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Original Article

Study of factors that influence the outcome of ^{131}I treatment in hyperthyroidism secondary to nodular goitre☆

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ABSTRACT

Objective: To assess the outcome after ^{131}I treatment in patients with multinodular (MNG) and nodular toxic goitre (NTG) according to the administered dose (555 or 740 MBq) and other factors related to the patient, pathology, or previous treatments.
Material and methods: A retrospective study was conducted on 108 patients (67 MNG and 41 NTG) treated in our department, with a follow-up period of at least 2 years. Development of hypothyroidism and treatment failure were evaluated along with their relationship with the administered dose and other factors such as age, sex, grade of hyperthyroidism, type of goitre, presence of autoimmunity, or previous antithyroid medication.
Results: More than one-third (36.9%) of MNG patients, and even higher proportion of NTG patients (51.2%) developed non-transient hypothyroidism, particularly in those receiving 740 MBq (66.7%). No relationship was found with any other variable. The development of early hypothyroidism (before one year) was also not related to any variable. Treatment failure was not related to the dose, but in MNG there was a relationship with male gender, presence of autoimmunity, or previous antithyroid drugs use.
Conclusions: The high rate of hypothyroidism obtained with high doses of ^{131}I in hyperthyroidism secondary to nodular goitre treatment suggests that lower doses might be sufficient to control the disease without an increase in treatment failures. Only patients with positive autoimmunity, in previous antithyroid medication, and perhaps male gender in MNG might be given higher doses, as the failure rate increases, but further studies are required.

Estudio de los factores que influyen en el resultado del tratamiento con ^{131}I en el hipertiroidismo por bocio nodular

Palabras clave:
Hipertiroidismo
Bocio nodular
Tratamiento ^{131}I
Hipotiroidismo
Fracaso de tratamiento

RESUMEN

Objetivo: Determinar el resultado obtenido tras tratamiento con ^{131}I en pacientes con bocio multinodular (BMN) y nódulo autónomo tóxico (NAT) en función de la dosis administrada (555 o 740 MBq) y de otros factores relacionados con el paciente, la enfermedad o tratamientos previos.
Material y métodos: Es un estudio retrospectivo sobre 108 pacientes (67 BMN y 41 NAT) tratados en nuestra unidad y con un seguimiento mínimo de 2 años. Se valoró el desarrollo de hipotiroidismo y el fracaso del tratamiento así como su relación con la dosis administrada u otros factores dependientes del paciente (edad o sexo), de la enfermedad (autoinmunidad, grado de hipertiroidismo o tipo de bocio) o la toma previa de antitiroideos.
Resultados: El 36,9% de los pacientes con BMN desarrollaron hipotiroidismo no transitorio llegando al 51,2% en el caso de los NAT y sobre todo en aquellos que recibieron 740 MBq (66,7%) sin encontrarse relación con ninguna otra variable así como tampoco en el desarrollo precoz del hipotiroidismo antes de un año. El fracaso del tratamiento no tuvo relación significativa con la dosis administrada pero sí con el sexo varón, la presencia de autoinmunidad o la toma previa de antitiroideos en el caso de los BMN.
Conclusiones: La elevada tasa de hipotiroidismo obtenida con dosis altas en el tratamiento de hipertiroidismo en el bocio nodular indica que dosis más bajas podrían ser suficientes para controlar la enfermedad sin producir un aumento de fracasos del tratamiento. Únicamente en los pacientes con BMN de sexo masculino, con autoinmunidad positiva o toma previa de antitiroideos se podría estudiar la posibilidad de administrar una dosis mayor pues tienen una tasa de fracasos más elevada.

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Introduction

Hyperthyroidism is caused by an elevation of thyroid hormones in the organism. Several thyroid diseases may lead to hyperthyroidism. Although there are multiple causes for this elevation the most frequent is due to hypersecretion of these hormones by the thyroid gland by hyperstimulation of immunological origin such as in Graves disease or the formation of secretor nodules as in the toxic nodular goiter (TNG) or multinodular goiter (MNG).

Among the therapeutic options available, the use of iodine 131 (^{131}I) is a good alternative to surgical or medical treatment. Treatment with ^{131}I is simple, induces little patient discomfort and has scarce secondary effects. It allows definitive long-term disease control, avoiding frequent monitoring and the secondary effects of medical treatment and definitive hypothyroidism in many cases as well as surgery-related risks.

The optimal dose is not well established. Some authors use fixed high or low doses or doses calculated taking into account most of the thyroid volume methods and the percentage of ^{131}I uptake at 24 h. The Marinelli et al.[1] method is one of the methods most commonly used.

One of the problems related to ^{131}I treatment is the rate of hypothyroidism produced, which according to different studies[2,3] varies greatly, ranging from 1% to 64%. It is known that high doses of ^{131}I produce a higher rate of cure than low doses, albeit at the expense of inducing a high rate of hypothyroidism.

