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Intensity-modulated radiation therapy reduces late salivary toxicity and mandibular osteoradionecrosis in the treatment of oral cavity cancer: Retrospective study

Şiddet modülasyonlu radyasyon tedavisi, oral kavite kanseri tedavisinde geç tükürük toksisitesini ve mandibular osteoradionekrozu azaltır: Retrospektif çalışma

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Abstract

Aim: It is increasingly being recognized that oral cavity cancer incidences are rising globally. Irradiation using 3D conformal radiotherapy results in high incidence of late radiation side-effects. Xerostomia and mandibular osteoradionecrosis result in most significant effects on patients quality of life. Intensive modulated radiotherapy (IMRT) is an advanced approach to 3D treatment planning and conformal radiotherapy. It optimizes the delivery of irradiation to irregularly-shaped volumes and has the ability to spare normal tissue while delivering adequate doses to the tumor volumes. In present retrospective analysis, we aimed to analyze the clinical and dosimetric characteristics with the dose constraints in patients followed for oral cavity cancer and treated by IMRT.

Methods: 19 patients followed for non-metastatic oral cavity cancer who were treated with IMRT, were retrospectively analyzed at the radiotherapy department Hassan II University hospital, Fes, Morocco between January 2016 and December 2016.

Results: The mean age was 58.5 years. The predominant histological type was epidermoid carcinoma. RCC was received in 79% of cases versus 15.8% of exclusive radiotherapy. 68.4% of cases received 70Gy for HR PTV, the mean dose delivered to the homolateral and controlateral parotid glands was 36Gy and 22Gy respectively, the average dose delivered to the mandible was 51.9Gy.

Conclusion: IMRT of oral cavity tumors offers reduces the risks of xerostomia and ORN through parotid and mandibular sparing, without compromising on target volume coverage.

Keywords: Intensive modulated radiotherapy, Oral cavity cancer, Xerostomia, Mandibular osteoradionecrosis

Öz

Amaç: Dünyada oral kavite kanseri vakalarının giderek arttığı artan bir şekilde bilinmektedir. 3D konformal radyoterapi kullanılarak ışınlama, geç radyasyon yan etkilerinin yüksek insidansına neden olur. Xerostomia ve mandibular osteoradionekroz, hastaların yaşam kalitesi üzerinde en önemli etkilerle sonuçlanır. Yoğun modüle radyoterapi (IMRT), 3D tedavi planlaması ve konformal radyoterapiye ileri bir yaklaşımdır. İrradyasyonun düzensiz şekilli hacimlere ulaştırılmasını optimize eder ve tümör hacimlerine yeterli dozları verirken normal dokuları yedekleme özelliğine sahiptir. Bu retrospektif analizde, oral kavite kanseri için takip edilen ve IMRT ile tedavi edilen hastalarda doz kısıtları ile klinik ve dozimetrik özellikleri analiz etmeyi amaçladık.

Yöntemler: IMRT ile tedavi edilen metastatik olmayan oral kavite kanseri nedeniyle takip edilen 19 hasta retrospektif olarak Ocak 2016-Aralık 2016 tarihleri arasında Fes, Fas'taki radyoterapi bölümü II'de kayıt edildi.

Bulgular: Ortalama yaş 58,5 idi. Baskın histolojik tip epidermoid karsinomdu. Olguların %79'unda RCC, %15.8'inde özel radyoterapi görüldü. Olguların %68,4'ünde HR PTV için 70Gy, homolateral ve kontrolateral parotis bezlerine verilen ortalama doz sırasıyla 36Gy ve 22Gy, mandibula verilen ortalama doz 51,9Gy idi.

Sonuç: Oral kavite tümörlerinin IMRT'si, hedef hacim kapsamından ödün vermeden, parotis ve mandibular koruma ile kserostomi ve ORN riskini azaltmaktadır.

Anahtar kelimeler: Yoğun modüle radyoterapi, Oral kavite kanseri, Kserostomi, Mandibular osteoradionekroz

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Introduction

Oral cavity cancer is the sixth most common cancer worldwide [1]. Incidences vary widely across geographical areas with the UK demonstrating a relatively low incidence of 3500 cases per year, [2] compared to parts of South East Asia where a third of all male cancers in India originate in the oral cavity [3]. Etiological factors for some squamous cell oral cavity cancer such as high tobacco and alcohol consumption, and betel quid chewing, may account for these geographical variations [4]. Recently infection with human papilloma virus had been identified as a causal factor for the rising incidence of oropharyngeal cancers in non-smokers. However, the relationship with oral cavity cancer is not yet established.

Treatments of oral cavity cancer

External beam radiotherapy is used in the treatment of OCC, primarily in the post-operative setting but also as first definitive treatment when surgery is felt to be inappropriate [5]. In these early stage patients, risk stratification is based on thickness and grade of tumor [6]. Patients with oral tongue tumors or floor of mouth tumors with a clinically node-negative neck require surgical resection of the primary lesion and elective neck dissection at the very least. In 1972, a study by Lindberg demonstrated that the lymph node groups most frequently involved in patients with carcinoma of the oral cavity are the jugulodigastric and midjugular nodes (levels II and III). In patients with carcinoma of the floor of the mouth, anterior oral tongue, and buccal mucosa, the nodes most frequently involved are in the submandibular triangle (level I). Lindberg also noted that cancers frequently metastasize to both sides of the neck and can skip the submandibular and jugulodigastric nodes, metastasizing first to the midjugular region. Supra-omohyoid neck dissection (dissection of nodal compartments level I to III) offers similar rates of locoregional control and survival as a modified radical neck dissection [7]. Most surgical groups advocate the use of an extended supraomohyoid dissection in oral tongue tumors and deem it compulsory for the node positive patient due to the risk of skip metastasis to nodal compartment level IV while some groups will recommend the extended supra-omohyoid dissection for floor of mouth tumors in addition to tongue tumors [8]. Tumors approaching the midline require dissection of the contralateral neck. Post-operative radiotherapy is administered in selected high risk groups [9].

