar et al. (DRCR.net) [23]	3	3,226	0.093
Moshfeghi et al [24]	12	60,322	0.020
Inoue et al. [25]	5	5,236	0.095
Shah et al. [26]	23	27,736	0.083
Inman & Anderson [27]	0	4,690	0
Chen et al. [28]	11	29,995	0.037
Bhatt et al. [29]	5	7,054	0.071
Martin et al. (CATT group) [30]	6	10,957	0.055
Lad et al. [31]	8	8,802	0.045
Cheung et al. [32]	7	14,893	0.047
Total	141	291,328	0.048

The major route of transmission of the bacteria contaminating the vitreous body during intravitreal injection is considered to be direct inoculation via the needle during injection. As mentioned above, to obtain transient sterilization of the conjunctiva, it is essential to use a volume of povidone–iodine that infiltrates the complicated structure [3], wait for the bactericidal effect to take place [4], and inject through the povidone–iodine used in washing [6, 7].

First, the povidone–iodine concentration has to be nontoxic for ocular tissues. The bactericidal effect of povidone–iodine has been observed over a wide range of concentrations from 0.005 % [37] to 10 %. Jiang et al. [38] reported that corneal epithelial cell damage was observed with 0.5 ml of 2.5 % povidone–iodine, and endothelial cell damage with 0.05 ml of 1.5 % povidone–iodine, and therefore recommended that povidone–iodine at 1.0 % or lower is safe. No damage to rabbit retina was observed after intravitreal injection of 0.1 ml of 0.4 % povidone–iodine [39] or 0.1 ml of 0.5 % povidone–iodine [40]. From their studies, Trost et al. [40] stated that 0.05 0.5 % povidone–iodine is safe for ocular tissues. The 0.25 % solution that we use is the intermediate value between 0.05 and 0.5 %, and a concentration that is safe even if introduced into the intraocular environment [6, 7].

Second, the volume of povidone–iodine has to be large enough to infiltrate the conjunctival structures. Since bacteria of the conjunctival flora are sheltered between complex structures of the conjunctiva, applying a few drops of povidone–iodine does not attain sufficient bactericidal effect. Miño de Kaspar et al. [3] reported that irrigation of the conjunctival fornices with 10 ml of 5 % povidone–iodine before cataract surgery significantly reduced conjunctival bacterial flora compared to applying two drops of povidone–iodine on the conjunctiva.

Third, adequate time has to be allowed for povidone–iodine to act. The time taken for povidone–iodine to kill bacteria is shorter at concentrations of 0.1 1.0 % (15 sec) than at concentrations of 2.5 10 % (30 120 sec) [4]. We use 0.25 % povidone–iodine to wash the surgical field, and wait for 30 seconds before performing intravitreal injection through povidone–iodine. In Europe and America, 5 % povidone–iodine instillation is widely used during intravitreal injections. When 5 % povidone–iodine is used, it is also essential to use a volume of at least 5 ml and wait for at least 30 seconds before injecting intravitreally.

During talking, coughing, or sneezing without a surgical mask, infectious droplets containing saliva and oral flora such as *Streptococcus* species may fall onto the ocular surface or needle [9, 28]. As is practiced in intraocular surgeries, the patient's face is covered with a drape as a substitute for a surgical mask, to prevent deposition of oral flora onto the injection site. Although silence has been reported to be effective to prevent contamination by oral

flora even without using a mask [36], surgical mask wearing is considered necessary if doctors, assistants, or patients with upper respiratory infections are involved in intravitreal injections [9].

In the present study, antibiotic was instilled 4 times a day for 3 days before intravitreal injection. In a survey of retinal specialists in the United States published in 2011, 34 % of the doctors used antibacterial eye drop before intravitreal injection [41]. Topical antibiotics require much longer killing time (approximately 60 minutes) than povidone–iodine (approximately 60 seconds). Therefore, when antibiotics are given immediately prior to an intravitreal injection, there is insufficient time for adequate bactericidal effect [42]. Therefore, injection of antibiotics either before the day of injection or immediately prior to injection is not generally recommended [43]. A recent prospective study found that topical moxifloxacin 0.5 % had no additional effect on reducing conjunctival bacterial counts beyond the effect of 5 % povidone–iodine alone [44].

