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Accelerated Radiation Therapy Using Weekend Boost with Concurrent Cisplatin in Head and Neck Squamous Cell Cancers: An Indian Institutional Experience

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ABSTRACT

Purpose: The purpose of the study was to evaluate the feasibility and efficacy of an accelerated radiotherapy schedule using weekend boost in terms of tumor response, compliance, and acute toxicities for head and neck squamous cell carcinoma, and to report long-term clinical outcomes.

Materials and methods: Twenty-six patients with stages III-IV head and neck squamous cell carcinoma receiving radical chemoradiotherapy were accrued prospectively into the study. External beam radiation therapy to a total dose of 66–70 Gy in 33–35 fractions, 1.8–2.0 Gy per fraction along with concurrent weekly cisplatin was planned. Radiation regimen included delivery of six fractions per week, with boost field delivered as the sixth fraction on the weekend. The compliance, tumor response, and toxicities were recorded. Survival curves were estimated using the Kaplan–Meier method.

Results: Twenty-one of 26 patients (81%) completed treatment as planned and five patients died during the course of treatment. Sixteen patients (62%) completed treatment in less than 44 days and, at the end of 3 months' follow-up, 18 patients (69%) showed complete response and two patients (8%) showed partial response. The 2- and 5-year actuarial disease-free survival were 90% and 65%, respectively, and 2- and 5-year actuarial overall survival were 60% and 38%, respectively.

Conclusion: Accelerated fractionation using weekend boost, along with concurrent weekly concurrent cisplatin, is an effective and promising approach with favorable impact on initial tumor response, comparable results, and acceptable toxicities.

RÉSUMÉ

Objet : Évaluer la faisabilité et l'efficacité d'un calendrier de radiothérapie accéléré utilisant un complément de dose (boost) le week-end en termes de réponse de la tumeur, conformité et toxicités pour l'épithélioma malpighien spinocellulaire de la tête et du cou (EMSTC) et présenter les résultats cliniques à long terme.

Matériel et méthodologie : Vingt-six patients atteints d'un EMSTC de stade III-IV recevant des traitements de chimiothérapie ont été ajoutés à l'étude de façon prospective. La planification comprenait des traitements de radiothérapie externe, pour une dose totale de 66-70 Gy, en 33-35 fractions, 1,8-2,0 Gy par fraction combinée à des injections hebdomadaires de cisplatine. Le régime de rayonnement prévoyait l'administration de six fractions par semaine, le complément de dose représentant la sixième fraction, administrée durant le week-end. La conformité, la réponse tumorale et les toxicités ont été compilées. Les courbes de survie ont été estimées par la méthode Kaplan–Meier.

Résultats : Vingt-et-un des 26 patients (81%) ont complété le traitement comme prévu et cinq patients sont morts avant la fin du traitement. Seize patients (62%) ont complété le traitement en moins de 44 jours, et à la fin de trois mois de suivi, 18 patients (69%) affichaient une réponse complète (CR) alors que deux patients (8%) affichaient une réponse partielle (RP). Le taux actuariel de survie sans maladie (SSM) après deux et cinq ans était respectivement de 90% et de 65%, alors que le taux actuariel de survie globale (SG) était respectivement de 60% et 38%.

Conclusion : Un fractionnement accéléré utilisant un complément de dose administré durant la fin de semaine avec injection hebdomadaire concurrente de cisplatine est une approche efficace et prometteuse avec des répercussions favorable sur la réponse tumorale initiale, des résultats comparables et des toxicités acceptables.

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Introduction

Among the various accelerated fractionation schedules studied in head and neck squamous cell carcinoma (HNSCC), acceleration of radiation by 1 week without dose reduction (ie, delivering six fractions instead of the conventional five fractions per week) is found to have a beneficial effect on locoregional control (LRC) along with a modest reduction in overall treatment time (OTT), and without an increase in late effects [1, 2]. However, results with this approach alone are widely variable, and improvement in survival has not been consistent [3, 4]. Substantial clinical investigations have demonstrated consistent survival gain along with favorable impact on LRC rates with concurrent chemoradiation. However, benefits of combined modality treatment come at the expense of additional acute mucocutaneous toxicities [5].

