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ROLE OF GAMMA AND DELTA TOCOTRIENOL (50%) IN RADIATION-INDUCED CONDITIONS OF ESOPHAGEAL, HEAD/NECK AND CERVICAL CANCER PATIENTS AFTER RADICAL RADIOTHERAPY TREATMENT: A STUDY

Radiology

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ABSTRACT

Background: The main aim of our research was to study the role of an isoprenoid compound's (gamma and delta Tocotrienol) in the radiation induced conditions like oesophageal stricture (dysphagia), trismus with neck stiffness, and cervical dystonia after radical radiotherapy treatment in cancer patients.
Method: In this study, histo-pathologically proved patients of oesophageal, head/neck and cervical cancer were selected after radical radiotherapy treatment which presented at Department of Radiation, Aadhar Hospital, Hisar, India. The patients who developed trismus with neck stiffness, cervical dystonia and oesophageal stricture after radical radiotherapy were divided into two group I & II. Group I patients were treated with gamma and delta tocotrienol (50%) capsules along with conventional treatment and group II patients were taken as reference group and was given conventional treatment.
Results: The selected patients were treated for six months with Tocotrienol capsules and evaluated for radiotherapy complications like dysphagia, trismus with neck stiffness, cervical dystonia, radiation induced fibrosis. The oesophageal stricture, trismus with neck stiffness, cervical dystonia conditions were improved up-to 80-90%. Other quality of life measures like emotional liability, depression, able to work normally at their workplaces/ general well-being of the patient were also analysed and were seen to be improved.
Conclusion: Gamma and delta Tocotrienol given after radical radiation treatment for six months have significant and subjective improvement of symptoms. Moreover, these patients quality of life like social life was also better, they feel good. Furthermore, a multi-centric randomized study will be more beneficial to evaluate the role of tocotrienols in radiotherapy complications.

KEYWORDS

INTRODUCTION

Now-a-days radiation is a common method of treatment for various cancers. The radiation method is also known by other names like irradiation, radiotherapy, radiation therapy or x-ray therapy. This method is used alone or combined with chemotherapies in treatment of cancers. In this method affected part of body of cancer patients were exposed to radiation or gamma rays or x-rays. With the development of modern technologies, sparing of healthy or normal tissue, thereby reducing the side effects is possible. Presently, sixty percent of cancer patients are exposed to the radiation therapy in their treatment as a part of their treatment regimen. But the radiation treatments still do have extensive range of adverse effects that can be severe and may cause permanent damage to the patient. Exposure of the surrounding normal tissues to radiation can lead to a number of acute and late complications. In an attempt to minimize these effects, many compounds have been identified and are in use clinically for the prevention and treatment of radiation associated toxicities. Furthermore, there are a number of emerging therapies being developed for use as agents that protects healthy normal tissue from radiation-induced damages [1-5].

The main aim of our research was to study the role of gamma and delta Tocotrienol (50%) in radiation induced conditions like oesophageal stricture (dysphagia), trismus with neck stiffness and cervical dystonia [6-10] after radical radiotherapy treatment in cancer patients of respective sites.

In this study, histo-pathologically proved patients of oesophageal, head/neck and cervical cancer were selected after radical radiotherapy treatment which presented at Department of Radiation, Aadhar Hospital, Hisar, India. In these patients who developed radiation induced conditions like oesophageal stricture (dysphagia), trismus with neck stiffness, and cervical dystonia were treated with gamma and delta tocotrienol (Brand name CA Probret) capsules along with conventional treatment. All selected patients were evaluated for radiotherapy complications like dysphagia, trismus, neck stiffness, cervical dystonia, radiation induced fibrosis. Other quality of life measures like emotional liability, depression, able to work normally at their workplaces/general well-being of the patient were also analysed.

