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Refractive error and visual acuity changes following systemic chemotherapy

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ABSTRACT

Background and Aims: The aim of this study was to compare refractive error, uncorrected and corrected distance visual acuity (UDVA and CDVA) changes in patients with different types of cancer before and after completing the course of systemic chemotherapy.

Material and Methods: Sixty-four right eyes of 64 consecutive patients with cancer were evaluated prospectively to compare the changes of UDVA and CDVA using standard Snellen chart and refractive errors using objective refraction before and after chemotherapy process.

Results: The mean age of patients was 52.7± 12.9 (range, 27-80) years [28(43.8%) males, and 36 (56.3%) females]. The most changes in refractive error were found in hyperopic patients in the component of "spherical equivalent" (0.69±1.34) and "spherical" (0.61±2.37) refractive error after the first course of chemotherapy. However, the other changes in deferent refractive error groups were under -0.25 diopter. Although the spherical refractive error in all patients' groups decreased, these reductions were not statistically significant (P>0.05). On the other hand, in all patients' groups, the amount of cylindrical refractive error was increased, but these changes were not statistically significant (P>0.05). Although the UDVA in different refractive error groups had insignificant changes after completing the course of chemotherapy, these changes were not statistically significant(P>0.05). In addition, the CDVA in different refractive error groups remained relatively stable following the chemotherapy process (P>0.05).

Conclusion: The refractive error, UCVA and CDVA after completing the course of systemic chemotherapy remained relatively unchanged. This study revealed that in patients with cancer, the refractive error and vision are not influenced by chemotherapy medication.

Keywords: Cancer; refractive error; visual acuity; chemotherapy

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Introduction

Cancer, also known as neoplasm or tumor, included a broad spectrum of diseases that may initiate at every body organ. This disease results from uncontrolled cell growth and the subsequent invasion of abnormal cells into the adjacent body structures (1). This process is known as metastasis and is the main factor that gives rise to death in affected patients (2). Accordingly, at most epidemiologic studies worldwide, cancer has been ranked as the first or second leading cause of death (3). According to the WHO Global Cancer Observatory (GLOBOCAN) 2018 registry, approximately 18 million cases of cancer have been newly identified in 2018 and the most common types of cancer were reported to be lung, prostate, and stomach for men, and breast, lung, and, cervix uteri for women (4, 5).

Three main types of cancer therapy are surgery, radiation therapy, and chemotherapy. These treatment protocols may be used independently or synergistically (6). Chemotherapy is the administration of chemical agents to destroy cancer cells and is frequently used as standard care of cancer therapy (7). Depending on the type and location of cancer cells, chemotherapy medications are administered through various methods(8).Primarily, this treatment plan is aggressive and may cause systemic complications (9, 10). The main underlying reason for comorbid complications of chemotherapy is its cytotoxic effects on healthy noncancerous cells (11, 12). Indeed, chemotherapy-induced toxicity can potentially adversely affect all body structures (12). The eye is one of the most sensitive organs of the body and may be influenced by toxicity of anti-cancer chemotherapy, as well. Ocular toxicity secondary to anticancer agents frequently occurs in patients who underwent chemotherapy (13). Consequently, various structures and functions of the ocular system may be influenced by chemotherapeutic agents (13-15). In addition to the clinical signs, patients who underwent chemotherapy may encounter ophthalmic-related symptoms including headache, body instability, vertigo, and visual uncertainty that are attributed to the toxicity-induced oculomotor deficiencies (16). Therefore, for early and effective interventions, it is recommended ophthalmologists, pharmacist, and oncologists to be familiar with expected ocular adverse effects of anti-cancer chemotherapy substances (14). From a clinical perspective, the best way to prevent irreversible vision problems is being aware of the possible ocular toxicity and tapering or changing the medication (17, 18).

Previous studies thoroughly evaluated consequences of various chemotherapy agents on different ocular structures, including anterior and posterior segment tissues and ocular adnexa (13-15). Fortunately, a few percentage of patients experience sight-threatening ocular consequences of systemic chemotherapy. These severe complications are reported predominantly in case studies (15, 19, 20). Most frequently encountered ocular adverse effects disappeared after discontinuing medications (21); however, some complications remained persistent and did not heal even after tapering or halting the drugs (21, 22). Alongside the structural consequences, previous studies on ocular function found significant changes in visual field, electroretinography (ERG), and visual evoked potential (VEP) following systemic chemotherapy (22, 23). Katz et al, observed bilateral central scotomas in visual field (VF) testing after intravenous Cisplatin therapy (22). They also found a remarkably decline in a-wave and the absence of b-wave in ERG recording of their patients. Despite the previous studies on refractive and visual acuity changes after administration of systemic medications (24, 25), no study evaluated these parameters after the course of systemic chemotherapy. The present study aimed to evaluate post-chemotherapy changes in refractive error and visual acuity in patients who accomplished different kinds of chemotherapy without any pathologic complications (26). The analyses were regardless of dosage, duration, and type of the medications.

