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ORIGINAL ARTICLE

Globe salvage in Group D and Group E Retinoblastoma after Intra-arterial chemotherapy (IAC).

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ABSTRACT… Objective: To evaluate the effectiveness of IAC in Group D and E retinoblastoma, with a specific focus on globe salvage, in a tertiary care center in Pakistan. **Study Design:** Retrospective study. **Setting:** Lahore General Hospital, Lahore. **Period:** 20th June 2025 to 20th August 2025. **Methods:** In which patients with group D and E retinoblastoma were included. Demographic and clinical data were retrieved from ophthalmology department of Lahore General Hospital. Patients received six cycles of intravenous chemotherapy followed by IAC. Up to four IAC sessions were administered. Tumor regression was assessed one-month post-IAC, and globe salvage was defined by sustained stability over six months. **Results:** There were 55 eyes of 55 patients. Mean age was 20.96±14.03 months. Twenty-nine eyes had group D and 26 had group E retinoblastoma. Tumor regression was noted in most of both groups, with no significant difference. Globe salvage with vision was observed more frequently in Group D (44.8%) compared to Group E (19.2%). Enucleation and loss of visual function were more common in Group E. Ischemic toxicity was rare, signifying the relative safety of IAC. **Conclusion:** Intra-arterial chemotherapy is an effective globe-sparing treatment for retinoblastoma, achieving high rates of tumor regression and globe salvage, even in advanced disease stages.

Key words: Chemotherapy, Etoposide, Melphalan, Ophthalmic Artery, Retinoblastoma, Vincristine.

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INTRODUCTION

Over the years, possibilities for treating retinoblastoma (RB) have improved significantly. Intravenous chemotherapy (IVC) and, if necessary, adjuvants, have formed the backbone of treatment for the past two decades.[1] As Reese-Ellsworth (RE) classification system was based on radiotherapy for intraocular retinoblastoma, it has mostly been replaced with International Classification of Retinoblastoma (ICRB) for managing this disease.[2] Based on this classification group E tumors require enucleation while groups A through C have shown considerable success after chemotherapy.[3] Since the advent of IVC, several centers have stopped using external beam radiation (EBRT) as their primary treatment for group D eyes and the eye globe salvage rate has improved.[4] However, globe salvage still remains a challenge in cases where only IVC is used. Recently, intra-arterial chemotherapy (IAC) has been adopted as a first-line therapy for group D tumors.[5] It has the advantage of higher concentration of chemotherapy drugs reaching the tumor, with negligible systemic side effects when compared with systemic IVC. It is effective in tumor control and eye salvage in cases of advanced and refractory RB. By achieving higher concentration in the target tumor, IAC has shown improved outcome in group D and E retinoblastoma. With these added benefits, IAC has emerged as the first-line management option in selected cases, and in developed countries the 5-year survival rate has reached 99% as the patients present with early disease.[6] However, in the developing countries, varying results are seen in terms of survival, vision saving and globe salvage especially in group D and E, retinoblastoma. In one study, globe salvage was achieved in 5 out of 6 eyes of group D and 3 out of 5 eyes of group E patients, after IAC.[7] The results were preliminary as the sample size was very small and all groups of RB were included.

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We planned this study in a larger sample size and focusing on the group D and E retinoblastoma.

The objectives of the study were to determine the frequency of globe salvage and compare the results of group D and group E retinoblastoma after IAC.

METHODS

It was a retrospective study which included all the patients who presented to Lahore General Hospital, which is a tertiary care center in Punjab after approval from the hospital ethical review committee Ref. No. (OSP-IRB/003-2025), medical records of retinoblastoma patients were retrieved from 2018 to 2024. Patients who underwent IAC in group D and E were selected. Globe salvage was defined as regression in terms of no active tumor vascularization, no hemorrhage, along with decrease in tumor size, increase in calcification and increase in scarring, and remaining stable on monthly examination under anesthesia for 6 months. A total of 55 records qualified the inclusion criteria which was defined as patients of either gender, age less than or equal to 5 years with diagnosed group D or group E retinoblastoma. Patients with retrolaminar tumor invasion, extraocular tumor extension and metastatic disease were excluded.

The demographic details (name, age, gender, group D or E) were recorded on a self-designed proforma. Data regarding history and examination was collected. Number of IVC and IAC sessions were recorded. Primary IVC consisted of six cycles of intravenous vincristine, etoposide, and carboplatin (VEC) every 3 weeks, followed by one cycle of IAC. The second IAC was given if needed (maximum of 4 injections were given). A micro-catheter was guided through the femoral artery to the ophthalmic artery in the treated eye. The melphalan was delivered directly into the artery. The dosage was determined by the child's age: 3mg for under 2 years old, 4mg for 2-3 years old, and 5mg for over 3 years old. Examination under anesthesia was conducted after one month following IAC to look for signs of regression. Patients showing complete regression in terms of no active tumor vascularization, no hemorrhage, along with decrease in tumor size, increase in calcification and increase in scarring were kept on one monthly follow up and the globe was considered salvaged if stable for 12 months.

