

## Ocular Toxicity after an Antineoplastic Drug Cyclophosphamide in Male Rat *Rattus Norvegicus*

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**Abstract:** Ocular toxicity induced by anti-cancer chemotherapy is common, but underestimated and under-reported. Use of newer agents and combination chemotherapies have resulted in a significant increase reported cases of chemotherapies induced ocular side effects. While studying the effect of an anticancer drug Cyclophosphamide on the reproductive system and of male rat, some ocular side effects were documented. Our observations are restricted to ocular surfaces including eyelids, conjunctiva, cornea and hemorrhage in the orbital area. This side effect was dose and duration dependent. Ocular toxicities induced by anticancer drugs are generally not preventable; therefore clinicians must be aware of potential vision threatening complications. Therefore, such studies would be useful to ophthalmologist, oncologists and in clinical management of oncology patients.

**Keywords:** Ocular toxicity, chemotherapy, anticancer drug, ophthalmologist, oncologists.

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### 1. INTRODUCTION

Chemotherapeutic drugs have a narrow therapeutic index and the dosage needed to achieve a therapeutic response usually proves toxic to the body's rapidly proliferating cells [1]. Visual changes have been attributed to a number of chemotherapeutic agents such as anti-metabolites, alkylating agents, taxanes and platinum agents [2]. Dealing with the side effects of chemotherapy has always been a major concern. Chemotherapy side effects can be debilitating and can make life very unpleasant. Traditional chemotherapeutic agents act by killing cells that divide rapidly, one of the main properties of most cancer cells [3,4]. In this background, the eye is usually considered a sanctuary site, but has a potentially high degree of sensitivity to toxic substances [5, 6, 7]. The present piece of work deals with ocular side effect of an anti-neoplastic drug Cyclophosphamide.

### 2. MATERIALS AND METHODS

#### 2.1. Antineoplastic Drug

The anticancer drug Cyclophosphamide (Endoxan-N, CAS no. 50-18-0) with molecular weight, 261.086 g/mol. manufactured by Candila Healthcare Limited, Goa was used for the present experiments.

#### 2.2. Animals

Male Wistar rat, *Rattus norvegicus* weighing between 250-300g were obtained from Department of Biochemistry, RTM Nagpur University, Nagpur. Animals were maintained in the laboratory under an absolute hygienic condition as per the recommended procedures, by fulfilling all the necessary ethical standards. They were fed ad libitum with standard pellet diet and had free access to water and kept on a 12hrs light-dark cycle.

#### 2.3. Treatments

Animals were allowed to acclimatized for a period of week before being treated. They were selected randomly and divided into three groups with six animals in each group. Vehicle-treated control (Group-I), 5mg, 7mg and 10mg/KgBW/day for 15days as a sub-chronic dose (Group-II). The drug was administered intraperitoneally.

### 3. RESULTS

Ocular toxicity was observed almost after every therapeutic protocols. Conjunctivitis was the most commonly recorded effect toxicity recorded after Cyclophosphamide treatment. In Cyclophosphamide treated groups (5mg, 7mg and 10mg/KgBW/day for 15days), the ocular toxicity observed were eyelids symmetrically retracted making some sclera visible above the iris, haemorrhage from the cornea of the eye due to impairment of venous drainage. These effects were more prominent with high doses.

### 4. DISCUSSION

Anti-neoplastic chemotherapies has eventual to produce acute and chronic organ damage in any organ system, but the eye is usually considered a protected site since the ocular-visual system has potentially a high degree of sensitivity to toxic substances [6, 8, 9]. In the present study number of side effect are observed after Cyclophosphamide treatment. The data from this report also provide sufficient evidence to relate ocular toxicity to the findings of earlier workers on Cyclophosphamide [10, 11]. The mechanism of visual toxicity induced by anti-neoplastic agent is unknown but may result from central nervous system accumulation of drug after repeated doses [5, 6, 12].

### 5. CONCLUSION

Given the findings of the study, ocular toxicity induced by Cyclophosphamide includes a broad spectrum of disorders, reflecting the unique anatomical, physiological and biochemical features of this essential organ can be minimize by proper and timely dosing also by focusing increase awareness through educational involvement, applying proper use of premedication and non pharmacological treatment for better worth of life.

### REFERENCES

- [1] Kirthi C., Afzal A., Reddy M., Ali S. A., Yerramill A. and Sharma S., A study on the adverse effects of anticancer drugs in an oncology center of a tertiary care hospital, *Int. J. Pharmacy Pharmaceutical Sci.* 6(2), 580-583 (2014).
- [2] Singh P. and Singh A., Ocular adverse effects of anti-cancer chemotherapy and targeted therapy, *J. Cancer Therap. Research.* [\(http://www.hoajonline.com/journals/pdf/2049-7962-1-5\)](http://www.hoajonline.com/journals/pdf/2049-7962-1-5). (2012)
- [3] Chandha V. and Shenoi S.D., Hair loss in cancer chemotherapeutic patients, *Ind. J. Dermatol. Venereol. Leprol.* 69, 131-132 (2004).
- [4] Kamil N., Kamil S., Ahmed S.P., Ashraf R., Khurram M. and Ali M.O., Toxic effects of multiple anticancer drugs on skin, *Pak. J. Pharm. Sci.* 27(1), 7-14(2010).
- [5] al-Tweigeri T., Nabholtz J.M. and Mackey J.R., Ocular toxicity and cancer chemotherapy. A review, *Cancer.* 78(7), 1359-1373(1996).
- [6] Omoti A.E. and Omoti C.E., Ocular toxicity of systemic anticancer chemotherapy, *Pharmacy Pract.* 2(4),55-59(2006).
- [7] Li, J., Tripathi R. C. and Tripathi B. J., Drug-induced ocular disorders, *Drug Saf.* 31(2),127-141 (2008).
- [8] Gonzalez F., Menendez D. and Gomez-Ulla F., Monocular visual loss in patient undergoing cisplatin chemotherapy, *Int. Ophthalmol.* 24(6), 301-304(2001).
- [9] Mulvihill A., Budning A., Jay V., Vandenhoven C., Heon E., Gallie B.L., Helen S.L. and Chan HS., Ocular motility changes after subtenon Carboplatin Chemotherapy for retinoblastoma., *Arch. Ophthalmol.* 121, 1120-1124 (2003).
- [10] Stevens A. and Spooner D., Lacrimal duct stenosis and other ocular drug toxicity associated with adjuvant Cyclophosphamide, Methotrexate and 5-fluorouracil combination chemotherapy for early stage breast cancer, *Clin. Oncol.* 13(6), 438-440 (2001).
- [11] Kashiwagi H., Ocular disorders of anticancer drugs-ocular side effects, *Gan To Kagaku Ryoho.* 37(9), 1639-1644 (2010).
- [12] Sastry M.S., Dighade S., Kashmiri Z., Gotmare V. and Dange M., Ocular side effects of some antineoplastic drugs in the male albino rat (*Rattus norvegicus*), *Innov. J. Medical Health Sci.* 2(3), 42-43 (2012).

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