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Original article

Intraluminal brachytherapy boost following external beam radiotherapy with concurrent chemotherapy of oesophagus carcinoma: Results of a prospective observational study

Curiethérapie endoluminale après chimioradiothérapie externe concomitante pour un carcinome de l'œsophage : résultats d'une étude prospective d'observation

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ABSTRACT

Purpose. – The main objective of our study is to evaluate response and toxicity profile in patients receiving external beam radiotherapy with concurrent chemotherapy followed by intraluminal brachytherapy boost for a carcinoma of the oesophagus.

Material and methods. – Twenty patients with biopsy-proven carcinoma of the oesophagus received external beam radiotherapy (50 Gy in 25 fractions) with concurrent chemotherapy (cisplatin: 40 mg/m²). After a gap of two to three weeks, intraluminal brachytherapy (10 Gy in two fractions each 1 week apart by a high dose rate ⁶⁰Co source) was given. Response was evaluated at 1 month and at 1 year of completion of treatment. In addition, acute and chronic toxicity was evaluated at 1 month and 6 months of treatment.

Results. – Complete response were seen in 80% of patients and partial response in 20% at 1 month. Moreover, there were 65% complete response, 10% local recurrences, 15% patients showed local control with distant metastasis and 10% patients died at 1 year. Grade 1, grade 2 and grade 3 oesophagitis were seen in 10%, 70% and 20% of patients respectively. Stricture was seen in 40% of patients and fistula in 10% of patients. There was no spinal cord, cardiac and nephrotoxicity found.

Conclusions. – With the concept that high tumoricidal dose for adequate tumor control achieved by intraluminal brachytherapy as a mean of dose escalation, while sparing surrounding normal tissue and potentially improving therapeutic ratio, external beam radiotherapy followed by intraluminal brachytherapy could be a better choice for oesophagus carcinoma.

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RÉSUMÉ

Objectif de l'étude. – L'objectif principal de l'étude était d'évaluer le profil de réponse et de toxicité chez les patients recevant une radiothérapie externe avec une chimiothérapie concomitante suivie d'une curiethérapie endoluminale pour un cancer de l'œsophage.

Matériel et méthodes. – Vingt patients ont reçu une radiothérapie externe de 50 Gy en 25 fractions et une chimiothérapie concomitante de 40 mg/m² par semaine, puis deux à trois semaines plus tard une curiethérapie endoluminale par une source de cobalt 60 de 10 Gy en deux fractions espacées d'une semaine. La réponse a été évaluée à 1 mois et 1 an après l'achèvement du traitement. La toxicité aiguë et chronique a également été évaluée à 1 mois et 6 mois de traitement.

Résultats. – Une réponse complète a été observée chez 80 % des patients et une réponse partielle chez 20 % à 1 mois. Il y a eu 65 % de réponses complètes, 10 % de récurrences locales, 15 % des patients étaient en situation de contrôle local avec une métastase à distance et 10 % de patients sont décédés à 1 an. Une œsophagite de grade 1, de grade 2 et de grade 3 a été observée chez respectivement 10 %, 70 % et 20 % des patients la première année. Une sténose a été observée chez 40 % des patients et une fistule chez 10 %. Il n'y pas eu de toxicité spinale, cardiaque et rénale.

Mots clés :

Curiethérapie de haut débit de dose

Cobalt 60

Curiethérapie endoluminale

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Toxicité

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Conclusions. – En réalisant une escalade de dose tout épargnant relativement les tissus sains avoisinants, une chimioradiothérapie suivie de curiethérapie pourrait s'avérer être le meilleur choix pour le cancer de l'œsophage.

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1. Introduction

Oesophageal cancer is the third most common cancer of the digestive tract and the seventh leading cause of cancer-related deaths worldwide [1]. Multidisciplinary treatment have been tried, which includes surgery, concurrent chemoradiation, external beam radiotherapy followed by high dose rate intraluminal brachytherapy in such patients to improve prognosis, however the results of the treatment of carcinoma of oesophagus have been poor despite advances in various treatment modalities [2]. Historical series of external beam radiation therapy alone report 5-year survival rates of 0–10%. Low survival rate followed initial radiotherapy alone could be due to loco regional persistence or recurrence of tumor, which is seen in as high as 85% of cases [3]. The combination of radiotherapy and concurrent chemotherapy with cisplatin and fluorouracil has led to long-term survival in approximately 20 to 30% of patients, an outcome similar to that associated with surgery alone but with an increased rate of local recurrence 77% when radiation therapy alone is used [4]. The above considerations have resulted in attempts to apply higher doses of radiation to the tumor but this lead to increased risk of late treatment related toxicity and 77% when radiation therapy alone is used.