Material and Methods

This prospective observational study was conducted on 64 cancer patients (64 eyes) administered systemic chemotherapy with different medications, regardless of the cancer type and location. The right eyes of the participants were included in the study analyses. All patients were evaluated before and after systemic chemotherapy for changes in the degree of refractive errors (hyperopia, myopia, and astigmatism). Participants were cancer patients referred to the chemotherapy department of Imam Hossein Hospital, Tehran, Iran, for their treatment course during the year 2019. All included patients were between 27 to 80 years old, regardless of their cancer and medication regimen. All subjects experienced systemic chemotherapy for the first time and did not have general weakness during all examinations. Patients with poor general health who could not involve in examinations, and those who required the addition of radiotherapy to their treatment course, were excluded from the study. Before starting the baseline examinations, the presence of comorbid diseases was ruled out by an oncologist in all patients. Before performing both levels of examinations, all participants underwent thorough ophthalmoscopy and slit-lamp evaluation and patients with anterior or posterior segment ocular pathologies such as cataract, uveitis, retinal vein and artery occlusion, choroidal neovascularization, maculopathy, optic neuritis, central serous chorioretinopathy, and retinal detachment were also excluded from the study. All baseline examinations were carried out on the same days of starting the course of chemotherapy (before drug administration). Post-chemotherapy examinations were performed during the first week following the chemotherapy cessation.

The institutional ethics committee of the Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved the protocol for this study (ethics code: IR. SBMU. RETECH. REC. 1397.1006). All participants provided written informed consent, and the study adhered to the tenets of the Declaration of Helsinki.

Examination sequence:

Before and after the course of chemotherapy, the objective dry refraction of all participants was performed using an automated instrument (CHAROPS, CRK-9000) and was confirmed using manual retinoscopy (Heine, Beta200). Three measurements were recorded, and the average value was used for the analyses. Spherical refractive errors were assigned as hyperopia (> +0.75D), emmetropia (between +0.50 D to -0.25 D), and myopia (> -0.50 D). (27, 28) The changes in measured values of myopic, hyperopic, cylindrical, and spherical equivalent (the spherical value plus one-half of the cylindrical value) were analyzed. The measurements of uncorrected and best-corrected visual acuity (UCVA and BCVA) were accomplished using standard Snellen tumbling E-chart adjusted for a 6m viewing distance. The results of UCVA and CDVA were converted to the logMAR values for statistical analyses.

Statistical analysis:

The collected data was analyzed using SPSS-24 (IBM, Armonk, New York, USA) software for Windows. Normal data distribution was tested by Shapiro–Wilk. According to the normal distribution of the data, paired t-test was applied to compare the amount of different refractive error components before and after the first course of chemotherapy. P-values less than .05 were considered significant.

Results

The mean age of 64 patients was 52.7± 12.9 (range, 27-80) years. The age of twenty (31.3%) patients ranged from 50 to 60 years, and 15 (23.4%) cases were in the range of 40 to 50 years. The less frequent

age ranged was <30 and 70-80 years old, including only 2 and 6 patients, respectively. Twenty-eight (43.8%) patients were males, and 36 (56.3%) were females.

According to the definition of refractive error in this study, hyperopia, myopia and emmetropia were found in 22 (34.4%), 11 (17.2%) and 31 (48.4%), respectively. The mean age of patients in hyperopic, myopic and emmetropic patients' groups were 57.3±10.4 (range, 40-80), 44.5±16.6 (range, 27-74) and 52.3±11.9 (range, 33-77), respectively.

Table 1 provides information regarding the amount of refractive error in different groups of patients before and after the chemotherapy course. Although the spherical refractive error in all patients' groups decreased, these reductions were not statistically significant. On the other hand, in all patients' groups, the amount of cylindrical refractive error was increased, but the same as spherical refractive error, these changes were not statistically significant. The most changes in refractive error after cessation of chemotherapy process were found in hyperopic patients in the component of "spherical equivalent" (0.69±1.34) and "spherical" (0.61±2.37) refractive error. However, the other changes in deferent refractive error groups were under -0.25 diopter, which means the refractive error after the course of chemotherapy stayed relatively unchanged.