The collected data was entered into and analyzed through SPSS version 26.0. Mean+SD was calculated for quantitative variables like age. Frequencies and percentages were calculated for gender and outcome in each group. Frequency of globe salvage was determined in group D and group E and was compared using chi square test. Data was stratified for age, gender, and post stratification chi square test was applied to see the effect of these effect- modifiers on the outcome. P value of <0.05 was considered statistically significant.

RESULTS

Fifty-five eyes of 55 patients were included. Only one eye of patients with bilateral disease was included. Mean age of patients was 20.96 ± 14.03 months including 63.6% males and 36.3% females. Twenty-nine eyes had group D and 26 had group E retinoblastoma, classified according to ICRB. Tumor regression was noted in most of both groups, with no significant difference (Table-I). Globe salvage with vision was observed more frequently in Group D (44.8%) compared to Group E (19.2%), though this difference was not statistically significant. Enucleation and loss of visual function were more common in Group E, consistent with disease severity. Ischemic toxicity was rare, signifying the relative safety of IAC in experienced hands. Figures-1, 2 and 3 show three different cases with group D and E retinoblastoma.

FIGURE-1

Group D tumor pre and post intra-arterial chemotherapy

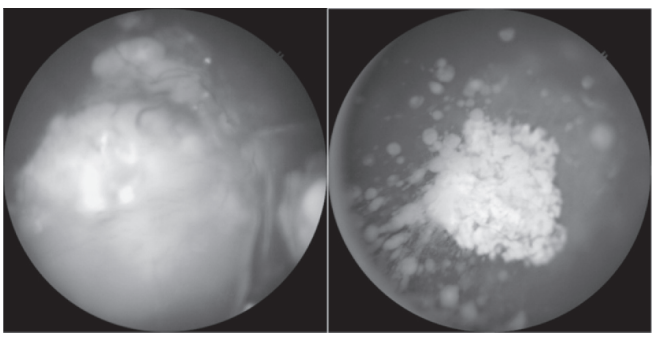


TABLE-I

Details of tumor response to intra-arterial chemotherapy in group D and E.

Variables		ICRB Group				P-Value
		D		E		
		Number	%age	Number	%age	
Side of eye	Left	12	41.4	15	57.7	0.227
	Right	17	58.6	11	42.3	
Procedure IAC	Single injection	4	13.8	4	15.4	
	2 to 4 injections	25	86.2	22	84.6	
	Tumor regression	22	75.9	17	65.4	0.867
	No regression	5	17.2	8	30.8	
	No follow up data	2	6.9	1	3.8	
Outcome	Globe salvaged with some vision	13	44.8	5	19.2	0.951
	Globe salvaged but no vision	7	24.1	10	38.5	
	Enucleation	5	17.2	8	30.8	
	Lost to follow up	4	13.8	3	11.5	
Ischemic chorioretinal toxicity	Lost to follow up	4	13.8	3	11.5	.0.556
	Present	0	0.0	1	3.8	
	Not seen	25	86.2	22	84.6	

FIGURE-2

Group E tumor pre and post intra-arterial chemotherapy

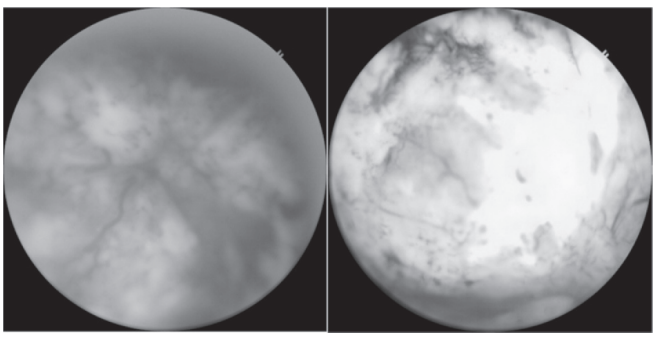
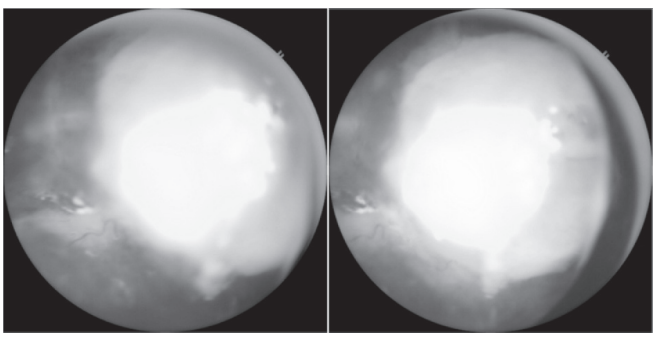


