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Risk factors for post-traumatic endophthalmitis in patients with positive intraocular cultures

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PURPOSE. *To determine the risk factors for post-traumatic endophthalmitis in patients with positive intraocular culture.*

METHODS. *An institutional-based prospective nonrandomized interventional study of patients older than 15 years who presented for primary repair of open globe injury between June 2003 and April 2005 was undertaken. The main outcomes measured were initial and final visual acuity, type of injury, presence of uveal and vitreous prolapse, time interval between injury and primary repair of the globe, length of wound, location of wound, and virulence of organism. Statistical analysis tests used were Student t-test, Fisher exact test, and chi-square test.*

RESULTS. *Fifty patients were included in the study. They were divided into two groups: Group 1 (n=19) patients, who developed clinically significant endophthalmitis; and Group 2 (n=31) patients, who did not develop clinically significant endophthalmitis. Delay in primary repair more than 36 hours (p=0.042), length of wound more than 8 mm (p=0.050), and isolation of organisms like fungus (p=0.006, OR=14),* Bacillus cereus *(p=0.01, OR=11.25), and* Pseudomonas aeruginosa *(p=0.05–0.10, OR=11.3) significantly increased the risk of endophthalmitis. Mean initial and final visual acuity was better in Group 2 but was not statistically significant (p=0.21).*

CONCLUSIONS. *Final visual outcome in the presence of positive intraocular culture is poor. Isolation of virulent organisms, longer length of laceration, and delayed primary repair of open globe injuries have high risk of developing endophthalmitis. Prophylactic intraocular antibiotics should be considered in cases with longer length of wound and delayed primary closure. (Eur J Ophthalmol 2007; 17: 642-7)*

KEY WORDS. *Open globe injuries, Intraocular positive culture, Post-traumatic endophthalmitis,* Bacillus cereus, Pseudomonas aeruginosa, *Prophylactic antibiotics*

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INTRODUCTION

Endophthalmitis is one of the dreaded complications of penetrating ocular trauma with a dismal outcome (1-3). The prognosis of post-traumatic endophthalmitis is worse than that of postoperative endophthalmitis, which may partially be the result of intraocular damage from the initial injury or infection with more virulent organisms after trauma (4). Risk factors for post-traumatic endophthalmitis include delayed primary closure of open globe injuries, presence of an intraocular foreign body, rural setting of injury or soil-associated injury, positive intraocular culture of virulent organism, presence of uveal tissue or vitreous prolapse, and longer length of wound.

It has been shown in various studies that microbiology of traumatic endophthalmitis is distinct from other subgroups of exogenous endophthalmitis (5, 6). Gram-positive organisms such as *Bacillus*, *Staphylococci*, and *Streptococci* are frequently isolated pathogens (6-8). Positive intraocular culture is an important risk factor in the

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development of endophthalmitis but mere isolation of microorganisms from the intraocular tissue does not necessarily mean that the patient will develop endophthalmitis. Organisms have been cultured from anterior chamber even after uncomplicated cataract surgery (9).

In the present study we attempted to identify risk factors for the development of endophthalmitis in cases of open globe injuries with positive intraocular cultures by comparing patients who subsequently developed endophthalmitis with patients who did not develop endophthalmitis despite positive intraocular culture.

METHODS

Patients older than 15 years who presented to us between September 2003 and April 2005 for primary repair of open globe injury following trauma and were found to have positive intraocular culture were included in the study. Patients with irreparably damaged globe at the time of presentation were excluded from the study. Patients younger than 15 years were excluded from the study because of the difference in response by children to trauma as compared to adults.

All patients were admitted and were taken for surgical exploration and repair of the injured globe on an emergency basis. At the time of surgical intervention, the aqueous aspirate in cases of injuries involving the anterior chamber was sent for microbiological examination. In cases of uveal tissue prolapse, the tissue was abscised and sent for microbiological evaluation. Prolapsed vitreous was cut flush to the wound with a cellulose sponge and was also sent for microbiological evaluation (10). The surgical intervention was carried out by experienced surgeons in all cases.