Table 1: Comparative analysis of refractive error in 64 consecutive patients with different cancers before and after completing the course of chemotherapy. *Paired t-test, N=number

	Study groups		**Minimum**	**Maximum**	**Mean+-SD**	**Mean difference**	**95% confidence interval of the difference**		***P*-value***
							Lower	**Upper**	
Sphere	Hyperopia (n=22)	Before	0.75	10.50	2.10±2.70	0.61±2.37	-0.44	1.67	.239
		After	-0.50	6.75	1.49±1.37				
	Myopia (n=11)	Before	-7.00	-0.50	-2.36±2.01	-0.11±0.38	-0.37	0.14	.341
		After	-7.00	0.00	-2.25±2.12				
	Emmetropia (n=31)	Before	-0.25	0.50	0.15±0.24	0.02±0.21	-0.06	0.09	.677
		After	-0.50	0.75	0.13±0.33				
	Total (n=64)	Before	-7.00	10.50	0.39±2.34	-0.20±1.42	-0.16	0.55	.266
		After	-7.00	6.75	0.19±1.74				
Cylinder	Hyperopia (n=22)	Before	-1.75	0.00	-0.66±0.56	0.16±0.98	-0.27	0.59	.454
		After	-4.00	0.00	-0.82±0.87				
	Myopia	Before	-0.25	-2.50	-1.16±0.76	-0.16±0.20	-0.02	-0.29	.026

	(n=11)	After	-0.50	-2.75	-1.32±0.77				
	Emmetropia (n=31)	Before	-3.00	0.00	-0.94±0.67	0.03±0.23	-0.05	0.12	.442
		After	-3.50	0.00	-0.98±0.77				
	Total (n=64)	Before	-3.00	0.00	-0.88±0.67	-0.10±0.60	-0.05	0.25	.194
		After	-4.00	0.00	-0.98±0.80				
Spherical equivalent	Hyperopia (n=22)	Before	-0.13	10.50	1.77±2.81	0.69±1.34	-0.51	1.89	.243
		After	-1.38	4.75	1.08±1.16				
	Myopia (n=11)	Before	-0.63	-7.50	-2.94±2.07	-0.03±0.62	-0.30	0.23	.783
		After	-0.25	-7.50	-2.91±2.20				
	Emmetropia (n=31)	Before	-1.50	0.50	-0.33±0.41	0.03±0.23	-0.05	0.12	.437
		After	-2.00	0.50	-0.36±0.52				
	Total (n=64)	Before	-7.50	10.50	-0.05±2.46	0.25±١,٦١	-0.15	0.65	.223
		After	-7.50	4.75	-0.30±1.79				

Table 2 demonstrates the UDVA and CDVA in 64 consecutive patients with different cancers before and after completing the course of chemotherapy. It can be inferred that although the UDVA in different refractive error groups had inconsiderable changes after completing the course of chemotherapy compared with before starting chemotherapy, these changes were not statistically significant. However, the CDVA in different refractive error groups remained relatively stable after completing the course of chemotherapy.

Table 2: Comparative analysis of corrected and uncorrected visual acuity in 64 consecutive patients with different cancers before and after completing the course of chemotherapy. *Paired t test N, number; UDVA, uncorrected distance visual acuity; CDVA, corrected distance visual acuity.

	Study groups		**Minimum**	**Maximum**	**Mean+-SD**	**Mean difference**	**95% confidence interval of the difference**		***P*-value***
							Lower	**Upper**	
UDVA	Hyperopia (n=22)	Before	0.03	2.00	0.42±0.51	0.07±0.25	-0.04	0.18	.193
		After	0.00	2.00	0.34±0.44				
	Myopia	Before	0.15	1.30	0.71±0.39	0.06±0.18	-0.06	0.18	.294