There are different studies on the influence of not only the dose administered but also other patient-associated factors such as age or sex or others related to the disease itself (autoimmunity, grade of hyperthyroidism or type of goiter) as well as treatments such as previous antithyroid therapy (AT) or the dose of ^{131}I administered.

The primary objective of this study was to evaluate the development of hypothyroidism following treatment with ^{131}I in nodular goiter, differentiating the patients according to the presence of MNG or TNG as well as their possible relationship with the previously mentioned factors. The secondary objectives were to evaluate the same relationship with early development of hypothyroidism, defined as the time of manifestation within one year after treatment and maintained over time, and treatment failure and the need to administer a second dose.

Material and methods

We performed an observational, retrospective study collecting data from all the patients diagnosed with hyperthyroidism with nodular type disease referred for treatment in our center from March 2004 to December 2012. All the patients had previously undergone scintigraphy with ^{99m}Tc-pertechnetate to determine the type and morphofunctional characteristics of the goiter.

The electronic clinical histories of the patients were reviewed and a database was created including the following variables: age, sex, type of thyroid disease (based on scintigraphy results), type of hyperthyroidism (clinical/subclinical) at the time of treatment, immune status, previous AT treatment (methimazole) and the dose received.

The dose received by the patients (555 or 740 MBq) was empirically decided taking into account the size of the goiter in the scintigraphic image, the intensity of nodule uptake, suppression or not of normal thyroid tissue in TNG and the predominance of increased or decreased uptake in MNG. Thyroid uptake was not determined.

Hyperthyroidism was considered to be subclinical with a TSH value <0.35 μU/ml and a normal free T4 (0.7–1.75 ng/dl) and clinical with an elevated free T4 and/or T3.

Table 1
Characteristics of the patients studied.

	MNG (n = 67)	TNG (n = 41)	Total (n = 108)
Mean age	67.7 (31–92)	65.2 (33–89)	66.7 (31–92)
Sex			
Men	11 (16%)	11 (27%)	22 (20%)
Women	56 (84%)	30 (73%)	86 (80%)
Hyperthyroidism status			
Clinical	11 (17%)	5 (12.5%)	16 (15.5%)
Subclinical	52 (83%)	35 (87.5%)	87 (84.5%)
Previous AT	18 (27%)	13 (32%)	31 (29%)
Autoimmunity	16 (24%)	3 (7%)	19 (18%)
Dose 15 mCi	34 (51%)	20 (49%)	54 (50%)
Dose 20 mCi	33 (49%)	21 (51%)	54 (50%)

MNG: multinodular goiter; TNG: toxic nodular goiter; AT: antithyroid.

The immune status was considered as positive with the presence of positive antithyroglobulin antibodies, antiTPO or TSI above the reference values of our laboratory which are >40 IU/ml, >35 IU/ml and >1.75 IU/ml, respectively.

The administration of AT was discontinued in all the cases at least 4 days prior to treatment with ^{131}I. Table 1 shows the characteristics of the patients.

For the analysis of the results the patients were divided into 2 groups according to the type of nodular goiter. The first group was made up of patients with MNG and the second had TNG.

We studied the relationship of the variables described with the results obtained following treatment in both groups. The study variables were analyzed in relation to the development of hypothyroidism maintained over the follow up period. For the purposes of the study, transitory hypothyroidism was not considered as hypothyroidism. We also analyzed early development of hypothyroidism, which was considered as that produced within the first year after treatment and maintained thereafter, and treatment failure in patients who received a second dose of ^{131}I due to persistence or recurrence of hyperthyroidism.

In all the cases the study was performed after the first dose of ^{131}I.

Statistical analysis

For the statistical analyses the SPSS 21 program was used. Dichotomous variables were analyzed using the Chi-square or the bilateral Fisher's exact test as necessary. Quantitative variables were analyzed with the Student's t test in variables with a normal distribution and the Mann–Whitney U test for those without a normal distribution. A p value <0.05 was considered statistically significant.

Results

We included 108 patients in the study: 67 had MNG (62.03%) and 41 TNG (37.96%). The mean age of the sample was 66.75 (31–92) years, and 22 patients were men and 86 were women.

Principal analysis: development of hypothyroidism

During the study follow up after treatment with ^{131}I, 24 patients with MNG (36.9%) developed hypothyroidism within a mean time of 19.5 months (1–77 months). Among the patients with TNG there were 21 hypothyroidisms (51.2%) developed over a mean time of 18.2 months (1–72). Two patients were lost to follow up.

Influence of the dose of ^{131}I: The rate of hypothyroidism was elevated and more marked in patients with TNG. On analyzing the factors which may have influenced this rate, only the dose administered was significantly related to the development