Original article

Outcome of Radioiodine Therapy in a West African Population

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Abstract

Hyperthyroidism continues to be a pressing public health concern in West Africa. Its prevalence in Africa has been quoted as 1.2%-9.9%, with Graves' disease as its most common cause. Radioiodine-131 (RAI) therapy of hyperthyroidism recently commenced in two government hospitals in Ghana and Nigeria. This is a retrospective analysis of consecutive patients treated with RAI for primary hyperthyroidism at the National Centre for Radiotherapy and Nuclear Medicine (NCRNM) from 2008-2013, and in the University College Hospital (UCH) from 2006-2013. Cure was defined as euthyroidism or hypothyroidism occurring at 6 months post-RAI. Data were analysed using SPSS version 21 and Epi Info version, categorical data were evaluated with the Chi-square test and Fisher's exact test. 94 patients were studied, aged 20-74 years; 78 were females, and 16 were males. 38 were Ghanaian and 56 Nigerian. The presence of thyroid-associated ophthalmopathy (TAO) made cure less likely (χ^2 $P = 0.006$, odds ratio = 0.118; 95% confidence interval, 0.027-0.518). Other factors assessed proved to be insignificant. Our findings suggest that hyperthyroid patients with TAO will benefit from a higher RAI dose than their counterparts without TAO.

Keywords: Goitre, hyperthyroidism, nuclear medicine, radioiodine, West Africa

Introduction

Hyperthyroidism continues to be a pressing public health concern in West Africa. An African study quotes its prevalence as 1.2- 9.9%, with Graves' disease (GD) as its most common cause.[1] In Nigeria, a tertiary hospital incidence[2] of 8 cases per year had been quoted; the figure is presently on the increase. Thyrotoxicosis (TT) comprised 75% of 170 cases studied in Nigeria,[1] while in Ghana GD interestingly comprised 3.2% of all thyroid disorders from a hospital-based study of pathology specimens.[3] Nuclear medicine (NM) is a newly introduced medical discipline in government hospitals in both countries. Radioactive iodine (RAI) is relatively novel as a therapeutic option for primary hyperthyroidism in West Africa, despite the fact that RAI has been an established treatment option globally for more than 70 years.[4,5] However, a private establishment in Nigeria had been administering RAI as treatment for hyperthyroidism since 1991.[6] The more popular modalities are medical and surgical therapy, with patients being referred for RAI for indications that include hyperthyroidism refractory to antithyroid drugs (ATDs), recurrence post-operatively, or patients indicating their preference for it over the scalpel.

NM is rapidly advancing with novel tracers providing new prospects for imaging pathology and physiology at the molecular level. This offers new and exciting opportunities in understanding pathology with the view of improving disease treatment and follow-up.

In spite of the recent beehive of activities in the field of receptor imaging, which make it appear that NM is novel, NM therapy and molecular imaging have been used for several decades. They are applicable in the treatment of thyroid disease where the sodium iodide symporter (NIS)

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is the receptor, and radioiodine-131 (RAI) is the radiotracer that has formed the basis for most of the current knowledge and practice of NM therapy.[7]

The thyroid gland traps and concentrates iodide, which is organified and coupled, eventually resulting in the synthesis of thyroid hormones for the metabolic needs of the body. The NIS is responsible for the trapping of RAI in the thyroid gland. While NIS is abundant in the thyroid gland, it is not limited to this site. Thus, RAI is trapped by other parts of the body such as gastric mucosa and salivary glands. This may result in side effects of gastritis and sialadenitis, respectively, particularly when high doses of RAI are administered.[7,8] Thyroglobulin secretion, unlike the NIS, is unique to the thyroid gland. Thus storage of RAI only occurs only in thyroglobulin in colloid and not in other areas of the body where NIS receptors are located.[9]

The principles underlying the choice of dose of RAI to treat hyperthyroidism are based on studies and observations in populations that have generally not included subjects from Western Africa. Furthermore, the paucity of trained personnel in NM, logistics, and financial restraints[10] have generally left Western Africa lagging behind in the application of NM techniques to treat patients.[11]

It is for this reason that we sought to study the patients in this environment who have benefitted from RAI therapy to discern if there were any factors that could predict the outcome of therapy that might differ from factors observed in patients from other parts of the world.

This is the first of a series of studies in two public NM centers in two West African countries. The study aims to assess the outcome of RAI therapy for hyperthyroidism, and to assess factors affecting outcome, thus enabling prediction of outcome, and effecting a change in patient management as necessary.

