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Bacterial contamination of needle points after intravitreal injection

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PURPOSE. *Evaluation of the magnitude and pattern of bacterial contamination of needle points with conjunctival bacteria during the intravitreal injection. Analysis of the efficacy of preinjection prophylaxis.*

METHODS. *A total of 550 intravitreal injections were done in 414 patients (n=425 eyes). A total of 289 patients were injected once, while 125 patients received several injections. Before the intravitreal injection in the operation room, the following standard preoperative preparation of the eye–10% povidone iodine scrub on the eyelids, eyelashes and forehead and irrigation of the conjunctival sac with 1% povidone iodine–was carried out. Immediately after the injection, the needle points were rinsed three times in thioglycolate broth, which was cultured at 35°C for 5 days afterwards. As a negative control, 200 sterile unused needle points were treated the same way.*

RESULTS. *Only 2 out of 550 (0.36%) needle points were contaminated after intravitreal injection. In sensitivity testing, the isolated Staphylococcus epidermidis and Corynebacterium sp did not show multidrug resistance. All 200 unused needle points proved to be sterile after 5 days of cultivation.*

CONCLUSIONS. *Contamination of needle points is minimal after iodine irrigation prophylaxis before intravitreal injection. Therefore, we recommend this prophylaxis technique before intravitreal injections. The low incidence of contaminated needle points, however, shows that there still is a risk of bacteria entering into the eye during injection. (Eur J Ophthalmol 2009; 19: 268-72)*

KEY WORDS. *Bacterial contamination, Intravitreal injections, Microbiology, Preoperative prophylaxis*

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INTRODUCTION

Intravitreal injections have become the treatment of choice for several posterior segment diseases such as macular edema due to diabetic retinopathy or venous occlusive disease and particularly exudative age-related macular degeneration. In most of these diseases, several injections have to be performed in the course of time. Therefore the number of patients treated with intravitreal injections has considerably increased in the last few years. Infectious endophthalmitis after intravitreal injection is a rare but serious adverse event with possibly sight-threatening consequences even with adequate treatment. In a study by Moshfeghi et al, the mean visual acuity of eyes with postinjection endophthalmitis after intravitreal injections of triamcinolone (IVTA) was 20/400 with no light perception in 3 out of 8 cases and enucleation in one patient (1). A review of 14,886 IVT injections in 4,382 eyes showed a prevalence of infectious endophthalmitis of about 0.2% per injection (2). These results have been confirmed in recent publications, which noted 7 (0.16%) cases of infectious endophthalmitis following IVT injection

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of bevacizumab (Avastin™) in a large series of 4,303 injections (3). Current publications, however, noted infectious endophthalmitis after intravitreal injection of triamcinolone actenoide in up to 0.3% of cases (4-6). The exact origin of endophthalmitis following intravitreal injection is not known. Taking into account the data on postoperative endophthalmitis, the causative pathogens seem to be part of the patient's periocular flora, which are introduced into the eye during surgery (7, 8). On the basis of this most likely source of contamination, several guidelines regarding intravitreal injections have been introduced, emphasizing the need for adequate preinjection disinfection of the ocular surface and the surrounding skin with povidone iodine and a meticulous aseptic injection technique (9, 10). By emphasizing preoperative prophylaxis procedures, the rate of endophthalmitis after intravitreal injection of pegaptanib could be lowered during the VISION study (11).

Studies have shown that surgical instruments may become contaminated while penetrating the ocular surface and therefore present a possible cause for transmitting the bacteria into the intraocular space. Ten out of 39 (26%) microsurgical knifes used for paracentesis in cataract surgery were contaminated in a study by de Kaspar et al, while two other studies showed a contamination rate of 15.1% and 19% of needles used in strabismus surgery (12-14).

Despite the high frequency of intravitreal injections, knowledge about contamination of the needles used in this context is limited. Therefore, we conducted the following study in order to determine the magnitude and pattern of bacterial contamination of needle points during intravitreal injection and to analyze the efficacy of preoperative flush irrigation of the conjunctival sac.

