ISSN2515-8260 Volume08, Issue 04, 2021

# EVALUATION OF OCULAR STATUS IN PATIENTS UNDERGOING COMBINATION CANCER CHEMOTHERAPY

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## 1. INTRODUCTION

Chemotherapeutic agents have long been used to treat cancer either as a single drug or as a combination. Cancer drugs have a great potential to induce acute, chronic, reversible and irreversible damage in any organ system. Ocular toxicity produced by chemotherapeutic agents is relatively uncommon as eye is usually considered as a protected site. Many of the side effects in the eye are usually undetected either by the patient or by the clinician. However, some of these side effects which are potentially reversible and treatable in the early stages, turn out to be irreversible by the time the symptoms are detected. Hence, it is important for the ophthalmologist to be aware of the potential ophthalmic complications to treat them or sometimes even to prevent them.

Ophthalmic complications of these chemotherapeutic agents are sometimes underestimated and neglected. Priority is usually given to the life-threatening effects of the drugs. Ocular surface side effects have been extensively examined by many authors, though the possible underlying mechanisms are poorly understood [1][2].

The quality of life takes a huge hit when the patient develops side effects like continuous watering or dry eye some of which can be easily managed before potential irreversible side effects develop[3][4]. An ophthalmic baseline examination for all patients planned for multiple chemotherapeutic cycles and those undergoing these cycles becomes indispensable part of patient care.

The aim of our study was to compare the baseline ocular status of the patients undergoing combination chemotherapy before the start of chemotherapy and after a minimum of three chemotherapeutic cycles.

## 2. MATERIALS AND METHODS

This prospective non-interventional observational study was approved by institutional ethics committee. The study was conducted in university teaching hospital, Sri Ramachandra Institute of Higher Education and Research Institute, Chennai, India. Sixty-two patients who underwent combination chemotherapy for various cancers participated in our study. Patients undergoing chemotherapy with Intravenous route and oral route were included.All patients less than 18 years were excluded from our study, other routes of administration other than inclusion criteria were excluded from our study.Also, patients undergoing other modalities of treatment for cancer and patients with pre-existing ophthalmic conditions like ocular surface disorders, glaucoma, pre-existing cataract, diabetes, hypertension, dense media opacities changes were excluded.

The patients were subjected to baseline ophthalmic evaluation before the start of the chemotherapy procedure. All patients underwent complete examination of anterior and posterior segment which included visual acuity, slit lamp bio-microscopic evaluation of anterior segment, complete dry eye evaluation - using fluorescein staining, Rose Bengal staining, Schirmer'sI and II, Tear film breakup time test; intraocular pressure measurement, dilated fundus examination with 78 D lens and indirect ophthalmoscopic examination. After a minimum of 3 cycles of chemotherapy the patients were re-examined and underwent a complete ophthalmic re-examination.

All symptomatic patients were treated with tear substitutes and were followed up regularly until the end of their chemotherapeutic cycles.

## 3. RESULTS

There were 27 males and 35 females in the age group between 35 and 50. Among the 62 patients enrolled, the spectrum of effects observed were lid hyperpigmentation 63.5%), madarosis (63.5%), dry eye (50.8%) and blepharon-conjunctivitis (39.1%). The most common nonspecific symptoms which the patients presented with following a minimum of 3 cycles of chemotherapy were blurred vision, watering, photophobia and mild periorbital pain.

### 3.1. Anticancer drugs

The patients whom we evaluated, underwent treatment for the following cancers -colon, breast, cervix and lymphomas. All these patients receivedcombination chemotherapy with standard dose regimens. None of the patients underwent any additional therapeutic modalities like radiotherapy and immunomodulatory therapy.

### 3.2.Ocular adnexa and Lacrimal system side effects

The most common symptoms that the patients initially presented were blurring of vision, stringy discharge of the eye, redness and crusting of the lids. On examination, the most common ocular adnexal side-effect observed were posterior blepharitis with meibomian gland dysfunction which were seen in forty-two patients (67.74%). Other eyelid abnormalities commonly seen were lid hyperpigmentation and madarosis in thirty-eight of the patients (61.29%). Eyelash abnormalities were not noted in any of the patients.Thirty-one patients showed evidence of tear film abnormalities including reduced Schirmer's I&II and Tear Film Breakup Time (TBUT) (50%). Ocular surface staining with Rose Bengal and Lisamine green showed interpalpebral staining which was suggestive of aqueous tear deficiency. Also, inferior conjunctiva was taking up stain in patients with posterior

blepharitis. Epiphora, due to lacrimal duct obstruction at the level of puncta was found in twelve patients (19.35%) [Table 1].

**3.3Ocular side effects**

Photophobia as a symptom was common in most of the patients undergoing treatment with chemotherapeutic agents. All the combination regimens produced variable amount of conjunctival hyperaemia, without any associated symptoms. Twenty- five patients (40.32%) had associated blepharo-conjunctivitis during one of the cycles [Table 2].