Materials and Methods

Ethics

Research procedures followed were in accordance with the ethical standards of the institutional committees on human experimentation and with the Helsinki Declaration of 1975,[12] as revised in 2000. Patient confidentiality was strictly maintained, and data rendered anonymous except for the purpose of subject identification during statistical analysis.

Study design

Selection and description of participants

The study is a retrospective analysis of consecutive patients treated with RAI for primary hyperthyroidism at two institutions: the other in Ghana from 2008 to 2013, and one in Nigeria from August 2006 to April 2013. Patients' medical records were retrieved and data was extracted from them. If the records were incomplete or patients had been referred to another clinic for continuation of care, attempts were made to reach patients telephonically and obtain needed information. Only patients with RAI-naïve thyroid glands were studied.

The protocol at the National Centre for Radiotherapy and Nuclear Medicine (NCRNM) has changed over the years. Initially every patient was given an empirical dose of 10 mCi, and thyroid scintigraphy was not mandatory for every patient.

From the year 2010, the protocol changed to a higher range of 15-30 mCi. Patients with large glands, nodular glands, and patients for retreatment received higher doses of 30 mCi. Moreover, all patients received a Tc-99m pertechnetate thyroid scan before therapy. Patients with dysthyroid eye disease were referred to the ophthalmologist and were placed on 0.5mg/kg oral prednisolone for 14 days, starting from day of administration of RAI. ATDs were discontinued for 7-14 days prior to RAI therapy. All women underwent a blood pregnancy test and patients were counselled and asked to sign a consent form. Patients were reviewed at 1 month, 3 months and 6 months after therapy. Cure was defined as euthyroidism/hypothyroidism at 6 months post-RAI.

At the University College Hospital (UCH), the protocol involves empirical dosing, with a minimum of 10 mCi administered per patient. Nodular goitres and recurrent disease attract higher doses up to 30 mCi. Tc-99m pertechnetate thyroid scans were performed for all patients prior to therapy. ATDs were discontinued for 5 days prior to therapy. Patients with thyroid-associated ophthalmopathy (TAO) were referred for an ophthalmology review before being treated. Oral corticosteroids (prednisolone 0.5 mg/kg body weight) were prescribed for a month prior to treatment; this practice began around 2011. Counselling was performed, and similar precautions observed as at the NRNMC. Written informed consent was obtained. Patients are treated on an outpatient basis, and discharged after having been observed for possible adverse reactions. Routine administration of oral/parenteral metoclopramide commenced recently, in order to prevent emesis of this expensive medication. Patients are followed up at source of referral, or at the unit's thyroid clinic based on the tenor of referral. This usually took the form of three-monthly appointments which lengthened as patients became more stable.

In both establishments, the goal of RAI therapy presently is hypothyroid cure, in view of prevailing financial and logistic constraints. Thyroid uptake was not routinely

performed for all patients in the period of study, and thus was omitted from analysis.

Statistics

Data were analysed using SPSS version 21[13] and Epi Info version 7.1.4,[14] categorical data evaluated with the Chi-square test and Fisher's exact test. A bivariate odds ratio computation was also performed, with a 95% confidence interval. The level of statistical significance was taken as $P < 0.05$.

Results

Table 1 displays basic characteristics of patients. A total of 94 patients were studied, aged 20-74 years. Seventy-eight of these were females and 16 were males. At the UCH, there were 56 patients, aged 20-74 years; 47 females and 9 males. At the NCRNM, there were 38 patients aged 24-66 years; 31 females and 7 males. Thus the male-to-female ratios for both institutions were approximately 1:4 and 1:7, respectively, while the overall ratio was 1:5. [Figures 1 and 2] Overall, 77 (81.9%) patients had GD, 8 (8.5%) toxic multinodular goitres TMG, and 7 (7.4%) toxic solitary nodules TSN [Figure 3].

Cure

Six months following RAI therapy, 41 of 53 patients (77.3%) had developed euthyroidism or hypothyroidism, while at an earlier period of 3 months, 43 of 67 patients (64.2%) had been cured. The default rate increased from 28.7% to 43.6% at 3 and 6 months, respectively [Figures 4 and 5].

Predictors of cure

The following variables were assessed as possible predictors of outcome of RAI: age, gender, nationality, type of thyroid pathology (GD, toxic multinodular goitre [TMG] and toxic solitary nodule [TSN]), presence or absence of TAO, pretreatment with ATDs, thyroid status at presentation, and dose of RAI administered. Out of all of the variables evaluated, TAO was found to be significantly predictive of cure (χ^2 $P = 0.006$, odds ratio = 0.118; 95% CI, 0.027-0.518) [Table 2].