The samples were immediately cultured in blood agar, chocolate agar, thioglycollate broth, brain heart infusion, and Sabouraud dextrose medium. Thioglycollate broth was incubated for 1 week, Sabouraud dextrose for 6 weeks, while others were incubated for 3 days before being discarded as negative cultures. A positive culture was defined as growth on two media along the culture streak. Antibiotic sensitivity was done using standard minimum inhibitory concentration testing.

The corneal and scleral lacerations were sutured by 10-0 and 8-0 nylon sutures respectively. Cataract extraction was done only if the crystalline lens was damaged with liberation of cortical matter either into the anterior chamber or posterior segment. Primary intraocular lens was not implanted. In cases with scleral laceration extending beyond 4 mm from the limbus, two rows of cryotherapy were applied surrounding the area of repair. In the immediate postoperative period, patients were started on intravenous ciprofloxacin (200 mg 12th hourly) (11). However, antibiotic was changed according to the sensitivity of the organisms later. For patients with fungal contamination, oral fluconazole 200 mg 12th hourly was given (10). Topically, cycloplegic and steroid-antibiotic combination eyedrops were given postoperatively.

In the present study, eyes were divided into two groups: Group 1 included eyes in which clinically diagnosed endophthalmitis developed at some point during the clinical course after the primary repair of the globe was undertaken; Group 2 included eyes in which clinically diagnosed endophthalmitis did not develop during the entire clinical course. The criteria used for making a clinical diagnosis of endophthalmitis included one or more of the following clinical features: marked intraocular inflammation with or without hypopyon; retinal periphlebitis; and marked exudates in the vitreous (12).

Intraocular antibiotics were not used at the time of initial surgical intervention. Intraocular antibiotics (intravitreal vancomycin [1000 µm] and ceftazidime [2.25 mg] and amphotericin [5µm]) were given only in patients who subsequently developed either bacterial or fungal endophthalmitis. Cases with persistence of infection despite one intravitreal injection underwent pars plana vitrectomy along with intravitreal antibiotics according to the sensitivity of the organisms.

Potential risk factors for the development of clinically significant endophthalmitis were evaluated. Statistical analysis tests used were two-sample *t*-test, Fisher exact test, and chi-square test. The level of significance used in all tests was p=0.05.

RESULTS

The study included 19 patients in Group 1 and 31 patients in Group 2. The age group 30–40 years accounted for almost one-third of all the patients in both groups. Men were affected three times more than women. The median duration of follow-up in Group 1 and Group 2 was 14.3 and 11.2 months with a range of 5–19 months and 3–17 months, respectively. Four patients in Group 1 and one patient in Group 2 had intraocular foreign body. Two out of these four patients in Group 1 showed fungal organism

while one showed *Bacillus cereus*. All these three patients had final visual acuity less than 20/400. The organisms isolated in both groups are enumerated in Table I.

All patients of Group 1 received intravitreal antibiotics injection (either antibacterial or antifungal in accordance to the culture report obtained during initial repair) along with microbiological evaluation of the vitreous aspirate and aqueous aspirate. The organisms cultured from intraocular specimens after the development of endophthalmitis differed from those obtained at the time of repair of open globe injuries in 3 patients out of 15 (Tab. II). Thirteen patients (68.4%) in Group 1 subsequently underwent pars plana vitrectomy due to persistence of infection. Intravitreal antibiotics injected at the end of vitrectomy in all these patients were in accordance with the culture report of the intraocular specimens obtained during the first intravitreal injection of antibiotic. In Group 2 only 8 patients (25.8%) underwent pars plana vitrectomy but intravitreal antibiotics were not injected.

Different variables studied to determine the risk factors for the development of endophthalmitis are enumerated in Table III. The significant risk factors included culture of virulent organisms, delayed repair of the injured globe, and longer wound length. The mean wound length in Group 1 was 9.37 mm while in Group 2 it was 6.71 mm. The mean time lapse between injury and surgical repair in Group 1 was 52.5 hours while in Group 2 it was 25.5 hours. Isolation of fungal organisms was associated with a very high risk for developing endophthalmitis (p=0.006, OR=14, CI=1.46–383.9) followed by *B cereus* (p=0.01, OR=11.25, CI=1.1–270.7) and *Pseudomonas aeruginosa* (p=0.05–0.10, OR=11.3, CI=7.5–61, correction factor of 0.5 was added to all cells).

