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Original Article

Ten Year Experience of Radioiodine Dosimetry: is it Useful in the Management of Metastatic Differentiated Thyroid Cancer?

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Abstract

Aims: When a fixed activity of radioiodine is given for differentiated thyroid cancer (DTC), absorbed doses of radioiodine can vary widely and are not usually measured. Leeds Cancer Centre has routinely used a form of lesion-specific dosimetry for radioiodine patients. This study investigated if the results of dosimetry influenced treatment decisions for patients with advanced DTC.

Materials and methods: Since 2005, patients with regionally advanced/metastatic DTC, who underwent radioiodine treatment together with dosimetry, were included in this study. Patients were excluded if their radioiodine post-treatment scan showed no abnormal uptake. Dosimetry was calculated using images taken 2, 3 and 7 days post-radioiodine. Regions of interest were drawn around lesions that required dosimetry and a time–dose activity curve was created. The total cumulative activity was equal to the area under the curve. Each patient's results were prospectively assessed by their oncologist regarding the usefulness of dosimetry in making management decisions.

Results: Thirty patients were studied and underwent 102 admissions of radioiodine between them. Dosimetry was carried out during 83 of 102 admissions. An absorbed dose of >20 Gy was taken as significant from dosimetry calculations, following which further radioiodine was considered. In 80% of patients, dosimetry was found to be useful when making treatment decisions. Only on 1/19 admissions did dosimetry calculate a minimum dose above 20 Gy in patients who had a total of four or more admissions for radioiodine. Ten per cent (3/30) had a complete response to radioiodine, both biochemically and radiologically, with a median follow-up of 6.7 months. Thirty-three per cent had a partial response/stable disease to radioiodine. The remainder had progressive disease. The decision to discontinue radioiodine therapy was often based on dosimetry and thyroglobulin results. Dosimetry was very useful for patients with thyroglobulin antibodies.

Conclusion: Only 10% had a complete response. Therefore, a significant number of patients became refractory to radioiodine during a course of repeat admissions for treatment. Dosimetry (often together with thyroglobulin and anatomical scans) helped to identify these patients to avoid further futile radioiodine therapy.

Key words: Differentiated thyroid cancer; lesion-based dosimetry; radioactive iodine; radioiodine; response to radioiodine; thyroid cancer metastases

Introduction

Differentiated thyroid cancer (DTC) is the most common form of thyroid malignancy, with an increasing incidence across the developed world [1,2]. In the UK alone, there has been a doubling of the incidence of thyroid cancer since the 1990s [3]. Treatment of DTC commonly involves total thyroidectomy followed by an empirical activity of radioiodine [4]. Radioiodine makes use of the radionuclide I-131, which emits both beta particles and gamma radiation. The short range beta radiation is thought to be involved in cell kill, whereas the gamma radiation can be picked up by radioiodine whole body scintigraphy [5] for the purpose of detecting the site of radioiodine uptake. For patients with metastatic disease the standard practice is to use repeat admissions for radioiodine until either a complete response or evidence of radioiodine resistance is reached.

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Standard practice is to administer a fixed activity (in MBq) of radioiodine to a patient with DTC as opposed to treating to a given absorbed dose in the tumour or critical organ. This means that the actual absorbed dose to the tumour is not known. If there is uptake of radioiodine in a thyroid cancer metastasis the dose delivered could be between less than 1 Gy and 100s of Gy. It would be useful to have knowledge of the absorbed dose when deciding on further radioiodine treatments.

Dosimetry for radioiodine treatments is rarely carried out in the UK, even though the doses vary widely [6]. The 2013/59/Euratom directive states that radiotherapeutic treatments should be individually planned and their delivery verified [7]. Good standardised dosimetry is essential in trials to allow multicentre comparisons or to assess radioiodine sensitisation by drugs such as new generation kinase inhibitors.

