Risk Factors of Postoperative Endophthalmitis in Intravitreal AntiVEGF Injection

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Abstract

Purpose: This retrospective study aims to understand the human and environmental risk factors associated with intravitreal injections and proposes methods to reduce the incidence of intraocular infection at Thammasat University Hospital.

Design: Retrospective study

Methods: A total of 1,552 cases from 2017 to 2019 underwent intravitreous injection which included diagnoses relating to retinal vein occlusion, diabetic macular edema, choroidal neovascularization, and age-related macular degeneration. The data collected was divided into two groups: before and after 16 July 2018 and this was used to calculate endophthalmitis risk.

Main outcome measures: The primary outcome measure was the risk of endophthalmitis following intravitrealintravitreous injection

Results: There was significant statistical difference in the incidence of endophthalmitis, CI 0.05 (P<0.05) after vitreal injection environment was adjusted. However, was no significant statistical difference in intraocular pressure, complications and ocular surface disease post-operatively (P>0.05). there was no The results before and after adjusting the vitreous injection environment werew statistically different with the confidence level of 0.05 (P<0.05), while intraocular pressure, complications, ocular surface disease, culture/organism, and surgical procedure were not statistically different (P>0.05).

Conclusion: We concluded that the operative environment can have important repercussions on reducing the risk of endophthalmitis associated with intravitreal injections as there was a statistically significant reduction in the incidence. After investigating the risk of endophthalmitis following intravitreal injection, In the investigation of endophthalmitis risk following intravitrealintravitreous injection, we concluded that the the data characteristics of illness and treatment of the patients who received the intravitreous injection before and after adjusting the vitreous injection environment were compared. It was found that the diagnosed endophthalmitis disease and medicines the patients received before and after adjusting the vitreous injection environment were statistically different at the level of 0.05 (P <0.05). Environmental conditions can influence the development of infection.

Keywords: Risk, Endophthalmitis, Vitreous, Injection, Environment

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Introduction

Endophthalmitis is a sight threatening everely ophthalmological emergency secondary to circumstance caused by inflammation and infection. It can progress to rapid vision loss could possibly emerge as the loss of vision if left

untreatedproper and accurate treatment was not applied. In severe cases, the illness could be life-threatening. The diagnosis of this illness is based on physical examination as the symptoms vary and are nonspecific. Therefore, an accurate and timely diagnosis is extremely vital may depend on the awareness of physicians.

Endophthalmitis can be divided into two types: exogenous endophthalmitis and endogenous endophthalmitis. Exogenous endophthalmitis mostly occurs following appears after medical operations or procedures, 90 percent of which is associated with cataract operation. while 90 percent of this postoperative endophthalmitis is found after the cataract operation. Additionally,However, exogenous endophthalmitis can also occur following be found after another kind of medical operative or procedure, which is intravitrealintravitreous injection.

IntravitrealIntravitreous injection contains recently used widely is Anti VEGF, and is used to manage aiming to treat neovascular AMD, diabetic macular edema, and retinal vein occlusion. Vascular endothelial growth factor (VEGF) promotes is one of the essential molecules associated with the development of new blood vessels (angiogenesis) and is a main contributor to the pathophysiology of neovascular ocular diseases. It can indicate the medical conditions of neovascular ocular disease. Therefore, the use of Intravitreous Anti VEGF plays an essential role in the present day.

In current practice, The intravitrealintravitreous injection is is administered alongside Povidone-Iodine via aseptic technique generally operated with topical anesthesia in a sealed room, where the aseptic technique is applied along with the use of Povidone-Iodine to minimize contamination of the conjunctiva with normal flora. the normal flora around the conjunctiva area.

Prior to July 16, intravitreal injection was administered in a procedure room in the outpatient ophthalmology department which has been kept open for access to various patients, students, nurses and clinicians. In the Outpatient Ophthalmology Department in Thammasat Hospital before 16 July 2018, an intravitreous injection had to be operated in a procedure room where there were other patients, students, nurses, and doctors walking in and out regularly. The injection could be administered done at any time of the day, and occasionally, the medicine was divided for the injection in advance, making it prone to contamination. which could simply cause infection after the injection.