FIGURE-3

Group D tumor pre and post intra-arterial chemotherapy showing no response and was enucleated



DISCUSSION

Our results showed that globe salvage with some vision was observed more frequently in Group D (44.8%) compared to Group E (19.2%), though this difference was not statistically significant. None of the patients reported mortality although a total of 7 patients out of 55 (12.7%) lost to follow up.

Retinoblastoma is a rare tumor of the eye and the data from the low- and middle-income countries is scarce.[8] Due to the high mortality associated with the condition, previously the focus was on saving the life of the patient. Over the last couple of decades, globe salvage and preservation of vision has been widely considered. Present-day globe-sparing treatments for RB include chemotherapy, radiotherapy, thermotherapy, cryotherapy, and laser photocoagulation.[9] Chemotherapy may be administered through various routes, including intravenous, intravitreal, and intra-arterial delivery.[9] Over 26 countries have adopted intra-arterial chemotherapy as part of the treatment approach for retinoblastoma.[10] Since IAC is delivered locally, it helps prevent the adverse effects typically associated with systemic chemotherapy.[11] Prior to the advent of intra-arterial chemotherapy (IAC),

nearly 80% of patients with advanced retinoblastoma required enucleation to prevent the risk of central nervous system invasion and hematogenous dissemination.[12,13]

The effectiveness of IAC in preserving the eye has been well-established through various studies. According to a meta-analysis, globe salvage rates with IAC were 35% for groups D and E, and 63.3% for Groups A to C.[14] In our study the globe salvage rate was 68.9% and 57.7% for group D and E respectively. However, our follow up was only for one year.

In this study, initial tumor regression following IAC was achieved in both D and E groups. These findings support the growing body of evidence suggesting that IAC is an effective primary treatment modality for advanced intraocular RB. The globe salvage rate with preserved vision was comparable in both groups—44.8% in group D and 19.2% in Group E. Additionally, the enucleation rates were relatively low (17.2% in Group D and 30.8% in Group E). However, the rates could have been different if the patients follow up record was more than one year.

Complications such as ischemic chorioretinal toxicity were rare. Only one case (3.8%) in group E experienced such toxicity, and no cases were reported in group D. This suggests a favorable safety profile for IAC.

In an early report, Abramson et al. found that intra-arterial chemotherapy successfully prevented enucleation in 7 out of 9 eyes.[15] Peterson et al. examined 17 eyes diagnosed with Group D retinoblastoma that had not responded to systemic chemotherapy and were subsequently treated with IAC, resulting in globe salvage in 13 cases (76%).[16] Eyes that eventually required enucleation typically showed widespread recurrence of subretinal or vitreous seeding. Gunduz et al. identified that the primary causes of treatment failure after chemo-reduction were subretinal seeding, vitreous seeding, and the presence of subretinal fluid, features that are frequently associated with Group D retinoblastoma.[17]

Intra-arterial chemotherapy (IAC), when used in combination with intravenous chemotherapy (IVC) and focal therapies, has been shown to be an effective treatment strategy for advanced retinoblastoma.[18,19] Studies also indicate that IAC contributes not only to tumor regression but may also play a role in reducing the risk of metastasis.[20]

Limitations of this study include retrospective design, limited follow up and a notable proportion of patients who were lost to follow-up (13.8% in Group D and 11.5% in Group E), which may affect the accuracy of outcome assessments, particularly regarding long-term visual and globe salvage rates. The study did not include genetic and molecular data and vision was examined only subjectively.

CONCLUSION

Intra-arterial chemotherapy demonstrates high effectiveness in achieving globe salvage, even in advanced retinoblastoma, with minimal complications, reinforcing its role as a key globe-sparing treatment option.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Khuda Bukhsh Saleemi:** Design, data collection.
2	**Tayyaba Gul Malik:** Methods, design.
3	**Iqra Khalid:** Data collection.
4	**Mian Hassan Ali:** Literature review.
5	**Hina Khalid:** Data entry.
6	**Chaudhary Abdul Fatir:** Data analysis.
7	**Muhammad Farqaleet:** Interpretation.
8	**Muhammad Shahid:** Critical intervention.