Clinical Profile and Outcomes of Patients with Endophthalmitis Treated with Pars Plana Vitrectomy: A Retrospective Study of 10 Years

Perfil Clínico e Resultados dos Doentes com Endoftalmite Submetidos a Vitrectomia Via *Pars Plana*: Estudo Retrospetivo de Dez Anos

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ABSTRACT

INTRODUCTION: Endophthalmitis is a sight-threatening emergency that requires prompt diagnosis and treatment. In the last few years, the role of early vitrectomy in endophthalmitis has been reconsidered. This study aims to describe the clinical profile and outcomes in endophthalmitis patients undergoing pars plana vitrectomy (PPV) and evaluate the effects of early PPV.

METHODS: Retrospective study of 13 eyes from 13 patients with clinical diagnosis of endophthalmitis treated with PPV at Hospital Pedro Hispano, Portugal, between September 2013 and August 2023. Demographics and clinical data were collected from the patients' medical records.

RESULTS: The mean age of patients was 69.0 ± 2.5 years and 8 (61.5%) were male. Two cases (15.4%) of endogenous endophthalmitis in the setting of infectious endocarditis were observed. Eleven (84.6%) cases of exogenous endophthalmitis were observed: 5 (38.5%) after intravitreal injection, 2 (15.4%) after cataract surgery, 2 (15.4%) related to late complications of glaucoma surgery, 1 (7.7%) after phaco-vitrectomy, and 1 (7.7%) after penetrating trauma. Most patients presented an initial visual acuity (VA) of hand motion (58.3%). PPV was performed an average of 3.9 ± 1.2 days after admission. The final VA improved in the majority of patients (66.7%), with 38.5% of patients reaching a final VA ≥20/40, 23.0% reaching 20/200-20/50, and 38.5% ≤20/400. Patients submitted to early PPV in the first 48 hours from admission (N=7) showed a tendency for a more favorable final visual outcome compared with patients submitted to PPV >48 hours (100% *vs* 33.3% improved their vision and 42.9% *vs* 33.3% achieved a final VA ≥20/40, respectively).

CONCLUSION: The most common cause of endophthalmitis among our patients was post-ophthalmic surgery, which reinforces the importance of sterile techniques and proper patient education for alarm symptoms. Vitrectomy for endophthalmitis results in VA improvement in some cases, and early vitrectomy may provide more favorable outcomes.

KEYWORDS: Endophthalmitis; Treatment Outcome; Vitrectomy.

RESUMO

INTRODUÇÃO: A endoftalmite é uma emergência ameaçadora da visão e requer diagnóstico e tratamento imediatos. Nos últimos anos, o papel da vitrectomia precoce nos casos de endoftalmite tem sido reconsiderado. Este estudo tem como objetivo descrever o perfil clínico e resultados nos doentes com endoftalmite submetidos a vitrectomia via *pars plana* (VVPP) e avaliar os efeitos da VVPP precoce.

MÉTODOS: Estudo retrospetivo de 13 olhos de 13 doentes com diagnóstico clínico de endoftalmite tratados com VVPP no Hospital Pedro Hispano, Portugal, entre setembro de 2013 e agosto de 2023. Os dados demográficos e clínicos foram recolhidos dos processos dos doentes.

RESULTADOS: A idade média dos doentes era de 69,0 ± 2,5 anos e 8 (61,5%) eram do sexo masculino. Foram observados 2 casos (15,4%) de endoftalmite endógena no contexto de endocardite infeciosa. Onze (84,6%) casos de endoftalmite exógena foram registados: 5 (38,5%) após injeção intravítrea, 2 (15,4%) após cirurgia de catarata, 2 (15,4%) relacionados com complicações tardias de cirurgia de glaucoma, 1 (7,7%) após faco-vitrectomia e 1 (7,7%) após trauma ocular penetrante. A maioria dos doentes apresentava uma acuidade visual (AV) inicial de movimentos de mão (58,3%). A VVPP foi realizada em média 3,9 ± 1,2 dias após a admissão. A AV final melhorou na maioria dos doentes (66,7%), com 38,5% a atingir uma AV final ≥20/40, 23,0% entre 20/200-20/50 e 38,5% ≤20/400. Os doentes submetidos a VVPP precoce nas primeiras 48 horas após a admissão (N=7) apresentaram uma tendência para um resultado visual final mais favorável comparativamente aos doentes submetidos a VVPP>48 horas (100% *vs* 33,3% apresentaram melhoria da AV, e 42,9% *vs* 33,3% atingiu uma AV final ≥20/40, respetivamente).