In the present study, antibiotic was instilled 4 times a day for 3 days after intravitreal injection. In a survey of retinal specialists in the United States, 81 % of the doctors use antibacterial eye drop after intravitreal injection [41]. In the case of bacterial contamination in intravitreal injection, bacteria are inoculated into the vitreous. However, the antibacterial eye drop used after intravitreal injection does not penetrate the vitreous adequately [45]. Since topical fluoroquinolone instillation before and after intravitreal injection is repeatedly used in a patient, the emergence of resistant bacteria is an issue [46]. A study reported a higher incidence of endophthalmitis when antibiotic prophylaxis was used after intravitreal injections compared with no antibiotic use [32]. The common practice of repeated use of fluoroquinolone before and after intravitreal injection in many facilities has to be re-examined.

This study was conducted in a single center. All the patients were followed for at least 2 months after surgery. Review of all the clinical charts found no case of endophthalmitis after intravitreal injection detected in our department and no case treated for endophthalmitis in other facilities. Therefore, we are confident that the endophthalmitis rate was 0 per 15,144 injections.

A limitation of the present study is that it was a retrospective single-center consecutive case series and not a controlled study. Without a control group, it is not possible to delineate which factors are important. Apart from the factors discussed above, other measures that we undertake routinely, such as perioperative topical antibiotics may also contribute to the low rate. However, this study does show that if the exact protocol described by the current paper is followed, it may be possible to achieve the same low risk of endophthalmitis.

If use of surgical mask further reduces the incidence of streptococcal endophthalmitis by 50 %, a trial with 700,000 patients would be required to demonstrate a significant difference [47]. This result suggests that endophthalmitis can be reduced to a minimum by preventing normal flora of the conjunctiva and bacteria in oral cavity from entering the vitreous. For this purpose, an infection control manual that requires nurses and doctors to wear surgical mask and drape the patient's face, irrigate the conjunctiva with 0.25 % povidone–iodine and wait at least 30 seconds before performing intravitreal injection is useful.

From the perspective of cost-effectiveness, the cost per injection for implementing our preventive measures, including masks, drapes, povidone–iodine and perioperative topical antibiotics, is around ¥2,500 (about US$28). Assuming that 15,000 intravitreal injections are performed each year, the annual cost amounts to ¥37,500,000 (US$420,000). On the other hand, the cost for clinical management of a case of endophthalmitis is around ¥3,000,000 (US$3,300). Assuming that 7–8 cases of endophthalmitis can be prevented per year, our infection control measures may be low in terms of cost-effectiveness. However, rather than the cost, the prevention of endophthalmitis, which has devastating clinical consequences, is a priority in many countrie, including Japan.

In summary, this retrospective study of 15,144 intravitreal injections demonstrated that a very low rate of endophthalmitis can be achieved by following a protocol that includes wearing surgical masks by doctors and nurses, draping patient's face, irrigating the conjunctiva with 0.25 % povidone–iodine and waiting at least 30 seconds before performing intravitreal injection.

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References

1. Moss JM, Sanislo SR, Ta CN (2009) A prospective randomized evaluation of topical gatifloxacin on conjunctival flora in patients undergoing intravitreal injections. Ophthalmology 116:1498 1501
2. Stewart JM, Srivastava SK, Fung AE, Mahmoud TH, Telander DG, Hariprasad SM, Ober MD, Mruthyunjaya P (2011) Bacterial contamination of needles used for intravitreal injections: a pro spective, multicenter study. Ocul Immunol Inflamm 19:32 38
3. Miño de Kaspar H, Chang RT, Singh K, Egbert PR, Blumenkranz MS, Ta CN (2005) Prospective randomized comparison of 2 dif ferent methods of 5 % povidone iodine applications for anterior segment intraocular surgery. Arch Ophthalmol 123:161 165
4. Berkelman RL, Holland BW, Anderson RL (1982) Increased bac tericidal activity of dilute preparations of povidone iodine solu tions. J Clin Microbiol 15:635 639