METHODS

A total of 550 intravitreal injections were done in 414 patients (n=425 eyes). A total of 289 patients were injected only once, while 125 patients received several injections. All patients were eligible for enrolment into this study after informed consent and approval from the Institutional Review Board at the Ludwig-Maximilian University, Munich, between January and March 2007. In total, 414 consecutive patients (median age 76 years) were enrolled (Tab. I, study group). The majority of patients (93.7%; n=388) were treated with anti-VEGF-drugs (Avastin™, Genentech, San Francisco, CA; Lucentis™, Genentech; Macugen™, Pfizer, New York, NY). Twenty-one patients (5.1%) had intravitreal injections of 4 mg triamcinolone acetonide and five patients had intravitreal injections of other drugs (dexamethasone, rTPA+C_2F_6, methotrexate).

Before the intravitreal injection, all patients underwent standard periorbital disinfection using a povidone iodine scrub on the eyelids and surrounding skin followed by application of gauze soaked with 10% povidone iodine on the closed lids for 5 minutes. After the patient had been transferred into the operation room, topical anesthetic eyedrops were applied and the brow, upper and lower eyelids, eyelashes and the adjacent forehead, nose, cheeks and temporal orbital area were again scrubbed with 10% povidone-iodine three times. Afterwards, the conjunctival sac was flush irrigated with 10 mL of 1% povidone iodine solution. The patient's head was then covered with sterile drape and a speculum was put in place. The intravitreal injection was performed in accordance with the guidelines: 3.5 mm posterior to the limbus in pseudophakic eyes and 4 mm in phakic eyes using 27 gauge needles (BD Microlance™ 3, 27 G x 3/4 in., No. 20, 0.4 mm x 19 mm, Becton Dickinson GmbH, Germany). Di-

TABLE I - DEMOGRAPHIC AND DISEASE DATA

	No.	%
Total patients	414	
Total eyes	425	
Total IVT injections	550	
Single injection	289	
Several injections	125	
Patients		
Female	265	64
Male	149	36
Total	414	100
Eyes		
Right	226	53
Left	199	47
Total	425	100
Diagnoses		
ARMD, CNV	217	52
ZVT	25	6
AVT	19	5
DME	22	5
Others	131	32
Total	414	100

ARMD = age-related macular degeneration; CNV = choroidal neovascularization; DME = diabetic macular edema.

rectly after the injection in the operation room, the needle points were rinsed three times in thioglycolate broth and cultivated for 5 days at 35 °C. As a control group, 200 unused, sterile needle points were treated the same way again in the operation room to simulate the study group as closely as possible. During 5 days, the broth was checked for growth daily. In case of any growth, the bacteria were isolated and identified and susceptibility testing was done using the automated Vitek 2 Compact System® (bioMérieux® GmbH, Nuertingen, Germany). All culture media were supplied by bioMérieux® GmbH.

RESULTS

In the study group, only 2 out of 550 needle points showed bacterial growth in the thioglycolate broth (0.36%). The identified bacteria were *Staphylococcus epidermidis* and *Corynebacterium sp.* The identified *S epidermidis* showed some resistance to a few standard antibiotics (Tab. II) while the *Corynebacterium sp* did not show any resistance. Therefore, no multidrug resistance to topical antibiotics could be found. All 200 unused needle points proved to be sterile after 5 days of cultivation.