CONCLUSÃO: A causa mais comum de endoftalmite nos nossos doentes foi pós-cirurgia oftalmológica, o que reforça a importância das técnicas de assepsia e educação dos doentes para os sinais de alarme. A vitrectomia melhora a AV em alguns casos de endoftalmite, e a vitrectomia precoce pode proporcionar resultados mais favoráveis.

PALAVRAS-CHAVE: Endoftalmite; Resultado do Tratamento; Vitrectomia.

INTRODUCTION

Endophthalmitis is a serious, sight-threatening condition that requires urgent diagnosis and treatment.[1] It has a poor prognosis, with a final visual acuity (VA) inferior to 20/100 in 44% of the cases.[2] The disease can be caused by intraocular surgery, open globe trauma, or hematogenous spread.[3]

Classically, the results of the Endophthalmitis Vitrectomy Study (EVS), a multicenter, randomized clinical trial published in 1995, postulated that routine immediate vitrectomy was indicated in patients with initial VA of light perception at diagnosis, but it was not necessary for those with initial VA of hand motion or better since there was no difference in visual outcome in this group, whether or not an immediate vitrectomy was performed.[4] However, in the last few years, the role of early vitrectomy in endophthalmitis has been reconsidered as vitrectomy techniques have markedly developed, knowledge of the physiopathology of endophthalmitis has increased, and several studies have suggested more favorable outcomes with early surgery.[5–7] Immediate pars plana vitrectomy (PPV) can allow the removal of the microbiologic agent and its toxins from the vitreous cavity, vitreous sampling for microbiological analysis, clearing of vitreous opacities, removal of vitreous membranes that can induce pathological vitreoretinal adhesion, and allow a better distribution of intravitreal antibiotics.[4,8]

This study aims to describe the clinical profile and results of endophthalmitis patients treated with PPV at our center and evaluate the impact of early PPV in the final visual outcome.

METHODS

The present study was conducted in accordance with the tenets of the Declaration of Helsinki. This was a retrospective study of the patients with clinical diagnosis of endophthalmitis who were treated with PPV at the Ophthalmology Department of Hospital Pedro Hispano, Portugal, in the last 10 years (between September 2013 and August 2023). Data collected from the patients' medical records included demographics, past medical history, etiology, date of admission, date of symptoms occurrence, treatment modalities and date, culture results, and VA on admission and last observation. VA was assessed using the decimal scale chart and converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. VA of counting fingers (CF), hand movement (HM), light perception (LP), and no light perception (NPL) were converted to 2.10, 2.40, 2.70, and 3.00 logMAR,

respectively, as used in publications from the Royal College of Ophthalmologists' National Ophthalmology Database,[9] using a tool by Moussa *et al*.[10] The diagnosis of endophthalmitis was presumed based on the patient's clinical presentation and later established by positive culture in some cases.

All patients received intravitreal injections of vancomycin 1 mg/0.1 mL and ceftazidime 2.25 mg/0.1 mL. These were initially administered until PPV was performed. All patients underwent a complete 23- or 25-gauge PPV (involving core and peripheral vitrectomy) as soon as possible according to the operating room's logistics and the patient's ocular and systemic status. At the beginning of the procedure, aqueous humor samples and vitreous samples were obtained by limbal paracentesis and dry vitrectomy, respectively, and sent for microbiological analysis. At the end of the surgery, intravitreal vancomycin and ceftazidime were administered in all cases. Eyes with important inflammation in the postoperative time received additional intravitreal injections of vancomycin and ceftazidime in the following days. Topical treatment included fortified vancomycin 50 mg/mL and fortified ceftazidime 50 mg/mL, as well as corticosteroids and cycloplegic agents. Systemic ciprofloxacin and prednisolone were given in most cases, and systemic fluconazole was given in one case. Endogenous endophthalmitis patients were treated with systemic ampicillin and ceftriaxone (and gentamycin in one patient).