5. Jaffe GJ, Martin D, Callanan D, Pearson PA, Levy B, Comstock T, Fluocinolone Acetonide Uveitis Study Group (2006) Fluocinolone acetonide implant (Retisert) for noninfectious posterior uveitis: thirty four week results of a multicenter randomized clinical study. Ophthalmology 113:1020 1027
6. Shimada H, Arai S, Nakashizuka H, Hattori T, Yuzawa M (2011) Reduction of anterior chamber contamination rate after cataract surgery by intraoperative irrigation with 0.25 % povidone iodine. Am J Ophthalmol 151:11 17
7. Shimada H, Nakashizuka H, Hattori T, Mori R, Mizutani Y, Yuzawa M (2013) Reduction of vitreous contamination rate after 25 gauge vitrectomy by surface irrigation with 0.25 % povidone iodine. Retina 33(1):143 151
8. Schimel AM, Scott IU, Flynn HW Jr (2011) Endophthalmitis after intravitreal injections: should the use of face masks be the standard of care? Arch Ophthalmol 129:1607 1609
9. McCannel CA (2011) Meta analysis of endophthalmitis after intra vitreal injection of anti vascular endothelial growth factor agents: causative organisms and possible prevention strategies. Retina 31:654 661
10. Doshi RR, Leng T, Fung AE (2012) Reducing oral flora contam ination of intravitreal injection with face mask or silence. Retina 32:473 476
11. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, Kim RY, MARINA Study Group (2006) Ranibizumab for neovascular age related macular degeneration. N Engl J Med 355:1419 1431
12. Fung AE, Rosenfeld PJ, Reichel E (2006) The International Intravitreal Bevacizumab Safety Survey: using the internet to assess drug safety worldwide. Br J Ophthalmol 90:1344 1349
13. Singerman LJ, Masonson H, Patel M, Adamis AP, Buggage R, Cunningham E, Goldbaum M, Katz B, Guyer D (2008) Pegaptanib sodium for neovascular age related macular degeneration: third year safety results of the VEGF Inhibition Study in Ocular Neovascularisation (VISION) trial. Br J Ophthalmol 92:1606 1611
14. Fintak DR, Shah GK, Blinder KJ, Regillo CD, Pollack J, Heier JS, Hollands H, Sharma S (2008) Incidence of endophthalmitis related to intravitreal injection of bevacizumab and ranibizumab. Retina 28:1395 1399
15. Mason JO 3rd, White MF, Feist RM, Thomley ML, Albert MA, Persaud TO, Yunker JJ, Vail RS (2008) Incidence of acute onset endophthalmitis following intravitreal bevacizumab (Avastin) in jection. Retina 28:564 567
16. Pilli S, Kotsolis A, Spaide RF, Slakter J, Freund KB, Sorenson J, Klancnik J, Cooney M (2008) Endophthalmitis associated with intravitreal anti vascular endothelial growth factor therapy injec tions in an office setting. Am J Ophthalmol 145:879 882
17. Wu L, Martínez Castellanos MA, Quiroz Mercado H, Arevalo JF, Berrocal MH, Farah ME, Maia M, Roca JA, Rodriguez FJ, Pan American Collaborative Retina Group (PACORES) (2008) Twelve month safety of intravitreal injections of bevacizumab (Avastin): results of the Pan American Collaborative Retina Study Group (PACORES). Graefes Arch Clin Exp Ophthalmol 246:81 87
18. Diago T, McCannel CA, Bakri SJ, Pulido JS, Edwards AO, Pach JM (2009) Infectious endophthalmitis after intravitreal injection of antiangiogenic agents. Retina 29:601 605
19. Artunay O, Yuzbasioglu E, Rasier R, Sengül A, Bahcecioglu H (2009) Incidence and management of acute endophthalmitis after intravitreal bevacizumab (Avastin) injection. Eye (Lond) 23:2187 2193
20. Klein KS, Walsh MK, Hassan TS, Halperin LS, Castellarin AA, Roth D, Driscoll S, Prenner JL (2009) Endophthalmitis after anti VEGF injections. Ophthalmology 116:1225
21. Brown DM, Michels M, Kaiser PK, Heier JS, Sy JP, Ianchulev T, ANCHOR Study Group (2009) Ranibizumab versus verteporfin photodynamic therapy for neovascular age related macular degen eration: Two year results of the ANCHOR study. Ophthalmology 116:57 65