DISCUSSION

While the number of intravitreal injections has increased considerably in the past few years due to newly developed and Food and Drug Administration approved medications for the treatment of posterior segment diseases, care has to be taken to minimize the risks associated with the application of these medications. The high number of patients and the need for continuous injections over time, i.e., more than one injection for each patient, render intravitreal injections an important cause of infective endophthalmitis. The guidelines for intravitreal injections aim at standardizing the procedure including issues before, during and after the injection and therefore reducing the risks associated with this procedure. In the study on pegaptanib for age-related macular degeneration by Gragoudas et al, 8/12 (67%) cases of infective endophthalmitis were due to protocol violations, mainly the lack of using a lid speculum (11). This stresses that the injection technique plays an important role in the prevention of infectious endophthalmitis and therefore the need for following a standardized application protocol as outlined in the Guidelines for intravitreal injections (9, 10). One important factor in this context is the conjunctiva and the eyelids as a possible source of pathogens causing postoperative endophthalmitis. Thus, correct disinfection of the ocular surface and the periorbital area to reduce the number of bacteria plays an important role in the prevention of infective endophthalmitis. To achieve this goal, several strategies are commonly used, such as the application of topical antibiotics or povidone-iodine and eyelid hygiene. Both topical antibiotics and povidone-iodine have shown to reduce the quantity of bacteria found on the ocular surface (15-18). Only the use of povidone-iodine, however, has proven to significantly reduce the rate of postoperative endophthalmitis after cataract surgery (evidence level II) (15). This effect has never been established for topical antibiotic prophylaxis. Similarly, controversy exists regarding the postoperative use of antibiotic eyedrops as a prophylaxis of infective endophthalmitis. While there are data on the outbreak of postoperative endophthalmitis despite treatment with modern forth-generation fluoroquinolones, many authors recommend this prophylaxis due to the breakdown of the conjunctival barrier by the injection itself (19, 20). Common recommendations therefore state that povidone-iodine should routinely be included in the preoperative preparation of the patient. In this study, the ocular surface and the periorbital area were meticulously

TABLE II - IDENTIFIED BACTERIA AND SUSCEPTIBILITY TO ANTIBIOTICS

	Sensitive	**Resistant**
Staphylococcus epidermidis	Oxacillin, ciprofloxacin, norfloxacin, levofloxacin, moxifloxacin, gentamicin, tobramycin, tetracycline, vancomycin	Penicillin, ampicillin-amoxicillin, cefazolin, cefotaxime, ceftazidime, erythromycin, clindamycin, fosfomycin
Corynebacterium sp	All commonly used antibiotics	No resistance noted

cleaned using 10% povidone-iodine scrub for the periorbital area and 10 mL of 1% povidone-iodine for flush irrigation of the conjunctival sac. Intense disinfection of the eyelids and the periorbital area has not been found to be routinely included in the preoperative preparation of the patients.

A limitation of this study is the fact that no conjunctival swabs were taken and that therefore no correlation between the bacteria found in the needle points and the conjunctival flora can be done. However, our primary goal was to establish the rate and pattern of contaminated needle points during intravitreal injections after prophylaxis with povidone-iodine in a consecutive series of patients. One might state that the two cases of contamination found in our study might be due to external contamination. However, since we cultivated the needle's tips only, we conclude external contamination to be minimal. This prospective study shows that needle points may become contaminated during intravitreal injections and therefore present a possible risk for introducing bacteria into the vitreous cavity. However, during the whole time the study was conducted and up to October 2007 no case of postoperative endophthalmitis was seen in our hospital. In comparison with two studies on the bacterial contamination of needles during strabismus surgery and microsurgical knifes in cataract surgery, the contamination rate of 0.36% in this study is extremely low, as the other studies showed contamination rates of 19% and 26%, respectively (12, 13). In a recent publication, de Caro et al reported a contamination rate of 2 out of 114 needles used for intravitreal injections after preinjection prophylaxis with topical antibiotics and 5% povidone-iodine (18). This low contamination rate might partly be explained either by the short contact time of the needle with the conjunctiva or by the small contact area during injection. As preoperative povidone-iodine irrigation resulted in a contamination of only 2 out of 550 needle points (0.36%) in our study, we regard this regimen to be a strong protective means in the prevention of infective endophthalmitis after intravitreal injections. At the Department of Ophthalmology, Ludwig-Maximilian University, Munich, we routinely perform this meticulous disinfection technique for all intraocular surgeries and have not had a single case of endophthalmitis in more than 3000 intraocular operations from January to October 2007.

Due to the high number of intravitreal injections, every effort should be taken to minimize the risk of postinjection infectious endophthalmitis. Contamination of needle points is minimal after iodine irrigation prophylaxis before intravitreal injection. Therefore, we recommend this prophylaxis technique before intravitreal injection as well as a meticulous aseptic injection technique. Despite the low incidence of contaminated needle points, our results show that there still is a risk of bacteria entering the eye during injection.

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