The research aims to is to investigate study and compare the environmental factors associated with endophthalmitis and ocular complications following intravitreal injection at Thammasat University Hospital. s where the intravitreous injection was is operated and the incidence of intraocular infection at Thammasat Hospital. Since Due to the resolution on 16 July 2018, the operating room was changed from a general procedure room to a specific room for injection to minimize the incidence of intraocular infection at Thammasat Hospital.

This research aims to seek the way to reduce the infection incidence from intravitrealintravitreous injection by studying the risk and environmental factors namely, the operating room and, method of medication preparation and dividing medicine for injection at Thammasat University Hospital. to find out whether these factors could reduce the incidence of the disease.

Materials and Methods

This research was conducted at the Outpatient Department, Ophthalmology Clinic, Thammasat University Hospital, Thailand, from 16 July 2017 - 16 July 2019. The data of this retrospective study was were collected from medical records in which the ICD-10 contains diagnoses related to retinal vein occlusion, diabetic macular edema, choroidal neovascularization, and age-related macular degeneration. The researchers compared the environmental factors causing endophthalmitis after intravitreous injection by ddividing divided the subjects them into two study groups: before and after adjusting the environment. A new protocol was implemented since The resolution on 16 July 2018 which required the operating

room to d that the operating room be changed from a general procedure room into a specific injection room. The protocol implemented specified that The criteria for changing the Intravitreous injection site after 16 July 2018 are as follows: the room must be sealed and specifically organized for intravitrealintravitreous injection only, the number of people involved in the injection must be minimized, the medicine for the injection will not be divided, and all the injections must be operated in the afternoon, with masks and head covers worn to must be worn to prevent the infection to minimize infection risks. Other aseptic techniques, such as the administration of Povidone Iodine, disinfectant eye drop, and mask and caps to prevent the infection from operators, were are required as usual.

The researchers compared the risk of endophthalmitis between before and after adjusting the environment by age, sex, occupation, underlying disease, laterality, medication, IOP, risk of endopthalmitis, and causative organism.

Calculation of the sample size

In order to estimate the sample size, the researchers used two-sided testing with the significance of 5% and power of 80%. The calculation showed that the sample size should include 496 patients per group based on data from a previous study (13) (Fileta J, Scott I, Flynn H. Meta-Analysis of Infectious Endophthalmitis After Intravitreal Injection of Anti-Vascular Endothelial Growth Factor Agents. Ophthalmic Surgery, Lasers and)

Statistical analysis

The data waswere collected in a standardized form and stored in an electronic data sheet (Microsoft Excel). A Paired t-test was used to compare pre-and post-adjusting the environment.

A p-value of less than 0.05 was considered statistically significant.

Results

Table 1 Baseline characteristics

	Total (n-1552)	Before (n-828)	After (n-724)	P-value
Sex,n(%)				
Male	870 (56.01)	445(53.7)	425(58.7)	0.050*
Female	682 (43.9)	383 (46.3)	299 (41.3)	
Age (year),mean±	59.09±11.08	60.75±11.47	57.19±10.31	<0.001*
Occupation, n(%)				
Unemployed/Retire	536 (34.5)	322 (38.9)	214 (29.6)	<0.001*
Self-employed	233 (15.0)	90 (10.9)	143 (19.8)	
Employee	226 (14.6)	111 (13.4)	115 (15.9)	
Government officer	203 (13.1)	134 (16.2)	69 (9.5)	
Private company	65 (4.2)	30 (3.6)	35 (4.8)	
employee				
Agriculturist	45 (2.9)	23 (2.8)	22 (3.0)	
Student	11 (0.7)	3 (0.4)	8 (1.1)	
Not specified	233 (15.0)	115 (13.9)	118 (16.3)	
Underlying disease, n(%)				
DM	1,090 (70.2)	531 (64.1)	559 (77.2)	<0.001*
HT	736 (47.4)	391 (47.2)	345(47.7)	0.866
DLP	263 (16.9)	135 (16.3)	128 (17.7)	0.471
IHD	13 (0.8)	6 (0.7)	7 (1.0)	0.601
Old CVA	13 (0.8)	10 (1.2)	3 (0.4)	0.087
CKD	13 (0.8)	8 (1.0)	5 (0.7)	0.522
Goud	12 (0.8)	5 (0.6)	7 (1.0)	0.415
COPD	10 (0.6)	9 (1.1)	1 0.1)	0.024*
IFG	7 (0.5)	7 (0.8)	0 (0.0)	0.017*
Thyroid	7 (0.5)	6 (0.7)	1 (0.1)	0.130
Asthma	5 (0.3)	3 (0.4)	2 (0.3)	1.000
other	8 (0.5)	8 (1.0)	0 (0.0)	0.009*