None of our patients developed any corneal pathology or associated uveitis was seen. Early anterior cortical opacities and posterior subcapsular opacities were seen intwo patients (3.22%) on slit lamp biomicroscopic examination. Intraocular pressures measured by Goldman applanation tonometry were found to be in the high normal range in seven patients, though no associated signs of structural damage were seen on clinical examination. These patients had no family history of glaucoma. Posterior segment changes in some of these patients included non-specific pigmentary changes in the macula and optic disc pallor with no visual significance.

## 4. DISCUSSION

Cancer chemotherapy includes a wide spectrum of drugs which are now used in higher doses and different regimens. Newer drugs are being developed with limited knowledge of ocular side effects. Since the advent of advanced screening and diagnostic modalities for cancer, more people are diagnosed with cancer at an early stage. Therefore, the survival of the patient is enhanced. Hence the recognition and monitoring of eye diseases resulting from chemotherapy is essential for improved patient care and management[5]. Ocular toxicity can greatly impact the quality of life even though these effects are non-fatal[6].

In this present study, we sought to understand and have a comprehensive experience about the ocular side effects of the combination chemotherapy regimen, at a tertiary care hospital. Ocular status of each patient's eye was assessed before the start of combination chemotherapy and the status was assessed after a minimum of 3 cycles. We broadly evaluated the ocular effects of these chemotherapeutic agents especially in the anterior segment before and after the start of chemotherapeutic cycle. We did not attempt to correlate the side-effects with the specific chemotherapeutic agents, the patients were taking. Majority of thepatients in our study, who were in combination chemotherapy presented with symptoms like blurred vision, stringy discharge of the eye, grittiness, burning sensation and crusting of the eyelids which was mainly due to Posterior blepharitis and associated meibomian gland dysfunction [7].The blurred vision in many of the patients in our study could be attributed to ocular surface and tear film disturbances in these patients. Statistically significant Dry eye and tear film disturbances were most seenamongthe patients in our study undergoing treatment with chemotherapeutic agents[8]. None of our study patients presenting with pain had any evidence of signs of acute inflammation like optic neuritis or uveitis. Epiphora due to puncta occlusion could have also contributed to the blurring. Some patientsalso developed Blepharo-conjunctivitis, which could be attributed to the profound immunosuppression caused by these drugs[9]. Few patients in our study also were found to have early onset anterior cortical and posterior subcapsular opacities[10]. Non-specific adnexal findings like eyelid hyperpigmentation and madarosiswere found as general sideeffects in most of our study

patients. Lacrimal puncta occlusion with associated epiphora was seen in few patients which could be due to the fibrosis induced by these drugs[10]. Pigmentary mottling changes were noted in some of our patients with no significant clinical correlation. Mild optic disc pallor was found in some patients undergoing chemotherapy which could be attributed to the low Hb and poor nutritional status of those patients[10].

Our study has few limitations. Firstly, we could have had a much larger sample size. Secondly, the side-effects could not be correlated directly to a particular drug as we analysed combination chemotherapy. Thirdly, we may not have identified all the possible clinical cases. Despite these limitations, it is important to draw several important conclusions, chief of which is that most of these patients can develop ocular surface disorders if not monitored carefully. Moreover, we feel that newer studies are warranted at every stage of the cancer patient's life to accurately know the immediate, medium-term and long-term side effects of these drugs in both their standard dose regimens and high dose regimens.

## 5. LIMITATIONS

The sample size in our study is small and there is a need for larger sample size to attribute a specific side-effect to individual drugs.

## 6. CONCLUSION

Some ocular toxicities by chemotherapeutic agents can be preventable. Hence clinicians must be aware of the potential of these drugs for these complications. Early consultation with ophthalmologist can lead to appropriate diagnosis and therapeutic interventions. Based on the results from our study every patient undergoing chemotherapy should at least undergo a baseline ophthalmic examination as these patients will require tear substitutes which can greatly improve their quality of life.

## 7. ACKNOWLEDGMENTS – Nil

## 8. CONFLICT OF INTEREST – Nil

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**TABLES**

Table 1: Ocular adnexal side effects

| OCULAR ADNEXAL SIDE-EFFECTS | FREQUENCY (%) |
|---|---|
| Lid hyperpigmentation | 38 (61.29%) |
| Madarosis | 38 (61.29%) |
| Posterior Blepharitis & Meibomian gland dysfunction | 42 (67.74%) |
| Lacrimal puncta-occlusion | 12 (19.35%) |
| Tear film disturbances | 31 (50%) |

Table 2: Ocular side effects

| OCULAR SIDE-EFFECTS | FREQUENCY (%) |
|---|---|
| Blepharo-conjunctivitis | 25 (40.32%) |
| Cataract | 2 (3.22%) |