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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Post-injection endophthalmitis in eyes receiving vs. not receiving topical antibiotic prophylaxis in Northern Thailand

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Introduction

Endophthalmitis following intravitreous anti-vascular endothelial growth factor (VEGF) injection is a rare sight-threatening condition. Several Western references suggest lower rates of post-injection endophthalmitis can be achieved without topical antibiotic prophylaxis [1–3]. However, a majority of physicians in the Asia-Pacific region still prescribe antibiotic prophylaxis [4], anecdotally stating concern that differences in environmental factors (e.g., tropical climates) or patient factors in the region might cause higher risk of endophthalmitis, comparing to the Western settings, to warrant this prophylaxis, despite little scientific rationale supporting such use. To our knowledge, little is known regarding incidence of post-injection endophthalmitis without antibiotic prophylaxis in a developing countries in Asia or elsewhere. Therefore, this study determined incidence of post-injection endophthalmitis with vs. without topical antibiotic prophylaxis at a university-based practice in Northern Thailand.

Materials and methods

IRB-approved prospective case series of patients receiving anti-VEGF injections at Chiang Mai University Hospital between May 2015 and September 2016 with follow-up anticipated for ≥3 weeks after injections were recruited. Before injections, study eyes were examined by slit-lamp biomicroscopy, ensuring no intraocular inflammation. Endophthalmitis was evaluated at 4 ± 1 weeks after the injection, and defined as severe inflammation in both anterior chamber and vitreous cavity associated with pain, redness, or decreased vision, regardless of whether subsequent cultures were positive.

A standardized intravitreous anti-VEGF injection protocol was strictly applied, including use of sterile drape, sterile eyelid speculum, sterile glove, procedure mask, and application of povidone-iodine, twice, over eyelid and conjunctival sac, and over injection site using a povidone-iodine soaked cotton tip for ≥30 s before injection.

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Table 1 Demographics of participants and study eyes in each subgroup (receiving vs. not receiving antibiotics) and overall

	Topical antibiotic prophylaxis		**Overall**, 1043 participants (%)
	Receiving, 381 participants (%)	**Not receiving,** 662 participants (%)	
Age (mean ± SD, years)	61.6 ± 7.8	60.4 ± 7.8	60.8 ± 7.8
Gender			
Men	193 (50.7)	333 (50.3)	526 (50.4)
Women	188 (49.3)	329 (49.7)	517 (49.6)
Nationality			
Thai	377 (99.0)	656 (99.1)	1033 (99.0)
Hill-tribe	4 (1.0)	6 (0.9)	10 (1.0)
Occupation			
Office workers/indoor workers/retirees	317 (83.2)	539 (81.4)	856 (82.1)
Outdoor workers[a]	64 (16.8)	123 (18.6)	187 (17.9)
Educational level			
Primary school or lower	219 (57.5)	408(61.6)	627 (60.1)
Secondary school or higher	162 (42.5)	254 (38.4)	416 (39.9)
Study eye			
Unilateral	346 (90.8)	565 (85.3)	911 (87.3)
Bilateral	35 (9.2)	97 (14.7)	132 (12.7)
	Receiving, 1407 injections (%)	**Not receiving, 2856 injections (%)**	**Overall, 4263 injections (%)**
Indication for injection[b]			
DME	445 (31.6)	1124 (39.4)	1569 (36.8)
PCV	206 (14.6)	574 (20.1)	780 (18.3)
NV AMD	303 (21.5)	371 (13.0)	674 (15.8)
RVO with ME	253 (18.0)	441 (15.4)	694 (16.3)
PDR-related condition e.g., VH	138 (9.8)	220 (7.7)	358 (8.4)
Others	62 (4.4)	126 (4.4)	188 (4.4)
Anti-VEGF agents[c]			
Aflibercept	216 (15.4)	758 (26.5)	974 (22.8)
Bevacizumab	1104 (78.5)	2011(70.4)	3115 (73.1)
Ranibizumab	87 (6.2)	87 (3.0)	174 (4.1)

[a]For example, agricultural workers, construction workers

[b]DME diabetic macular edema, PCV polypoidal choroidal vasculopathy, NV AMD neovascular age-related macular degeneration, RVO retinal vein occlusion, ME macular edema, PDR proliferative diabetic retinopathy, VH vitreous hemorrhage, anti-VEGF anti-vascular endothelial growth factor

[c]Bevacizumab was re-packaged in sterile fashion by the hospital pharmacy department into multiple doses of 1.25 mg/0.05 ml. Each dose was stored in a sterile insulin syringe, while ranibizumab (0.5 mg/0.05 ml) and aflibercept (2.0 mg/0.05 ml) were prepared by physicians at the time of each injection

Subsequently, participants received or did not receive topical antibiotics depending on their physicians' preferences. Three of six retina specialists (DP, PK, NI) always prescribed antibiotics (Tobramycin®) before or after injections for 5–7 days; the other three (JC, NW, VC) did not prescribe any antibiotics as part of standard care.

Results

Of 4263 injections (1043 participants) meeting eligibility criteria, 1407 (33%) received antibiotic prophylaxis, and 2856 (67%) did not receive any antibiotics. Demographics are shown in Table 1. There was one case of culture-negative post-injection endophthalmitis, which subsequently underwent vitrectomy, among eyes

Table 2 Incidence of endophthalmitis in eyes receiving vs. not receiving antibiotic prophylaxis

	Topical antibiotic prophylaxis		Difference of incidence (95% confidential interval)	*P* value
	Receiving[a]	Not receiving		
Number of intravitreous injections	1407	2856		
Incidence of endophthalmitis	1 (0.07%)	−(0%)	0.07% (−0.12% to 0.26%)	0.72

[a]Tobramycin eye drops for 5–7 days before or after intravitreous injection or both before and after injection

receiving antibiotics (1/1407 injections; 0.07%). No endophthalmitis occurred among eyes not receiving antibiotics (0/2856 injections; 0%) for a difference of 0.07% (95% confidence interval: −0.12 to 0.26%, $P = 0.728$; Table 2).

Discussion

To our knowledge, this study is among the first to explore an incidence of post-injection endophthalmitis when no antibiotic prophylaxis was given in a developing-country setting. The setting, a government hospital which mainly serves lower socioeconomic patients within geographically tropical climates, may be a good representative for individuals believed by some to be at higher risk for post-injection endophthalmitis in developing countries. The results, though not a randomized clinical trial, did not reveal an increased incidence of endophthalmitis in eyes not receiving antibiotic prophylaxis, similar to Western reports [1–3]. These data support continued use of povidone-iodine for ≥30 s prior to intravitreous injection [5] but not topical antibiotics for prophylaxis against post-injection endophthalmitis.

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Compliance with ethical standards

Conflict of interest All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. VC reported receiving research grant from Bayer and ThromboGenics; and receiving honoraria and travel reimbursement from Allergan and Novartis. ON reported no financial disclosure. DP reported working as a consultant, receiving honoraria and travel reimbursement from Bayer and Novartis; and receiving honoraria and travel reimbursement from Alcon. JC and NW reported receiving honoraria and travel reimbursement from Alcon, Allergan, Bayer and Novartis. PK reported receiving honoraria and travel reimbursement from Novartis. NI reported no financial disclosure. NMB reported receiving grants to employer, Johns Hopkins University; and from Bayer, Novartis, Roche (Genentech) and Samsung. No other disclosures were reported.

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