22. Lima LH, Zweifel SA, Engelbert M, Sorenson JA, Slakter JS, Cooney MJ, Klancnik JM, Yannuzzi LA, Freund KB (2009) Evaluation of safety for bilateral same day intravitreal injections of antivascular endothelial growth factor therapy. Retina 29:1213 1217
23. Bhavsar AR, Googe JM Jr, Stockdale CR, Bressler NM, Brucker AJ, Elman MJ, Glassman AR (2009) Diabetic Retinopathy Clinical Research Network. Risk of endophthalmitis after intra vitreal drug injection when topical antibiotics are not required: the diabetic retinopathy clinical research network laser ranibizumab triamcinolone clinical trials. Arch Ophthalmol 127:1581 1583
24. Moshfeghi AA, Rosenfeld PJ, Flynn HW Jr, Schwartz SG, Davis JL, Murray TG, Smiddy WE, Berrocal AM, Dubovy SR, Lee WH, Albini TA, Lalwani GA, Kovach JL, Puliafito CA (2011) Endophthalmitis after intravitreal anti vascular endothelial growth factor antagonists: a six year experience at a university referral center. Retina 31:662 668
25. Inoue M, Kobayakawa S, Sotozono C, Komori H, Tanaka K, Suda Y, Matsushima H, Kinoshita S, Senoo T, Tochikubo T, Kadonosono K (2011) Evaluation of the incidence of endophthal mitis after intravitreal injection of anti vascular endothelial growth factor. Ophthalmologica 226:145 150
26. Shah CP, Garg SJ, Vander JF, Brown GC, Kaiser RS, Haller JA, Post Injection Endophthalmitis (PIE) Study Team (2011) Outcomes and risk factors associated with endophthalmitis after intravitreal injection of anti vascular endothelial growth factor agents. Ophthalmology 118:2028 2034
27. Inman ZD, Anderson NG (2011) Incidence of endophthalmitis after intravitreal injection of antivascular endothelial growth factor medications using topical lidocaine gel anesthesia. Retina 31:669 672
28. Chen E, Lin MY, Cox J, Brown DM (2011) Endophthalmitis after intravitreal injection: the importance of viridans streptococci. Retina 31:1525 1533
29. Bhatt SS, Stepien KE, Joshi K (2011) Prophylactic antibiotic use after intravitreal injection: effect on endophthalmitis rate. Retina 31:2032 2036
30. Martin DF, Maguire MG, Ying GS, Grunwald JE, Fine SL, Jaffe GJ; CATT Research Group (2011) Ranibizumab and bevacizumab for neovascular age related macular degeneration. N Engl J Med 364:1897 1908
31. Lad EM, Maltenfort MG, Leng T (2012) Effect of lidocaine gel anesthesia on endophthalmitis rates following intravitreal injec tion. Ophthalmic Surg Lasers Imaging 43:115 120
32. Cheung CS, Wong AW, Lui A, Kertes PJ, Devenyi RG, Lam WC (2012) Incidence of endophthalmitis and use of antibiotic prophy laxis after intravitreal injections. Ophthalmology 119:1609 1614
33. Lundström M, Wejde G, Stenevi U, Thorburn W, Montan P (2007) Endophthalmitis after cataract surgery: a nationwide prospective study evaluating incidence in relation to incision type and location. Ophthalmology 114:866 870
34. Oshika T, Hatano H, Kuwayama Y, Ogura Y, Ohashi Y, Oki K, Uno T, Usui N, Yoshitomi F (2007) Incidence of endophthalmitis after cataract surgery in Japan. Acta Ophthalmol Scand 85:848 851
35. Doshi RR, Leng T, Fung AE (2011) Povidone iodine before lidocaine gel anesthesia achieves surface antisepsis. Ophthalmic Surg Lasers Imaging 42:346 349
36. Wen JC, McCannel CA, Mochon AB, Garner OB (2011) Bacterial dispersal associated with speech in the setting of intravitreous injections. Arch Ophthalmol 129:1551 1554
37. Van den Broek PJ, Buys LF, Van Furth R (1982) Interaction of povidone iodine compounds, phagocytic cells, and microorgan isms. Antimicrob Agents Chemother 22:593 597

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