Data were analyzed with Chi-square test/Fisher exact test, Independent T-test
*Statistically significant at the 0.05 level

Table 1 outlines shows sthe personal characteristic data of patients the demographic and medical history of the studied subjects. who received the intravitreous injection. TOut of 1,552 cases from 2017 to 2019, t The majority of the patients were male (56.1%). , followed by female (43.9%). The average age was 59.09 ± 11.08 years old. Most patients were unemployed or retired (34.5%)., followed by self-employed and merchanting (15.0%), and employees (14.6%), respectively. The majority of the patients had diabetic disease (70.2%), followed by hypertension (47.4%), and hyperlipidemia (16.9%), respectively.

Before adjusting the vitreous injection environmental conditions, there were 828 participating subjectspatients, the majority of which were most of which were male (53.7%), followed by female (46.3%). The average age was 60.75 ± 11.47 years old. Most patients were unemployed or retired (38.9%), followed by government officers (16.2%), and employees (13.4%), respectively. The majority of the patients had diabetes diabetic disease (64.1%), followed by hypertension (47.2%) and hyperlipidemia (16.3%), respectively.

In the new operative setting, there were 724 patients, After adjusting the vitreous injection environmental conditions, there were 724 patients, most of which were male (58.7%), followed by female (41.3%). The average age was 57.19 ± 10.31 years old. Most patients were unemployed or retired patients (29.6%), followed by self-employed (19.8%) and employees (15.9%), respectively. The majority of the patients had diabetes diabetic disease (77.2%), followed by hypertension (47.7%), and hyperlipidemia (17.7%), respectively.

Table 2 Illnesses and treatment

	Total (n-1552)	**Before (n-828)**	**After (n-724)**	**P-value**
Diagnosis, n(%)				
DME	749 (48.3)	334 (40.3)	415 (57.3)	<0.001*
CRVO with ME	296 (19.1)	165 (19.9)	131 (18.1)	
BRVO with ME	171 (11.0)	110 (13.3)	61 (8.4)	
PCV	153 (9.9)	108 (13.0)	45 (6.2)	
AMD	114 (7.3)	57 (6.9)	57 (7.9)	
CNV	34 (2.2)	33 (4.0)	1 (0.1)	
HRVO with ME	12 (0.8)	11 (1.3)	1 (0.1)	
CRVO	10 (0.6)	2 (0.2)	8 (1.1)	
OIS	5 (0.3)	5 (0.6)	0. (0.0)	
HRVO	4 (0.3)	2 (0.2)	2 (0.2)	
other	4 (0.3)	1 (0.1)	3 (0.4)	
Laterelity, n(%)				
OD	795 (51.2)	435 (52.5)	360 (49.7)	<0.001*
OS	723 (46.6)	388 (46.9)	335 (46.3)	
OU	34 (2.2)	5 (0.6)	29 (4.0)	
Medication, n(%)				
Avastin	667 (43.0)	336 (40.6)	331 (45.7)	<0.001*

Table 2 Illnesses and treatment (Cont.)