MATERIAL AND METHOD

In this study, histo-pathologically proved 160 patients (from Nov. 2016 to May 2019) included both males and females of 30 to 70 years age groups were presented at Department of Radiation, Aadhar Hospital, Hisar were taken. After metastatic work up, patients were evaluated for further treatment. Out of 160 patients; 20 patients are excluded due to advance stage of cancer and the remaining patients after radical RT therapy with or without chemotherapy or surgery were enrolled in the study and were divided into two groups with equal number of patients (Table 1).

Table 1: The patients groups & their complications

Group	Type of cancer	Condition's after RT treatment		No. of patients	Treatment
I (Test)	Oesophageal cancer	Oesophageal stricture	With stent & dilatation when necessary	5	Gamma & Delta Tocotrienol capsules (CA Probret) after radiotherapy
			Without stent & dilatation	25	
	Head & neck cancer	Trismus with neck stiffness & cervical dystonia		35	
	Cervical cancer	Difficulty to passing stool		5	
Total patients				70	
II (Reference)	Oesophageal cancer	Oesophageal stricture	With stent & dilatation when necessary	5	without Tocotrienol capsules
			Without stent & dilatation	25	
	Head & neck cancer	Trismus with neck stiffness & cervical dystonia		35	
	Cervical cancer	Difficulty to passing stool		5	
Total patients				**70**	
Grand total patients				**140**	

The first group patients were treated with combination of gamma and delta tocotrienol 50% (400 mg capsules twice a day for six month) after RT along with conventional treatment (antioxidant therapy & triamcinolone acetonide 10mg/ml injection once weekly or wherever required) and the second group was as reference group (conventional treatment, antioxidant therapy & triamcinolone acetonide 10mg/ml injection once weekly or wherever required without tocotrienol capsules). The patient's parameters were monitored before as well as after treatment and measured their improvement in terms of percentages. The samples of gamma and delta tocotrienol (50%) capsules were provided by Jenome Biophar Pvt. Ltd., India for this study.

RESULT AND DISCUSSION

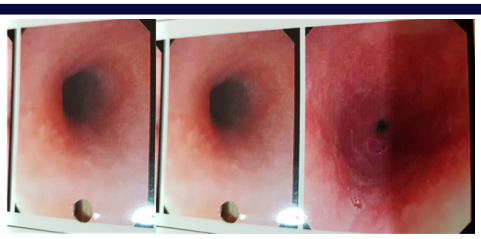
The study was carried out on selected patients (thirty patients out of 70 of group I) conditions of oesophageal stricture developed after radical radiotherapy treatment of oesophageal cancer. The patients divided in term of dysphagia stage and their criteria (Table 2). The sixteen (16) patients and fourteen patients (14) at stage 3 and stage 2 of dysphagia were taken respectively after radical radiotherapy.

The oesophageal stricture patients (different stage of dysphagia) of group I (30 patients) were treated with soft gel capsules of tocotrienol capsules and compared with or without treatment group II. The results demonstrated that condition of Eleven (11) patients were improved up-to normal swallowing mechanism (stage 0) and 05 patients reached at minimal dysphagia (stage 1) out of 16 patients of dysphagia (stage 3). Besides this, the 14 patients were at stage 2 conditions was improved and reached at stage 0 after treatment of tocotrienol soft gel capsules up-to six months. Where-as in reference group 5 patients of each stages of stage 2 & stage 3 reached at stage 1 (minimal dysphagia) after conventional treatment without tocotrienol capsules. Overall results showed that 83.33 % oesophageal stricture condition (25 patients out of 30) has shown improved as compared to reference group nil patients (0 out of 30) reached up-to normal swallowing mechanism. Furthermore the 16.67 % (05 out of 30) patient condition was reached at minimal dysphagia after treatment with tocotrienol capsules as compared to reference group condition (33.3%; 10 out of 30) after treatment without tocotrienol capsules. The patients were observed month-wise and obtained results depicted in Table 3 and Figure 1.