Consequently, concurrent chemoradiotherapy is the preferred nonsurgical treatment modality for locally advanced diseases, whereas altered fractionation is generally selected for early and intermediate stage tumors or for patients who are medically unfit for chemotherapy [6, 7]. Furthermore, evidence is needed for combining an altered fractionation regimen with concurrent chemotherapy without resulting significant compromise in normal tissues. Theoretically, delivery of a smaller boost field on a weekend as sixth fraction of the week, instead of a larger field, will effectively reduce OTT by one week, and without much increase in toxicity. With an aim to evaluate the feasibility and efficacy of this approach, we undertook this study. In this study, we intend to reduce OTT by delivering six fractions per week, wherein the sixth fraction is a boost field encompassing only gross tumor volume on the weekend, along with concurrent weekly cisplatin chemotherapy.

Methods and Materials

Study Design

The trial was designed as a prospective, single-center, one-armed study to assess the efficacy and safety of accelerated fractionation schedule using weekend boost (WEB) and concurrent chemotherapy for locally advanced head and neck cancers.

The study protocol was approved by the institutional ethics committee. Written informed consent was obtained from each eligible patient before inclusion into the study after explaining in detail the nature, scope and possible consequences of participation in the trial.

Data Collection and Inclusion–Exclusion Criteria

Between December 2011 and July 2013, all histopathologically proven HNSCC patients receiving concurrent chemoradiotherapy with radical intent at M.S. Ramaiah Hospitals, Bengaluru were considered. Patients aged between 18 and 80 years, with Karnofsky performance status $\geq$70 and adequate baseline bone marrow function (hemoglobin $>$10 gram%, absolute neutrophil count $>$1500 per microliter, platelets $>$100,000 per microliter), normal hepatic and renal function were accrued. Nasopharyngeal, early laryngeal (T1 and T2), postoperative cases, history of prior radiation or chemotherapy, any previous or synchronous malignancy and hypersensitivity to platinum agents were excluded.

Sample Size Calculation

The sample size was estimated in consultation with a biostatistician using "*n-Master*" Software based on previous trial by Skladowski et al [8] which compared 7-day continuous accelerated irradiation (CAIR) with conventional fractionation schedule in a randomized clinical trial. Considering 25% precision and 90% desired confidence limit, minimum sample size required accruing in one and half year period was 25. A total of 26 patients were accrued into study in the previously mentioned study period.

Pretreatment Evaluation

Initial work up consisted of clinical examination, laboratory tests including complete blood count, and renal and hepatic function tests were done for all patients to assess the general condition of the patient. Computed tomography and/or magnetic resonance imaging of head and neck region was done to document local extent of disease. Chest radiograph and abdominal sonography were done to rule out metastases. Each patient was clinically staged as per American Joint Committee on Cancer Tumor Node Metastasis, 2010 staging system after complete work up.

Treatment

All patients were immobilized with four-clamp head and neck thermoplastic orfit and planning simulation done on a conventional x-ray or computed tomography simulator. During simulation, enlarged lymph nodes were externally delineated with a lead wire to ensure adequate encompass within portals. External beam radiation therapy either on telecobalt machine or linear accelerator (6 MV) using conventional or three-dimensional conformal radiation therapy techniques were permitted. A total dose of 66–70 Gy in 33–35 fractions with 1.8–2.0 Gy per fraction over a 6.5-week period was administered with parallel opposed lateral portals using shrinking field technique in three phases without any tissue compensators. Nodes were treated electively in all patients. A direct anterior lower neck field was used in selected patients.

Initial dose of 45 Gy was delivered to Phase 1 radiation portals, which encompassed gross tumor and microscopic