	Total (n-1552)	Before (n-828)	After (n-724)	P-value
Aflibercept	518 (33.4)	238 (28.7)	280 (38.7)	
Lucentis	367 (23.6)	254 (30.7)	113 (15.6)	
High intraocular pressure in 1 Month, n(%) (n=1525)	47 (3.1)	28 (3.4)	19 (2.7)	0.392
Complication, n(%)				
no complication	1,516 (97.7)	810 (97.8)	706 (97.5)	0.182
OHT	25 (1.6)	14 (1.4)	11 (1.5)	
NGV	5 (0.3)	0. (0.0)	5 (0.7)	
PAG	4 (0.3)	2 (0.2)	2 (0.3)	
SCH	1 (0.1)	1 (0.1)	0 (0.0)	
Endopthalmitis	1 (0.1)	1 (0.1)	0. (0.0)	

Table 2 demonstrates shows the morbidity and treatment data of patients who underwent undergoing intravitrealintravitreous intravitreal injection. The data showed that nearly half of the patients were diagnosed with DME (48.3%), followed by CRVO with ME (19.1%) and BRVO with ME (11.0%). Patients with right-sided morbidity accounted for 51.2%, followed by righ t left-sided morbidity 46.6%. The intravitreal injection administered was medications they received are mainly Avastin (43.0%), followed by Aflibercept (33.4%), and Lucentis (23.6%). Patients with high intraocular pressure (> 21 mm Hg) after injection into the Vitreous accounted for 3.1%, while 2.3% with complications, 1.6% with OHT, 0.3% with NVG and POAG each, followed by 0.1% with SCH and endophthalmitis, respectively. Only 0.1% of the patients had Hordeolum, and only one case (0.00064%) was infected with staphylococcus aureus from having PPV surgery together with IVT.

Before adjusting the environment in vitreous injection, it was found that the majority of patients were diagnosed with DME (40.3%), followed by CRVO with MEe (19.9%) and BRVO with ME (13.3%). The majority had right-sided ocular morbidity (52.5%), followed by left-sided (46.9%), and bilateral both sides (0.6%). The main intravitreal injection administered was the most of the medicine given were Avastin (40.6%), followed by Lucentis (30.7%), and Aflibercept (28.7%). Following intraocular injection, 3.4% of the patients had Patients with high intraocular pressure (>21 mm Hg) after intraocular injection accounted for 3.4%, with complications (2.2%), while 1.4% presented with OHT 1.4%, 0.2% POAG (0.2%), and 0.1%SCH (0.1%). It was noted that one patient had has eye infection infections (0.0012%).

After adjusting the environment in vitreous injection, it was found that the majority were diagnosed with DME (57.3%), followed by CRVO with Me (18.1%) and BRVO with ME (8.4%). The majority had right-sided morbidity (49.7%), followed by left-sided (46.3%), and both sides (4.0%). The main intravitreal injection administered was Most of the medicines given were Avastin (45.7%), followed by Aflibercept (38.7%), and Lucentis (15.6%), respectively. Patients with high intraocular pressure (>21 mm Hg) after intraocular injection accounted for 2.7%, with complications (2.5%), OHT 1.5%, NVG (0.7%), and POAG (0.3%). No endophthalmitis infection was found.

We found that there was a statistically significant reduction in the incidence of endophthalmitis after operative environmental adjustment (CI 0.05, P<0.05) after comparing the characteristics The comparison of characteristics of illness and treatment of the patients who received the intravitreous injection before and after adjusting the vitreous injection environment, showed that the diagnosed endophthalmitis disease and medicines the patients received before and after adjusting the vitreous injection environment were statistically different at the level of 0.05 (P<0.05). In contrast, intraocular pressure, other complications, ocular surface disease, culture/organism, and surgical procedure were not statistically different (P>0.05).