Endoesophageal brachytherapy makes it possible to use high doses of radiation to the tumor itself with concurrent protection of the adjoining healthy tissues due to rapid fall in dose with square in distance from the centre of the dose. The aim of brachytherapy is to reduce dysphagia, diminish pain and bleeding as well as improve patient well-being. Doses used in teletherapy were as high as 35 to 60 Gy, whereas those in high dose rate brachytherapy ranged between 10 and 25 Gy administered in two to four fractions. The combined treatment can be radical or palliative [5]. The above treatment also leads to a small proportion of late radiation complications.

However, there have been only few reports to confirm that the number of local remissions and long-term survival rates have been increased in patients treated with teletherapy combined with brachytherapy.

In this article, we report the findings of our observational study done on patients with oesophagus carcinoma who received concurrent chemotherapy and external beam radiotherapy followed by intraluminal brachytherapy boost and evaluated the clinical response and toxicity associated with it, especially the high dose rate intraluminal brachytherapy component.

2. Materials and methods

In this prospective observational study 20 patients with histopathologically proven oesophagus carcinoma were included with following criteria: Age between 30 and 65 years with Karnosky performance score of more than 70 with no metastasis or comorbidities and no previous treatment.

2.1. Treatment design

All patients received external radiotherapy to the whole length of oesophagus along with lymph nodes with a dose of 50 Gy in 25 fractions with 6 MV photons on high energy linear

accelerator Clinac DMX (Varian medical systems). Contouring of gross tumor volume, clinical target volume and organs at risk was done as per Radiotherapy Oncology Group (RTOG) guidelines. Patients also received concurrent chemotherapy with cisplatin 40 mg/m² once a week for five times. After completion of external radiotherapy, patients were assessed by endoscopy; intraluminal brachytherapy and two fractions was given by high dose rate brachytherapy machine "Co0.A86" (Eckert and Ziegler BEBIG, Germany) using a cobalt source with a dose of 5 Gy in two fractions (10 Gy/2 fractions) to the involved site one week apart. A gap of 10 to 15 days was given between external beam radiotherapy and intraluminal brachytherapy.

For the procedure of intraluminal brachytherapy, the patients were taken to the endoscopy room where a local anaesthesia endoscope was passed through the oral cavity with the help of a gastroenterologist to evaluate the extent of the tumor and mark the upper and lower margins of the tumor by applying radioopaque markers on the skin 3 cm above and 3 cm below the lesion under C arm guidance. Then, a 6-mm diameter oesophageal applicator (Nucletron Oesophageal applicator) was inserted on the guide wire into the oesophagus and fixed to the mouth piece for immobilization. The lower end of the applicator was placed 3 cm below lower end of the lesion. The patient was kept under observation for 15 min postprocedure and then moved for computed tomography (CT) scan of the thoracic area using Siemens SOMATOM definition AS scanner (Siemens Medical systems, Germany). CT images of 3 mm slice thickness were taken and were imported on treatment planning system (TPS) (Fig. 1a). A 100% of dose was calculated 0.5 cm from the surface of the source. Patient was lying down in lateral position in the brachytherapy room and the source tube was passed through the applicator lumen till its lower end and the patient was treated (Fig. 1b).

2.2. Response evaluation

After the completion of treatment, response was evaluated after 1 month and at 1 year of completion of treatment. Evaluation was done clinically (relief from dysphagia) as well as by endoscopy and CT scan. Response was evaluated as per RECIST criteria for solid tumors version 1.1. Local recurrence is defined as reappearance of primary lesion on endoscopy and CT scan. Local control with distant metastasis is defined as no primary lesion in oesophagus on endoscopy but patient present with lung and liver metastasis on CT scan. Toxicity was evaluated within 1 month as acute toxicity and within 6 months of treatment as chronic toxicity by history, physical examination and laboratory tests, endoscopy, CT scan. The grading of toxicity was done as per RTOG/European Organisation for Research and Treatment of Cancer (EORTC) radiation morbidity criteria.

2.3. Statistical analysis

All statistical analyses were done using Graph Pad (Demo Version). *P*-value was calculated. *P* value < 0.05 was considered as significant difference and *P* value > 0.05 as non significant difference. Chi-square test was applied to find the association of toxicity with 1 month and 1 year response.

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