All statistical analysis was performed using SPSS software version 26.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were described through mean (M) ± standard deviation (SD) and categorical variables through absolute (n) and relative (%) frequencies. Parametric tests were applied after the normality of the sample was assessed by the Kolmogorov-Smirnov test. A paired samples t-test was conducted to evaluate the differences in VA over time and an independent samples t-test to evaluate the differences in VA between groups. The global sample was divided into two groups according to PPV timing, and a mixed between-within subjects' analysis of variance was conducted to assess the impact of performing PPV in the first 48 hours after admission (Group 1) or after this period (Group 2) on patients' final visual outcome. Statistical significance was considered when p-value <0.05.

RESULTS

Thirteen eyes from 13 patients were studied (giving an average of 1.3 cases per year at our center). Baseline characteristics are summarized in Table 1. The mean age of patients was 69.0 ± 2.5 years and 8 (61.5%) were male. The mean follow-up time was 26.9 ± 6.0 (3-59) months.

Two cases (15.4%) of endogenous endophthalmitis in the setting of infectious endocarditis were observed. Eleven (84.6%) cases of exogenous endophthalmitis were observed: 5 (38.5%) after intravitreal injection, 2 (15.4%) after cataract surgery, two (15.4%) related to late complications of glaucoma surgery, one (7.7%) after phaco-vitrectomy, and one (7.7%) after penetrating ocular trauma. The two cases of late complications of glaucoma surgery included one eye with bleb-associated endophthalmitis three years after nonpenetrating deep sclerectomy complicated with late Seidel and development of an avascular bleb, and one eye with late tube exposure six years after Ahmed glaucoma valve implantation. Excluding these two cases, the remaining postoperative endophthalmitis cases occurred an average of 11.0 ± 2.9 (3-25) days after the procedure.

Patients' admission to the hospital occurred an average of 2.2 ± 0.5 days (1-4) from symptoms occurrence. Most

Table 1. Demographic and baseline characteristics.

Variables	
Number of patients, N	13
Number of eyes, N	13
Age (years), M±SD (range)	69.0 ± 2.5 (56-82)
Gender, N (%)	
Male	8 (61.5%)
Female	5 (38.5%)
Laterality, N (%)	
Right eye	4 (30.8%)
Left eye	9 (69.2%)
Lens status, N (%)	
Pseudophakic	7 (53.8%)
Phakic	6 (46.2%)
Comorbidities, N (%)	
Diabetes *mellitus*	5 (38.5%)
Rheumatoid arthritis	1 (7.7%)
Colorectal carcinoma	2 (15.4%)
Human immunodeficiency virus	1 (7.7%)
Endogenous *vs* exogenous endophthalmitis, N (%)	
Endogenous	2 (15.4%)
Exogenous	11 (84.6%)
Etiology, N (%)	
Infeccious endocarditis	2 (15.4%)
Intravitreal injection	5 (38.5%)
Cataract surgery	2 (15.4%)
Phaco-vitrectomy	1 (7.7%)
Penetrating ocular trauma	1 (7.7%)
Late complications of glaucoma surgery	2 (15.4%)
Culture results, N (%)	
Negative	6 (46.2%)
Positive	7 (53.8%)
Time between first symptoms and admission (days), M±SD (range)	2.2 ± 0.5 (1-4)
Number of antibiotic IV injections, M±SD (range)	3.6 ± 0.4 (2-6)
Time between admission and first antibiotic IV injection (days), M±SD (range)	0.8 ± 0.5 (0-6)
Time between admission and PPV (days), M±SD (range)	3.9 ± 1.2 (0-15)

IV, intravitreal; logMAR, logarithm of minimum angle of resolution; M, mean; N, absolute frequencies; PPV, pars plana vitrectomy; SD, standard deviation; %, relative frequencies.

patients presented an initial VA of hand motion (58.3%), counting fingers in 16.7%, light perception in 8.3%, 1.30 logMAR (Snellen equivalent of 20/400) in 8.3%, and 1.00 logMAR (20/200) in 8.3%.