Table 3 Visual Acuity

VA	LE				RE			
	Total (n=745)	**Before (n=393)**	**After (n=352)**	**P-value**	**Total (n=844)**	**Before (n=440)**	**After (n=404)**	**P-value**
5/200	21 (2.8)	13 (3.3)	8 (2.3)	<0.001*	30 (3.6)	20 (4.5)	10 (2.5)	<0.001*
10/200	69 (9.3)	16 (9.2)	33 (9.4)		79 (9.4)	48 (10.9)	31 (7.7)	
20/20	6 (0.8)	5 (1.3)	1 (0.3)		2 (0.2)	1 (0.2)	1 (0.2)	
20/25	27 (3.6)	22 (6.4)	2 (0.6)		11 (1.3)	7 (1.6)	4 (1.0)	
20/30	63 (8.5)	35 (8.9)	28 (8.0)		49 (5.8)	32 (7.3)	17 (4.2)	
20/40	67 (9.0)	23 (5.9)	44 (12.5)		44 (5.2)	18 (4.1)	26 (6.4)	
20/50	88 (5.7)	23 (5.9)	44 (12.5)		106 (12.6)	45 (10.2)	61 (15.1)	
20/60	44 (5.9)	15 (3.8)	29 (8.2)		76 (9.0)	31 (7.0)	45 (11.1)	
20/70	50 (6.7)	28 (7.1)	22 (6.3)		54 (6.4)	21 (4.8)	33 (8.2)	
20/80	26 (3.5)	14 (3.6)	12 (3.4)		46 (5.5)	23 (5.2)	23 (5.7)	
20/100	75 (10.1)	41 (10.4)	34 (9.7)		101 (12.0)	43 (9.8)	58 (14.4)	
20/150	81 (10.9)	51 (13.0)	30 (8.5)		72 (8.5)	40 (9.1)	32 (7.9)	
20/200	58 (7.8)	39 (9.9)	19 (5.4)		49 (5.8)	34 (7.7)	15 (3.7)	
Fc ½ ft	6 (0.8)	6 (1.5)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Fc 1 ft	22 (3.0)	11 (2.8)	11 (3.1)		56 (6.6)	35 (8.0)	21 (5.2)	
Fc 2 ft	14 (1.9)	10 (2.5)	4 (1.1)		22 (2.6)	12 (2.7)	10 (2.5)	
Fc 3 ft	10 (1.3))	8 (2.0)	2 (0.6)		13 (1.5)	3 (0.7)	10 (2.5)	
Fc 4 ft	1 (0.1)	1 (0.3)	0. (0.0)		3 (0.4)	1. (0.2)	2 (0.5)	
HM	17 (2.3)	9 (2.3)	8 (2.3)		31 (3.7)	26 (5.9)	5 (1.2)	

Data were analyzed with Chi-square test
*Statistically significant at the 0.05 level

Table 3 shows the visual acuity data of the intravitreous injection patients, both left and right. It was found that most patients had their left eye 20/150 (10.9%), followed by 20/100 (10.1%) and 10/200 (9.3%), respectively.

Discussion

In total, 1522 patients received intravitreal injection from July 16th-17th, 2019 for conditions including According to the study, patients with in retinal vein occlusion, diabetic macular edema, choroidal neovascularization and , age-related macular degeneration. who have received intravitreous injection from 16 July 2017 - 16 July 2019 totaled 1,552 cases. One single case of intraocular infection (0.00064%) was reportedfou=nd. It is a case of with the colonization of staphylococcus aureus and occured in the case of a patient infection while undergoing PPV with IVT surgery. In comparison to the research from of Fileta J, Scott I, Flynn H Meta-Analysis of Infectious Endophthalmitis After Intravitreal Injection of Anti-Vascular Endothelial Growth Factor Agents from 2005 to 2012, there were 350,535 patients who received an injection into the vitreous. Only 197 out of 350,535 were found to be infected, accounting for 0.056%. It is evident that our data are lower than the reference study. Other minor complications were found, such as ocular hypertension, neovascularizationneovascularized glaucoma, open-angle glaucoma, and subconjunctival hemorrhage.

The scenarios of before and after modifying the environment on 16 July 2018 were compared by utilizing a closed chamber for injecting into the vitreous only, reducing the number of people involved in injection to a minimum, not dividing the dose for injection in advance, compiling all injections in the afternoon of the day, hats and masks were worn every time to prevent transmission from the operator. It was found one patient had intraocular infections before 16 July 2018 or 0.0012%, whereas there were was no more intraocular infection found after 16 July 2018 at all. We also It is noticed that the environment may affect and increase the risk of infection in the eyeball.

Limitation

- It is a study of a single unit.
- The data retention period is only two years.

Conclusion: In the investigation of endophthalmitis risk following intravitreous injection, the data characteristics of illness and treatment of the patients who received the intravitreous injection before and after adjusting the vitreous injection environment were compared. It was found that the diagnosed endophthalmitis disease and medicines the patients received before and after adjusting the vitreous injection environment were statistically different at the level of 0.05 ($P < 0.05$). Environmental conditions can influence the development of infection.

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