Comparison of the initial and final visual acuity of the patients in both groups was made in Tables III and IV. The visual acuity improvement was seen in only 11 (57.9%) patients in Group 1 but was seen in 25 (80.7%) patients in Group 2. The final visual acuity was 20/200 or better in 12 (38.7%) and 20/40 or better in 6 (19.4%) in Group 2, while in Group 1 only 5 (26.3%) could achieve 20/200 or better vision and none achieved better than 20/40 vision. However, the difference was not statistically significant (p=0.21).

DISCUSSION

Isolation of microbes from the intraocular tissues does not always lead to endophthalmitis. Microbes have been cul-

TABLE I - ORGANISMS CULTURED IN BOTH GROUPS DURING REPAIR OF INJURED GLOBES

Serial no.	Organism	No. of patients	
		Group 1	Group 2
1	*Staphylococcus epidermidis*	1	9
2	*Staphylococcus aureus*	3	5
3	*Streptococcus pyogenes*	1	3
4	*Streptococcus pneumoniae*	0	4
5	*Haemophilus influenzae*	0	1
6	*Bacillus cereus*	5	0
7	*Bacillus subtilis*	1	2
8	*Pseudomonas aeruginosa*	3	0
9	*Enterobacter species*	0	3
10	*Proteus mirabilis*	0	2
11	*Actinomyces species*	1	1
12	*Acremonium curvulum*	1	0
13	*Aspergillus flavus*	1	0
14	*Candida albicans*	1	0
15	*Candida parapsilosis*	0	1
16	*Paecilomyces lilacinus*	1	0
17	*Fusarium solani*	2	0
18	*Aspergillus fumigatus*	1	0
	Total	**22**	**31**

Three patients in Group 1 were infected with two organisms

TABLE II - ORGANISMS CULTURED IN GROUP 1 PATIENTS AT THE TIME OF REPAIR AND AFTER DEVELOPING ENDOPHTHALMITIS

Serial no.	Organisms cultured	Group 1 patients	
		At the time of repair of open globe injury	After developing endophthalmitis
1	*Staphylococcus epidermidis*	1	1
2	*Staphylococcus aureus*	3	1
3	*Streptococcus pyogenes*	1	1
4	*Streptococcus pneumoniae*	0	1
5	*Haemophilus influenzae*	0	1
6	*Bacillus cereus*	5	4
7	*Bacillus subtilis*	1	1
8	*Pseudomonas aeruginosa*	4	4
9	*Proteus mirabilis*	0	1
10	*Actinomyces species*	1	1
11	*Acremonium curvulum*	1	1
12	*Candida albicans*	1	1
13	*Paecilomyces lilacinus*	1	1
14	*Fusarium solani*	2	2
15	*Aspergillus fumigatus*	1	1
	Total	**22**	**22**

Three patients in Group 1 showed positive cultures for two organisms both at the time of injury (intraocular culture) and after developing clinical endophthalmitis

TABLE III - VARIABLES AFFECTING THE DEVELOPMENT OF ENDOPHTHALMITIS

Serial no.	Variables	Number	No. of patients with endophthalmitis (% out of total)	No. of patients with no endophthalmitis (% out of total)	p value*
1	Type of injury				
	• Organic	30	10 (33.3)	20 (66.7)	0.405
	• Inorganic	20	9 (45.0)	11 (55.0)	
2	Time delay, h				
	• <36	37	11 (29.7)	26 (70.3)	0.042
	• >36	13	8 (61.5)	5 (38.5)	
3	Uveal tissue prolapse				
	• Present	38	12 (31.6)	26 (68.4)	0.096
	• Absent	12	7 (58.3)	5 (41.7)	
4	Vitreous prolapse				
	• Present	15	6 (40.0)	9 (60.0)	0.849
	• Absent	35	13 (37.1)	22 (62.3)	
5	Location of laceration				
	• Only cornea	24	8 (33.3)	16 (66.7)	0.191
	• Only sclera	14	6 (42.9)	8 (57.1)	
	• Both cornea and sclera	12	5 (41.7)	7 (58.3)	
6	Length of laceration, mm				
	• 0–4	9	6 (66.7)	3 (33.3)	0.050
	• 4.1–8	9	1 (11.1)	8 (88.9)	
	• >8	32	12 (37.5)	20 (62.5)	