	(n=11)	After	0.10	1.30	0.65±0.40				
	Emmetropia (n=31)	Before	0.00	0.50	0.12±0.15	-0.03±0.13	-0.08	0.02	.188
		After	0.00	0.50	0.15±0.15				
	Total (n=64)	Before	0.00	2.00	0.32±0.41	0.02±0.19	-0.03	0.07	.401
		After	0.00	2.00	0.30±0.37				
CDVA	Hyperopia (n=22)	Before	0.00	2.00	0.19±0.46	-0.01±0.09	-0.05	0.03	.747
		After	0.00	2.00	0.19±0.48				
	Myopia (n=11)	Before	0.00	0.20	0.04±0.07	0.01±0.03	-0.01	0.03	.272
		After	0.00	0.15	0.02±0.05				
	Emmetropia (n=31)	Before	0.00	0.20	0.02±0.05	0.00±0.05	-0.02	0.02	.818
		After	0.00	0.22	0.02±0.05				
	Total (n=64)	Before	0.00	2.00	0.08±0.28	0.00±0.06	-0.02	0.01	.891
		After	0.00	2.00	0.08±0.29				

Discussion

A broad range of cancer types could be managed with numerous systemic chemotherapeutic agents. These medications target metastatic cells and inhibit their growth or multiplication, and could result in cell death. Due to their systemic function, chemotherapeutic substances may encompass healthy cells of the body. One of the most sensitive organs that may be affected by chemotherapy medications is the eye. The severity of these adverse effects ranged from mild to severe and irreversible complications. Knowledge of visual adverse effects may aid the clinician to detect and manage such complications as early as possible. In addition, tapering or even discontinuing the drug therapy may be warranted following sight-threatening consequences. Both structural and functional consequences of the anticancer medications have been reported; however, no study has evaluated the post-chemotherapy changes of refractive errors in cancer patients. This article investigated changes in refractive error, UCVA, and BCVA of patients administered anticancer medications.

Vision problems and blurring following some chemotherapy agents such as Mitomycin C, Cyclophosphamide, 5-fluorouracil, Alkyl sulfonates, Platinum complexes, and Methotrexate have been documented (29, 30).Cisplatin which is an Alkylating agent, in higher concentration levels could cause papilledema, idiopathic blurred vision, and optic neuritis in affected patients (31). In a study by Wilding et al, they found that blur vision has been spontaneously managed after discontinuing the course of Cisplatin therapy in a group of patients who experienced post-chemotherapy blurred vision (32) .Carboplatin is another Alkylating agent that might impose self-limited blurred vision in patients who administer this substance in the form of Intravenous injection (33, 34).Cyclophosphamide is another chemotherapeutic medication that is a subgroup of Nitrogen mustard derivatives. It has been reported that this drug could induce reversible blur vision for the first 60 minutes to two weeks after the chemotherapy process (35).

Other anticancer agents that may induce nonspecific and transient blurred vision following chemotherapy cessation, especially when administered intravenously, are Busulfan, Carmustine, Cytosine arabinoside, Methotrexate, 5FU, and Mitomycin C (13, 36-39). Published studies attributed the post-chemotherapy vision changes to the optic nerve disorders, dry eye induced problems, and ciliary spasm or pupillary constriction (35). However, previous studies did not report whether refractive error changes could affect the visual ability of the patients or other structural disorders (30).

We found no significant differences between spherical (myopia and hyperopia) and cylindrical refractive errors in comparing baseline and after the course of chemotherapy in patients who underwent different anticancer medications. However, despite insignificant changes, we found reductions in the mean spherical refractive errors measurements and a rise in the mean values of cylindrical refractive errors in all patients' groups. In addition, SE measurements and emmetropic patients also showed no significant difference at the corresponding levels. In all studied patients, the mean values of UDVA and CDVA for all refractive errors did not significantly change when comparing before and after the chemotherapy course. The most remarkable changes in refractive errors after cessation of the chemotherapy processwere found in hyperopic patients in the component of "spherical equivalent" (0.69±1.34) and "spherical" (0.61±2.37) refractive error. Despite extensive literature review, the authors of the present study were unable to find any similar study for comparing the amount of refractive change after chemotherapy.

Some limitations of the present study were relatively small sample size, lack of categorization of drug and cancer types and their effects on different refractive and visual data, and lack of controlling medication dosage. We also could not adjust the timing of the chemotherapy process that was due to the unpredicted results of this management strategy in cancer patients. A larger study on different types of cancer and different anticancer medications with a comprehensive testing setup is recommended to unveil the chief reasons for the acute or chronic episodes of blurry vision in some patients who experience that after chemotherapy.

Conclusion

In conclusion, we found that regardless of the type of cancer and its administered medication during chemotherapy, no significant refractive and visual acuity changes were observed in the affected patients. Clinically, in patients who do not reveal pathologic structural and functional abnormalities of the eye, different components of refractive error, UDVA, and CDVA are not required to be monitored. Therefore, any post-chemotherapy symptom of blurry vision may be related to disorders other than refractive changes.

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