Our patients received a total of 3.6 ± 0.4 (2-6) intravitreal injections of vancomycin and ceftazidime; an average of 1.3 ± 1.1 (0-4) were performed before PPV. The mean time between diagnosis and the first antibiotic intravitreal injection was 0.8 ± 0.5 (0-6) days.

PPV was performed in all patients an average of 3.9 ± 1.2 days (0-15) after admission. Regarding cases of particularly delayed PPV, surgery was performed 15 days from presentation in one patient with exogenous endophthalmitis who initially refused PPV. One patient with endogenous endophthalmitis in the setting of bacteriemia and infectious endocarditis was submitted to PPV 10 days from admission because of the lack of systemic operative conditions. These patients were submitted to repeated antibiotic intravitreal injections until PPV was possible. In the remaining patients, PPV was performed as soon as feasible according to the operative room's availability and the patient's condition.

Primary silicone oil tamponade was used in four patients and sulfur hexafluoride (SF6) gas tamponade in one patient. Additional intraoperative procedures included anterior chamber washout, lensectomy in phakic eyes, and aspiration of septic foci. Ahmed glaucoma valve was removed in the patient with late tube exposure.

Culture results were positive in 7 cases (53.8%) and the most frequent microbiological agent was *Staphylococcus epidermidis* (N=3, 42.9%). Other agents identified in a single case included *Streptococcus anginosus*, *Cutibacterium acnes*, *Enterococcus faecalis*, and *Serratia marcescens*. Most were sensitive to vancomycin, fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin) and/or 3rd generation cephalosporins.

The final VA improved in the majority of patients (66.7%), with 38.5% reaching a final VA ≤ 0.30 logMAR (≥20/40), 23.0% reaching 0.40-1.00 logMAR (20/200-20/50), and 38.5% ≥1.30 logMAR (≤20/400). Two patients (15.4%) achieved a final VA of 0.00 logMAR (20/20). The lowest final visual outcomes (VA ≥1.30 logMAR) included 1 (7.7%) patient with NLP, 2 (15.4%) with LP, 1 (7.7%) with HM, and 1 (7.7%) with 1.30 logMAR (20/400).

The sample was divided into two groups according to PPV timing from admission: patients who underwent PPV ≤ 48 hours from admission (Group 1) and those who underwent PPV > 48 hours from admission (Group 2). In group 1 (N=7), the final VA improved in 100% of cases, with 14.2% reaching a final VA ≥ 1.30 logMAR (≤20/400), 42.9% between 0.40-1.00 logMAR (20/200-20/50), and 42.9% ≤ 0.30 logMAR (≥20/40). Regarding group 2 (N=6), the final VA improved in 33.3% of patients, with 66.7% reaching a final VA ≥ 1.30 logMAR (≤20/400), 0% between 0.40-1.00 logMAR (20/200-20/50), and 33.3% ≤ 0.30 logMAR (≥20/40).

Table 2 summarizes VA changes between diagnosis and last observation for both groups. The initial VA did not differ between the two groups (p=0.841), while the final VA was significantly better in Group 1, compared to Group 2 (p=0.026). VA significantly improved in the global sample (p=0.007) and Group 1 (p=0.002), but not in Group 2 (p=0.420). A mixed between-within subjects' analysis of variance was conducted to assess the impact of PPV timing on patients' final visual outcome. The main effect comparing the two groups did not reach statistical significance ($F(1,10) = 4.424$, p=0.062, partial eta squared = 0.307), although the results illustrated in the clustered bar chart (Fig. 1) suggest a tendency for a more favorable evolution of VA between the baseline and the final visit in Group 1.

