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Research

Is There a Hint Towards Clinico-Dosimetric Correlation of Fatigue Among Head and Neck Cancer (HNC) Patients Treated by Modulated Radiotherapy?

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Abstract

Introduction

Fatigue has always been a distressing symptom for patients of head and neck cancer (HNC) on radiotherapy. Modulated radiotherapy has been instrumental in reducing many of the acute and late side effects. Few recent publications hinted at possible correlation of fatigue with dosage to CNS structures. We have previously published our data on dose received to CNS structures while on IMRT. This study aims at correlating CNS structures dose with IMRT and Brief fatigue inventory (BFI) scale scores to arrive at an objective criteria to reduce fatigue.

Materials and Methods

This prospective analysis comprising of twenty eight (28) HNC patients receiving either postoperative or radical modulated RT. Patients were administered BFI scale before and after completion. CNS structures were additionally contoured besides standard contouring guideline. In planning CT scan brainstem and posterior fossa excluding brainstem were contoured and dose recorded. Spearman correlation was used to correlate between CNS structures dosage and their relation to fatigue scale score.

Results

There was 28 (male: 20, Female: 8) non nasopharyngeal HNC. BFI was available pre and post IMRT for all the patients. 20/28 patients had preexisting fatigue and on a scale of 10, majority reported score 3. Almost all the patients reported post IMRT fatigue with median score of 6. The main affected domain being mood and social life. The dosimetric correlation suggested that dose maximum (Dmax) of brainstem and post IMRT fatigue score and worst fatigue score (spearman correlation: 0.028 and 0.008) and Dmax of post fossa with post IMRT fatigue and worst fatigue score (spearman correlation: 0.051and 0.033) respectively. No definite dose cut off and BFI score change could be established.

Conclusion

This prospective study hinted possible correlation between CNS structures dose and increased fatigue. The future inclusion of dose constrained IMRT for CNS structures would help to reduce fatigue.

Introduction

Over the last decade intensity modulated radiotherapy (IMRT) has become the standard of care in the management of head and neck cancer (HNC). The prospective randomized data favoring better toxicity profile and in the long term an improved quality of life has been the biggest boon[1].

Fatigue is a known occurrence among HNC patients and factors like younger age, advanced stage, associated depressive symptoms and re irradiation have all been implicated[2]. The patterns of symptomatology although differs between survivors and non survivors of HNC. A recent article analyzed these issues and among the survivors there is improvement in different symptoms over time and EORTC QOL Q C-30 and H&N 35 were able to address these issues [3,4].Especially with IMRT newer organs at risk (OAR) and their acute and late effects have become paramount in deciding patients overall quality of life. Though incidental, but an important finding from PARSPORT trial was excessive fatigue among IMRT patients. Gulliford SL et al have analyzed the dosimetric explanation in these group of patients[5].We have already published our Institutional data on dose received to CNS structures on HNC IMRT among non-nasopharyngeal cancer patients[6].

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This prospective documentation aimed at correlating CNS structures dose with IMRT and Brief fatigue inventory (BFI) scale scores to arrive at an objective criteria to reduce fatigue.

Materials and Methods

Twenty eight (28) patients of HNC receiving postoperative (n=10) and radical radiotherapy (n=18) were prospectively evaluated. There were 5 females and 23 male patients. The median age of the patients was 56 years. The primary disease sites were oral cavity (10), oropharynx (6), larynx (7) and hypopharynx (5). Majority was locally advanced (25) and concurrent chemotherapy was given in 20 patients with cisplatin being the commonest drug. The IMRT dose planned was between 60 Gy to 70 Gy with conventional fractionation. The OAR concerned was delineated in radiotherapy planning scans. Standard contouring guideline was followed while contouring brainstem (BS) and posterior fossa (PF) excluding brainstem.

The volumes of BS and P were noted besides the dose received to 1,2,10 cc of these organs as well as dose means (Dmean) and maximum (Dmax) dosage.