Radiotherapy for oral cavity cancers

Stage III and IV tumors of the oral cavity generally require bilateral oral cavity and neck irradiation following surgery. The acute toxicity from bilateral oral cavity irradiation is severe, and the majority of patients develop grade 2/3 oral mucositis and dysphagia. However, these acute effects are self-limiting and it is the permanent nature of the late effects which become more problematic. Sixty-six percent of patients with stage III disease and 58% patients with stage IV undergoing appropriate surgical management and postoperative radiotherapy will survive five years or longer and are deemed cured beyond this point. They are therefore susceptible to lifelong consequences of irradiation.

Intensity modulated radiotherapy

Intensity modulated radiotherapy (IMRT) is an advanced approach to 3-D treatment planning and conformal therapy (3D-CRT). It optimizes the delivery of irradiation to irregularly shaped volumes and has the ability to produce concavities in radiation treatment volumes. Typically for head and neck cancer the clinical target volume 1 (CTV1), which includes the primary tumor and the involved nodes receives a higher radiation dose as compared to the clinical target volume 2 (CTV2). The different doses to CTV1 and 2 can be delivered simultaneously, while sparing the parotid salivary glands and the spinal cord. In the head and neck region, IMRT has a number of potential advantages:

- it allows for greater sparing of normal structures such as salivary glands, esophagus, optic nerves, brain stem, and spinal cord; [10,11]

- it allows treatment to be delivered in a single treatment phase without the requirement for matching additional fields to provide tumor boosts and eliminates the need for electron fields to the posterior (level II, V) neck nodes;

- it offers the possibility of simultaneously delivering higher radiation doses to regions of gross disease and lower doses to areas of microscopic disease, the so-called simultaneous integrated boost (SIB-IMRT) [12].

IMRT is the gold standard in the treatment of upper aerodigestive cancers. One of the goals is the protection of risk organs such as salivary glands and the mandible. The risks of hyposalivism, trismus and osteoradionecrosis must be reduced.

The objective of our retrospective study, carried out at the radiotherapy department Hassan II University hospital, Fes, Morocco between January 2016 and December 2016, is to analyze the clinical and dosimetric characteristics with the dose constraints in patients followed for oral cavity cancer and treated by IMRT.

Materials and methods

We collected 19 patients followed for non-metastatic oral cavity cancer who were treated with IMRT, including 9 cases of tongue cancer (47.3%), 4 cases of lip cancer (21%), 3 cases of cheek cancer (15.7%), 2 cases of the palate cancer (10.5%), and one case of the retro-molar trine cancer (5.2%).

Statistical analysis was obtained using Excel and SPSS computer software. The significance level of all observed differences was set for all statistical tests at a probability value $p \leq 0.05$.

Results

The mean age was 58.5 years, with a female predominance (sex ratio at 1.71). The predominant histological type was epidermoid carcinoma in 84.2% of cases; there was only one case of adenocarcinoma, one case of basal cell carcinoma and one case of sarcomatoid myoepithelial carcinoma. The number of patients with stage I, II, III and IV disease were 1, 3, 8, and 7 respectively. 8 patients underwent tumor excision (42.1%) against 57.8% of non-operated patients. RCC was received in 79% of cases versus 15.8% of exclusive radiotherapy.

68.4% of cases received 70Gy for HR PTV, 21% of cases received 66Gy, 5.2% of cases received 60Gy and 5.2% of cases received 46Gy. The mean dose delivered to the homolateral and controlateral parotid glands was 36Gy and 22Gy respectively.

The average dose delivered to the mandible was 51.9Gy. The mean dose delivered to the homolateral and contralateral TMJ was 23.2Gy and 19.3Gy respectively.

Discussion

Our study demonstrates the benefit of IMRT to reduce the risk of xerostomia by delivering a mean dose less than 22Gy to the parotid which concord perfectly with the data of literature. Eisbruch and al. Proposed an average contralateral parotid dose <26Gy as a parotid sparing goal to recover the initial salivary flow at 12 months [13]. In a recent analysis of a multicentric phase III trial (PARSPORT) compared the occurrence of a xerostomy in case of IMRT and 3D conformal radiotherapy in ENT cancers, a contralateral parotid constraint was defined with a mean dose <24Gy and which was concluded that there is a clear reduction in the risk of xerostomia with IMRT with no difference in overall survival or locoregional control [14].

No specific prospective study has been done to precisely define the exact doses to be received by the mandible and it is through the analysis of dosimetric data that proposals can be made. The average dose delivered to the mandible in our study was 51.9Gy and the radionecrosis risk is significantly reduced. In a review by Maignon et al. [15], he have evoked a notion of average dose less than 60 to 65Gy if the patient is toothless, with a radionecrosis risk of 5% at 5 years, or less than 60Gy if the patient is not edentulous, with a risk of radionecrosis from 5% to 5 years.

With regard to temporomandibular joints, the data are missing in the literature to be very reliable. A maximum dose below 65Gy (or D2% <65Gy), or even 60Gy seems advisable [16]. The results of our study are in perfect accord with the data from the literature.

In conclusion, IMRT of advanced oral cavity tumors offers the potential to reduce the risks of xerostomia and ORN through parotid and mandibular sparing. This can be performed without compromising on target volume coverage and hence treatment outcomes.

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