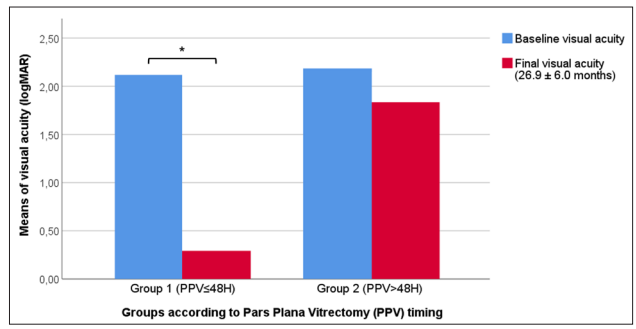

Figure 1. Clustered bar chart – Mean baseline visual acuity and mean final visual acuity for each group according to pars plana vitrectomy timing from admission (Group 1, PPV performed in the first 48 hours; Group 2, PPV performed after 48 hours). Note that a visual acuity of 0.00 logMAR corresponds to Snellen's equivalent of 20/20. H, hours; LogMAR, Logarithm of minimum angle of resolution; PPV, pars plana vitrectomy; *, statistical significance.

Early- and long-term complications included macular edema (N=2), choroidal detachment (N=2), vitreous cavity hemorrhage (N=2), phthisis bulbi (N=2), ocular hypertension (N=1) and ocular hypotony (N=1).

DISCUSSION

The most common cause of endophthalmitis among our patients was post-ophthalmic surgery, which reinforces the

Table 2. Visual acuity at diagnosis and last observation for the global sample and groups divided according to PPV timing (Group 1, PPV≤48 H; Group 2, PPV>48 H).

Groups	Initial VA (logMAR) M±SD (range)	Final VA (logMAR) M±SD (range)	Paired samples t-test
Group 1 (N=6)	2.12 ± 0.56 (1.00-2.40)	0.29 ± 0.26 (0.00-1.30)	t(5)=5.669; p=0.002*
Group 2 (N=6)	2.18 ± 0.56 (1.10-2.70)	1.83 ± 1.36 (0.00-3.00)	t(5)=0.879; p=0.420
Total (N=12)	2.15 ± 0.54 (1.00-2.70)	1.10 ± 1.23 (0.00-3.00)	t(11)=3.294; p=0.007*

H, hours; LogMAR, logarithm of minimum angle of resolution; M, mean; N, absolute frequencies; PPV, pars plana vitrectomy; SD, standard deviation; VA, visual acuity; *, statistical significance.

importance of sterile techniques and proper patient education for alarm symptoms. Our patients sought ophthalmological observation an average of 2.2 ± 0.5 days from symptoms occurrence, presenting low VA at diagnosis (from LP to 1.00 logMAR [20/200]). Systemic comorbidities were present in a considerable portion of patients.

The causative infecting agent and its susceptibility in endophthalmitis varies according to the etiology, geographic location, and local practices.[11] For endophthalmitis in general, the most common isolated bacteria is coagulase-negative *Staphylococcus*.[12] As expected, *Staphylococcus epidermidis* was the most common microbial agent in our study. No resistance to the antibiotics used in the standard treatment protocol was observed. These results are in accordance with another retrospective study of 32 patients who underwent PPV for endophthalmitis with microbial analysis. Gram-positive organisms, particularly streptococcal species and coagulase-negative *Staphylococcus*, were the most common organisms, and visual outcomes were significantly worse in patients with streptococcal endophthalmitis.[1]

Endophthalmitis is an ophthalmological emergency with a very poor prognosis and often results in severe vision loss. It has been postulated that retinal damage can occur soon, and it is mostly secondary to toxin production and host inflammatory response, which is why clearance of the microbial agent and purulence from the vitreous cavity through early and complete PPV can be advantageous over more conservative approaches.[7] In a more subacute phase, endophthalmitis is associated with abnormal vitreoretinal adhesions formation with consequent vitreoretinal traction. If surgery is delayed, progression of the inflammatory vitreoretinal interface, retinal ischemia, retinal breaks and preretinal fibrosis can develop and impede visual improvement.[5]