Historically, different dosimetry approaches were made to refine radioiodine therapy [8]. The 'bone marrow dose limit' approach tried to establish the ceiling of safe radioiodine activity that could be given to a patient, potentially individualising radioiodine treatment by serial blood sampling. However, this does not take into account individual patient/tumour radioiodine uptake. The other approach is 'lesion-specific dosimetry', which produces absorbed dose estimates for one or more lesions in a patient. In Leeds, UK, lesion-specific dosimetry has been used for the last 10 years. The aim of this study was to determine if carrying out dosimetry influenced treatment decisions for patients with advanced DTC.

Materials and Methods

Since 2005, in Leeds, most patients with regional advanced/metastatic DTC who underwent radioiodine treatments had dosimetry calculated using serial post-treatment scans. All of these patients were included in this study. Data collected included basic patient and tumour demographics, stimulated thyroglobulin levels at the time of each treatment and relevant imaging studies. The results of the above tests and the dosimetry information were used to decide if each patient should be re-admitted for more radioiodine. If the estimated tumour dose was low (<20 Gy) and the stimulated thyroglobulin/scans suggested progression of thyroid cancer then no further radioiodine was given. However, if there was evidence of good absorption of radioiodine in the metastasis, then radioiodine was repeated on the premise that the tumour had received a reasonable dose of radioiodine during the previous admission.

Patients with known regional node or distant metastases had dosimetry calculated from radioiodine uptake during their first admission for radioiodine. Some patients only had dosimetry carried out on subsequent admissions for radioiodine, particularly if metastases were first discovered on the whole body radioiodine post-ablation scan.

Patients were excluded if their radioiodine post-treatment whole body scan (WBS) showed no abnormal uptake on their first admission, because dose was assumed to be close to zero, so dosimetry was not carried out.

Each patient's results were prospectively assessed by their oncologist regarding the usefulness of dosimetry in making management decisions.

Leeds Dosimetry Method

Techniques for the estimation of radiation dose from nuclear medicine images have developed significantly in recent years and continue to develop [9]. These improvements have been facilitated by technological advances in nuclear medicine imaging, specifically: (i) the availability of gamma cameras incorporating high-quality X-ray computed tomography and (ii) the adoption and development of interactive image reconstruction techniques, which better correct for the effects of scattered photons [10] and improve the quantification of small lesions [11].

State-of-the-art imaging in nuclear medicine is being introduced into our practice, as new equipment is procured. However, for the purposes of this paper, all dose estimates were calculated using a methodology that has been achievable, both in terms of the equipment and the scanning time available, throughout the 10 year period covered by this study.

Patients were imaged 2, 3 and 7 days after administration of the I-131 capsule. On days 2 and 7, static images of different magnifications and a WBS were taken. On day 3, statics, WBS and a single photon emission computed tomography (SPECT/CT) (60 frames, 128 matrix) were acquired.

Regions of interest were drawn around any lesions that required dosimetry. The background corrected counts in the lesion were obtained and converted to retained activity, using the camera's measured sensitivity for I-131. This information was used to plot a time–activity curve. The total cumulative activity, $\tilde{A}_h$, was equal to the area under this curve. In its simplest form, it was calculated by equation 1 [12]:

$$\tilde{A}_h = 1.44 \times A_0 \times T\frac{1}{2}_{eff} \quad (1)$$

where A_0 is the activity in the lesion and $T\frac{1}{2}_{eff}$ is the effective half-life of the radiopharmaceutical in the lesion, i.e. combination of physical decay and biological clearance. $T\frac{1}{2}_{eff}$ was found from the gradient of the log of the clearance curve or via curve fitting methods.

The lesion mass was obtained from assessing the images. In the absence of a gold standard for measuring the total functional volume and mass, a range of probable masses were used to create a dose range for each lesion. A minimum and maximum mass were determined to cover the possible range of actual values. We used the minimum dose as a criterion for re-treating patients, but the range was also taken into consideration as well as other factors. Other forms of anatomical imaging (e.g. magnetic resonance scans) were often helpful to assess the mass of nodal metastases, although functional was not always equal to anatomic volume. Where necessary, radiologists aided the definition of ill-defined or equivocal lesions.

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