Table 2: Patient's dysphagia stages and their criteria

Stages	Criteria
0	Normal swallowing mechanism.
1	*Minimal dysphagia*—Patient reported a change in sensation during swallow. No change in diet is required.
2	*Mild dysphagia*—dysphagia to solids. Can take semi solids with ease
3	*Moderate dysphagia*—patient can take semi solids with difficulty or liquids only
4	*Severe dysphagia*—patients is unable to take anything by mouth, have difficulty even is taking liquids

Another group of selected patient's (according to the group I divided in table 1) conditions of Trismus with neck stiffness & cervical dystonia developed after radical radiotherapy (RT) treatment of head/neck cancer and results were compared with the patients in group II. After comparison, the results of this study showed that out of thirty-five patients (Table 4 and Figure 2); 12 patients conditions were improved to normal (34.30%) and remaining patients (19/35; 54.28%) condition was further improved in six month treatments with respect to starting stage of fibrosis conditions except, four patients (conditions improvement up-to three months only; 11.42%) as compared to reference group (34.28%) treatment without tocotrienol capsule.



A B C

Figure 1: The image of oesophageal stricture; A) after six month tretament; B) after three month treatment and C) after RT treatment

In cervical cancer patients conditions; five patients were difficulty of passing stool after radical RT treated with tocotrienol capsules for six months. The results of this study showed that difficulty of passing stool conditions improved and patients feel better after tocotrienol capsules treatment (07-10 days) interruption as compared to same number of patients difficulties in passing stool were seen from the group II treatment without tocotrienol. The treated patients conditions were remain stable for whole six month trial period treatment.

a)

b)

Figure 2: Patients neck conditions a) during RT b) after treatment up-to 06 month

CONCLUSION

In the last decade, biology of tocotrienols has been revealed, after its discovery half century ago. This study revealed that gamma and delta tocotrienols capsule has significant role in complication of radiotherapy treatment especially as a result of radiation fibrosis. The study has been shown that thirty-five patients of oesophageal cancer with oesophageal stricture condition improved up-to 83.33% (reference group 33.33%), where-as conditions of patients of head/neck cancer and cervical cancer with trismus with neck stiffness, cervical dystonia, conditions improved up-to 88.58% (reference group 34.28%) after six-month treatment with gamma and delta tocotrienols capsule as compared to conventional treatment without tocotrienols. To study the full potential of gamma and delta tocotrienol, a large multi-centric and randomized study is needed.

Table 3: Patients oesophageal stricture (dysphagia) stages after treatment up-to six month's

No of Patients In Group I	Type of Cancer & condition during RT treatment	Patients oesophageal stricture (dysphagia) stages after RT treatments				Patients condition improved after six-month conventional treatment with tocotrienol capsules			
	Oesophageal cancer & Oesophageal stricture	Stage 0	Stage 1	Stage 2	Stage 3	Stage 0	Stage 1	Stage 2	Stage 3
30		-	-	14	16	25	5	-	-
No of Patients In Group II	**Type of Cancer & condition during RT treatment**	**Patients oesophageal stricture (dysphagia) stages after RT treatments**				**Patients condition improved after six-month conventional treatment without tocotrienol capsules**			
30	Oesophageal cancer & Oesophageal stricture	Stage 0	Stage 1	Stage 2	Stage 3	Stage 0	Stage 1	Stage 2	Stage 3
		-	-	14	16	-	10	9	11

Table 4: Patients RT conditions of Trismus with neck stiffness & cervical dystonia stages after treatment up-to six month's

No of Patients In Group I	Type of Cancer & condition during RT treatment	Stage after RT treatments	Patients condition improved after six-month conventional treatment with tocotrienol capsules

35	Head/neck cancer and Trismus with neck stiffness & cervical dystonia stages	Neck fibrosis	Reduced	Further Reduced	Normal
			4	19	12
No of Patients In Group II	**Type of Cancer & condition during RT treatment**	**Stage after RT treatments**	**Patients condition improved after six-month conventional treatment without tocotrienol capsules**		
35	Head/neck cancer & Trismus with neck stiffness & cervical dystonia stages	Neck fibrosis	Reduced	Further Reduced	Normal
			12	Nil	Nil

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