Modern PPV techniques have changed how the conclusions of the EVS should be interpreted and applied in current practice.[11,13] Several more recent studies have suggested more favorable outcomes with early PPV for the treatment of endophthalmitis.[14,15] A retrospective study of 62 eyes with acute postcataract endophthalmitis suggested that complete and early vitrectomy should be the initial treatment for fundus-obscuring endophthalmitis, improving the recovery of a VA ≥20/40 by approximately 50% compared to a predominantly tap-and-inject treatment paradigm.[7] Another retrospective study of 33 patients concluded that PPV within 7 days resulted in improved final VA outcomes in patients with exogenous endophthalmitis. Complications included retinal detachment (24.2%), macular hole (3%), hypotony (6%), suprachoroidal hemorrhage (3%) and enucleation/evisceration (6%).[5] A prospective, comparative observational study of 41 endophthalmitis cases found that primary vitrectomy (within 6 hours) or, if not achievable, primary injection of intravitreal antibiotics locally followed by admission for vitrectomy (performed in a median time from primary intravitreal antibiotics to vitrectomy of 23 hours) centrally allowed for early vitrectomy for all cases of acute endophthalmitis, and most eyes in both groups achieved a clinically meaningful improvement in BCVA (defined as ≥0.3 logMAR, equivalent to 15 letters).[16]

Our patients were submitted to PPV an average of 3.9 ± 1.2 days from admission. PPV was particularly delayed in two patients for external reasons, the remaining patients were treated with PPV as soon as feasible. Ideally, a vitreoretinal surgeon and a staffed operating room would be instantly available, but this reality is not easy in everyday practice, especially in smaller centers. At our center, intravitreal injections of vancomycin and ceftazidime are immediately started until PPV, in an attempt to control the infection, if surgery is not readily performed. Intravitreal injections are once again administered in all cases at the end of the surgery. In our study, overall, VA improved in most patients (66.7%) after PPV and a final VA ≥20/40 was achieved in 38.5%. Initial VA did not differ between the two groups, suggesting that the severity of the clinical presentation did not significantly influence the PPV timing. More positive results were observed in the group of patients treated with PPV in the first 48 hours from admission: 100% of cases improved their vision, and a final VA ≥20/40 was achieved in 42.9%. Graph representation of VA evolution in the two groups divided according to PPV timing also illustrates a tendency for more favorable results when PPV is performed earlier. Similar results were described in a retrospective cohort study of 64 patients who underwent early PPV within 72 hours of presentation for the treatment of acute infective bacterial endophthalmitis, where a final VA equal to or better than 0.477 logMAR (20/60) was observed in 42%. Ophthalmology Departments should be prepared and develop protocols to avoid delays because if PPV is performed even earlier, it possibly can allow more positive visual outcomes.

Adjunctive systemic antibiotic therapy is a controversial but common practice, despite limited data, due to the severity of the disease and poor prognosis.[17] The EVS postulated that there was no significant role of systemic antibiotics in the management of postoperative endophthalmitis in patients treated with intravitreal antibiotics.[4] However, patients with severe endophthalmitis were excluded and nearly half of the patients received systemic ceftazidime or amikacin, which have poor intraocular penetration after systemic use. We verified that most of our patients were also treated with adjunctive systemic antibiotics, namely ciprofloxacin. The pharmacokinetic rationale behind its use is the rapid elimination of intravitreally applied antibiotics with almost complete removal after 24 hours, whereas systemic administration favors intraocular antibiotic accumulation over time. Ciprofloxacin has good intraocular penetration, and the use of silicone oil tamponade increases its intraocular levels substantially.[18] The best-documented agents achieving therapeutic levels in the vitreous seem to be meropenem, linezolid, and moxifloxacin.[17]

The limitations of this study include the retrospective design and the limited sample size due to the rarity of the disease. The small sample size does not allow us to reliably extrapolate these results, thus multicenter studies are needed to validate our conclusions.

CONCLUSION

The most common cause of endophthalmitis among our patients was post-ophthalmic surgery, which reinforces the importance of sterile techniques and proper patient education for alarm symptoms. Vitrectomy for endophthalmitis results in VA improvement in some cases, and early vitrectomy may provide more favorable outcomes. Multicenter studies are needed to validate these results.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

ARV: Study design, data collection, data analysis and manuscript writing.

CT, RC, BV, TM and PT: Study design, review of the manuscript and its scientific content.

All the authors approved the final version to be published.

ARV: Conceção do estudo, recolha de dados, análise de dados e redação do manuscrito.

CT, RC, BV, TM e PT: Conceção do estudo, revisão do manuscrito e do seu conteúdo científico.

Todos os autores aprovaram a versão final a ser publicada.

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