Table 1: Characteristics of hyperthyroid patients treated with RAI

	N (%)		
	NCRNM	**UCH**	**All patients**
Age (years)			
Mean (SD)	46.89±12.54	47.73±12.30	47.38±12.34
Range	23-66	20-74	20-74
Gender (F)	31 (81.6)	49 (87.5)	80 (85.1)
Gender (M)	7 (18.4)	7 (12.5)	14 (14.9)
Sex ratio (M:F)	1:4	1:7	1:6
GD	27 (71.0)	50 (89.3)	77 (81.9)
TMG	3 (7.9)	5 (8.9)	8 (8.5)
TSN	6 (15.8)	1 (1.8)	7 (7.4)
ATD Yes	33 (86.8)	52 (92.8)	85 (90.4)
ATD No		3 (5.3)	3 (3.2)
TAO present	21 (55.2)	19 (33.9)	40 (42.5)
TAO absent	17 (44.7)	15 (26.8)	32 (34.0)
TSH* at presentation (mIU/L)	0.01±3.88	2.47±5.69	0.015±0.007
First dose RAI (mCi)	17.49±7.28	13.70±6.75	15.27±7.19

*SD: Standard deviation; M: Male; F: Female; GD: Graves' disease; TMG: Toxic multinodular goitre; TSN: Toxic solitary nodule; ATD: Antithyroid drug; TAO: Thyroid-associated ophthalmopathy; TSH: Thyroid stimulating hormone; RAI: Radioiodine

Table 2: Factors affecting outcome of RAI therapy at 6-month follow-up

Parameter	*P* value	OR*(95% confidence interval)
Age	0.336	3.72 (0.21-64.48)
Gender	0.89	0.85 (0.08-9.00)
ATD pretreatment	0.79	Inconclusive
Thyroid pathology	0.05	1.00
TAO	0.005	0.118 (0.027-0.518)
Dose of RAI	0.69	0.56 (0.15-2.11)

*OR: Odds ratio; ATD: Antithyroid drugs; TAO: Thyroid-associated ophthalmopathy; RAI: Radioiodine