Brief fatigue inventory (BFI) scale was administered to these patients prior to starting radiotherapy and also at the completion. It is a simple 10 point Likert scale with different aspects of fatigue and related changes are documented. The score is a simple Likert type with 0 being no fatigue and 10 being worst fatigue. There were sub-divisions again on a scale of 0-10 on mood, activity and enjoyment of life. All the data were analyzed using SPSS version 18.0 and Spearman correlation was used to correlate between CNS structures dosage and their relation to fatigue scale score before and after IMRT.

Results

Among the 28 non nasopharyngeal HNC, the median BS and PF volumes were 23.3 cc and 252 cc respectively. The median Dmax of BS and PF were 38.37 Gy and 46.05 Gy respectively while the median Dmean of BS and PF 14.2 Gy and 8.85 Gy respectively.

Seven patients had pre IMRT existing fatigue with median pre IMRT fatigue score being 2 (range 0-7). In terms of worst fatigue, general activities, mood and walking the pre IMRT scores ranged between 2 to 3. Post IMRT the median fatigue score increased to 6.5 and the general activities, mood and worst fatigue all ranges between 5-7.

The main affected domain being mood and social life. The dosimetric correlation suggested that Dmax of brainstem and post IMRT fatigue score and worst fatigue score (spearman correlation: 0.028 and 0.008) and Dmax of post fossa with post IMRT fatigue and worst fatigue score (spearman correlation: 0.051and 0.033) respectively. It was also noted that higher the dosage to these structures (typically more than 40 Gy) higher the fatigue score. No definite dose cut off and BFI score change could be established.

Six patients had treatment gap varying between 2 days to 10 days, mostly due to hematological toxicities and oral mucositis and 4 of them had PF Dmean more than 10 Gy and BS Dmax over 40Gy. The same has been found in the recent Guliford SL et.al data from patients of PARSPORT trial[5].

Discussion

Gulliford SL et al. in their retrospective analysis of PARSPORT data have concluded "The excess fatigue reported in the IMRT arm of the trial may, at least in part, be attributed to the dose distribution to the posterior fossa, cerebellum and brainstem"[1,5].This aspect of cancer related fatigue is definitely a new observation.

Cancer related fatigue have been reported in several literature. Age, concurrent chemotherapy, low hemoglobin percentage and comorbidities have all been documented to be instrumental in causation. In 1998 Smets EM et.al. Have indicated that baseline pain and disease related disability can cause long term fatigue among cancer patients [7].The depression and fatigue symptoms increase during radiotherapy and about 50% patients of HNC experience them [8,9].

The prospective documentation of fatigue among HNC patients have already been validated with Modified Brief Fatigue Inventory (MBFI) scale[10].The scale actually analyses various aspects of cancer related fatigue with common questionnaires in Likert pattern. It is easy to administer and can record fatigue objectively. Compared to fatigue specific scale, quality of life scales like EORTC QLQ-C30 and QLQ-H&N35 questionnaires also reports about improvement in fatigue over time[4,5,11].Different scales have also identified concurrent chemo radiation to be responsible for increased fatigue among HNC patients[12].A recent Indian study also supported EORTC QLQ C15-PAL questionnaire and reported median score of 50 for fatigue [9].

The uniqueness of Guliford SL et.al. Study was the dosimetric explanation of excessive fatigue among HNC IMRT patients. Recently Powell et.al also analyzed the fatigue and dosimetric correlation among nasopharyngeal patients and basal ganglia, pituitary and cerebellum were additional OAR with significance to grade 2 fatigue been established [13].

We accept the shortcomings in view of co-relating with other confounding factors like age, comorbidities, use of chemotherapy. Fatigue is a multi-factorial entity and only contribution of IMRT may be difficult to establish.

We believe that our short and preliminary report among 28 Indian HNC patients and clinic-dosimetric data of BS and PF with BFI scale was encouraging in view of its uniqueness and International similarity to published literature. The definite dose cut-off level of BS and PF and changes in BFI scale on a large cohort of patients' needs to be seen. This might help in reducing untoward side effects of the treatment and will result in compliance and better outcome.

Conclusion

Clinico-dosimetric co-relation of fatigue among HNC patients is an ideal option for future IMRT planning. The already validated BFI scale and dose constrained IMRT to PF and BS would definitely help in reducing untoward side effects and will result in better compliance.

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