

Intra Arterial Chemotherapy (IAC) – Advantages and Pitfalls

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INTRODUCTION

Retinoblastoma is a blinding malignancy of childhood, which is curable when diagnosed early and treated properly, but retinoblastoma is dismal when the basic elements in diagnosis and treatment are lacking. Survival and ocular prognosis is 30% in Africa, 60% in Asia and 95% in Europe and United States and mirrors economic development of the countries.¹ In the past three decades there has been marked improvement in the prognosis among victims of childhood cancer; reporting more than 75% survival rates in the United States;² however, we cannot ignore the fact that 80% of retinoblastoma affects children in the developing countries.

The complexity of the required multi-disciplinary approach makes treatment difficult in the developing countries.³ We have set an example of a retinoblastoma treatment center that caters for early diagnosis, systemic chemotherapy, intra-arterial chemotherapy, intra vitreal chemotherapy, focal laser ablation and long term follow up assisted with retinal camera.

The treatment for retinoblastoma relies heavily on chemotherapy, which can be given through various routes. Systemic intra venous chemotherapy (IVC) has the advantage of addressing systemic metastasis, second tumor, lesser cost and bearable systemic toxicity.⁴ Early diagnoses, appropriate staging and International Classification of Retinoblastoma grouping remain crucial predictive factors regarding prognosis.

The major challenge is when we encounter eyes refractory to systemic intravenous chemotherapy (IVC), or showing early recurrence after systemic chemotherapy. Intra-arterial Chemotherapy (IAC) stands out as a hope to save these eyes and preserve useful vision, especially when this eye is the only eye. The developed countries have been using IAC as the primary treatment modality for unilateral retinoblastoma in order to avoid systemic side effects caused by IVC.⁵ Advanced tumors classified as group D and E commonly need a combination of IAC and IVC.⁴

IAC involves the cannulation of the femoral artery and navigating through the ipsilateral internal carotid artery. We use a Headway 17 micro-catheter manufactured by Microvention Terumo, California, USA. The ostium of the ophthalmic artery is selectively engaged in order to give targeted infusion of potent chemotherapeutic agent at tumor site and therefore, maximum drug concentration is achieved at the tumor bed.⁶ Successful cannulation of ophthalmic artery ostium is reported to be as high as 98% with no angiography related complications.⁷

The success of IAC is attributed to the ability of using a highly potent chemotherapeutic agent with short half-life, mainly Melphalan, which is otherwise highly toxic through intravenous route.⁸

IAC ensures maximum drug concentration in the tumor and in vitreous cavity to combat both sub-retinal and vitreous seeding. Shields et al reported 100% eye salvage in group B, C and D retinoblastoma and 33% eye salvage in group E retinoblastoma.⁹ Another retrospective study of 70 eyes reported 100% success with IAC in group B and C, 94% in group D and 36% in group E.⁵ This success is much higher compared to the rate of eye salvage achieved with IVC alone that is 93% for Group A, 83% for Group B, 73%

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for Group C, 40% for Group D, and 19% for Group E eyes.¹⁰

IAC being a local therapy, the treatment of systemic metastasis remains a challenge when IAC is used as the sole primary treating modality. Yousef et al reported 2.1% metastatic deaths in a meta-analysis including 613 eyes.¹² However, Abramson et al published <1% metastatic deaths among 6 centers treating retinoblastoma with IAC, which seems to be very reassuring.¹²

In Pakistan, the limited number of trained interventional neuro-radiologists and fluoroscopy suites form a significant limitation in offering IAC to victims of retinoblastoma. A developing country like Pakistan cannot ignore the burden of cost. At our center, Lahore General Hospital, only the disposable equipment costs about \$1,000 per session. Aziz et al estimated that 3 sessions of IAC require \$16,000. They also stated that enucleation is the cheapest treatment for retinoblastoma and IVC is relatively cheaper than IAC.¹³

We would like to mention that IAC delivers potent chemotherapeutic drug directly to ocular vasculature, which carries risk of retinal and choroidal vascular occlusion and toxicity. Munier et al reported choroidal or retinal ischemia in 3/13 patients.¹⁴ Shields et al reported choroidal vasculopathy or retinal arterial occlusion in 6/17 patients.⁹ Muen et al also reported cranial nerve palsy, orbital edema and vitreous hemorrhage.¹⁵ Dose adjustment according to patients age works as the best preventive factor according to what we observed in our practice. Gobin et al also support the role of age adjusted dose in preventing sight threatening complications.⁷

IAC is a promising treatment modality for retinoblastoma and it is an important option for refractory tumors. National support to IAC centers is the only hope to flourish IAC in the country in order to avoid enucleation and retinoblastoma related blindness.

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