*Statistical analysis tests used were two sample t-test, Fisher exact test, and chi-square test. The level of significance used in all tests was $\alpha = 0.05$

TABLE IV - GROUP 1 INITIAL VS FINAL VISUAL ACUITY

Initial visual acuity	Number of cases*	Final visual acuity of 20/400 or better, n (%)
Light perception	13	7 (53.8)
Hand movements	2	1 (50)
Better than hand movements to 3/200	1	1 (100)
Better than 3/200	1	0 (0)
Total	**17**	**9 (52.9)**

*Two patients had no light perception at presentation

TABLE V - GROUP 2 INITIAL V/S FINAL VISUAL ACUITY

Initial visual acuity	Number of cases*	Final visual acuity of 20/400 or better, n (%)
Light perception	16	7 (43.8)
Hand movements	12	9 (75)
Better than hand movements to 3/200	2	2 (100)
Better than 3/200	1	0 (0)
Total	**31**	**18 (58.1)**

tured from the anterior chamber even after uncomplicated cataract surgery without any evidence of endophthalmitis (9, 13). In a previous study despite positive microbial cultures after open globe injuries in 10 cases none of them developed endophthalmitis (14). The source of infectious organisms in post-traumatic endophthalmitis is either exogenous organism introduced into the eye during trauma or the patient's own ocular microbial flora (9). This ocular microbial flora may also be responsible for the contamination of intraocular fluids during intraocular surgeries. The

ocular microbial flora usually harbors less virulent organisms while the organisms from exogenous source are usually more virulent and are associated with poor visual outcome. Trauma sustained in rural settings is more frequently associated with contamination with *Bacillus* species and fungal organism and both are associated with poor visual outcome (7).

There have been varied reports on culture positivity and development of endophthalmitis with increasing length of corneoscleral laceration (14, 15). Longer corneoscleral wounds usually do not seal properly, expose the intraocular contents to the outside environment, and are associated with greater hypotony leading to ingress of extraocular fluids, which are likely to be contaminated and carry a high risk for endophthalmitis. Delay in repair of corneoscleral laceration increases the risk for colonization of microorganisms in the eye and development of endophthalmitis (16).

Organisms causing post-traumatic endophthalmitis are usually the same as obtained with the culture of intraocular contents at the time of primary repair of open globe injuries. However, they may differ in some cases, like in our series; three organisms that were not cultured at the time of primary repair of globe were found to be the causative organisms for endophthalmitis. This may be due to introduction of organisms during repair or failure of the organisms to be cultured in the first instance due to low infective inoculum but subsequent proliferation resulting in endophthalmitis.

Presence of uveal tissue or vitreous prolapse exposes the intraocular contents to the microbial flora of the conjunctival sac or exogenous organisms. However, in the current study the presence of uveal or vitreous prolapse did not significantly increase the risk of endophthalmitis. This may be due to the contamination with the organisms of conjunctival sac, which is usually less virulent, and thus the patient does not develop clinically significant endophthalmitis. The use of systemic and topical antibiotics, delayed use of steroid, the size of inoculum, virulence of the organism, and host factors play roles in preventing the manifestation of overt endophthalmitis.

Isolation of virulent organisms like fungus, *B cereus,* and *P aeruginosa* were associated with the occurrence of endophthalmitis. On the other hand, isolation of *Staphylococcus epidermidis* is rarely associated with endophthalmitis (only 1 out of 10 cases developed). Final visual acuity in Group 2 was better than in Group 1 (Tabs. IV and V) but was not statistically significant. This may be due to confounding factors like concurrent retinal detachment, posterior segment damage from the original trauma, macular scar, corneal edema and scar, and suprachoroidal hemorrhage, which may influence the final visual outcome.

The decision whether to administer prophylactic intraocular antibiotics in patients with open globe injuries in the absence of hypopyon or other classic signs of endophthalmitis remains controversial. In the light of the current study, prophylactic intraocular antibiotic should be strongly considered in cases with longer wound and delayed primary repair of the corneoscleral wound. The antibiotics we generally prefer are vancomycin for coverage of Gram-positive organisms (including *Bacillus*) and ceftazidime for coverage of Gram-negative organisms.

Proprietary interest: None

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