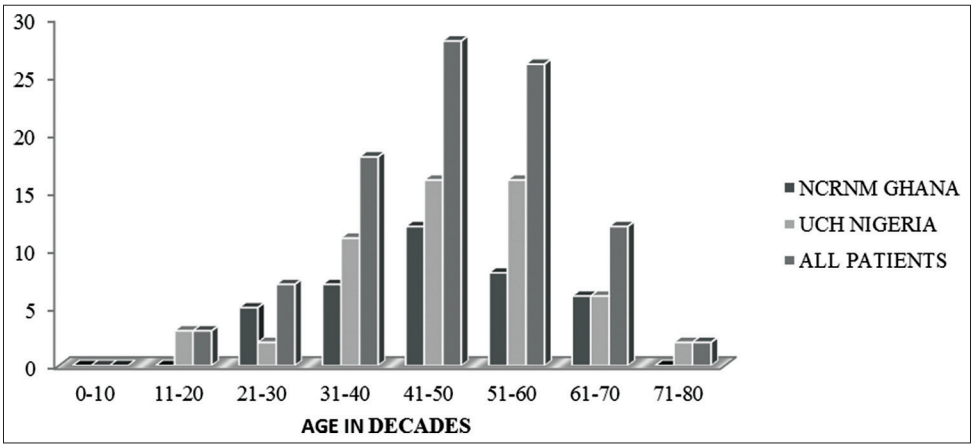

Figure 1: Patients' ages in years displayed for both centers

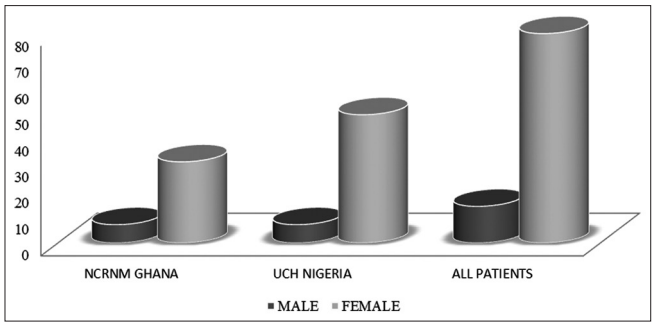

Figure 2: Gender distribution of hyperthyroid patients

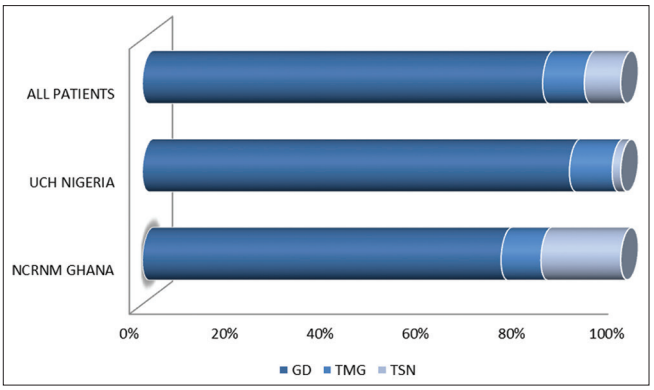

Figure 3: Thyroid pathology findings at both centers

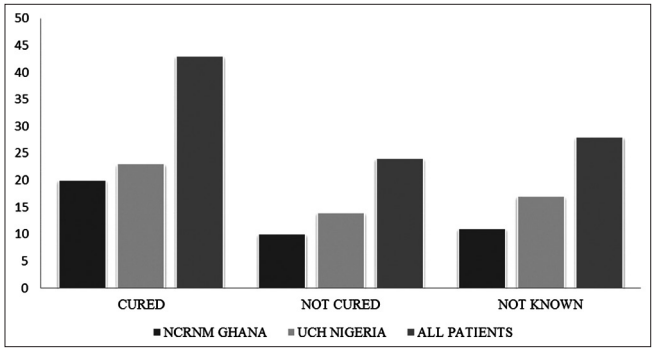

Figure 4: Outcome of RAI therapy at 3 months in both centers

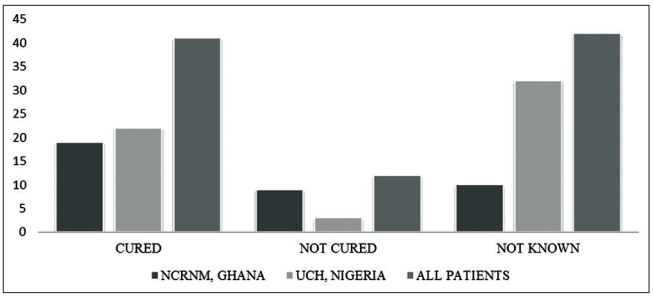

Figure 5: Outcome of RAI therapy at 6 months in both centers

Discussion

RAI therapy as an option in the management of hyperthyroidism continues to gain popularity among clinicians and patients alike in West Africa. There are other countries not involved in this study that also offer this service. It has advantages that include its being non-invasive, being an out-patient modality, offering high cure rates, and causing few side effects.

The majority of our patients were in the 4th to 7th decade of life and most had been diagnosed within a five-year period prior to receiving radioiodine therapy. In sub-Saharan Africa, hyperthyroidism has been described[15] as occurring in patients older than 50 years, who were mostly from rural areas. The most common aetiology then was attributed to GD, although at a lower figure of 50% compared to our overall figure of 81.9%. Our findings also indicate an increase in the hospital incidence of hyperthyroidism previously published.[2] As well, there has been a significant increase in the utility of RAI as a modality for treating hyperthyroidism; previously described as 7% for Nigerians.[11]

TAO

Its incidence is higher in female patients, with a prevalence of 0.25%.[16] Other risk factors are middle age, smoking, and RAI therapy.[17] Smoking has also been known to exacerbate the outcome of TAO following RAI. However in our study, only one patient admitted to a history of smoking prior to RAI; he was known to have TSN and had been cured by his 6-month follow-up visit. A female preponderance was also observed in our patients (32 females and 8 males). TAO was not a significant predictor of outcome at 3-month follow-up, but was at 6 months. This suggests that patients with TAO require a longer period to be cured. There is a significant dearth of literature regarding TAO and its effect on RAI therapy outcomes in Africa, especially in Western Africa.

Cure

At 6 months following RAI therapy, 77.8% of patients had developed euthyroidism or hypothyroidism requiring L-T4 replacement, while at an earlier period of 3 months, 64.7% had been cured. In a 7-year Nigerian review,[18] hypothyroidism post-RAI was 50% at one year in a study of 77 patients treated with 10 to 20 mCi of RAI. Our cure rate indicates greater efficacy than quoted for ATD therapy in a West African study (61%).[19]

Type of goitre

In both centers, nodular and larger glands generally received higher doses than smaller and diffuse toxic goiters. Despite having received relatively larger doses, nodular goitres were less likely to be cured after a single dose of RAI with an average dose of 25 mCi. However, this was not a significant finding. The relatively resistant nature of TMG to RAI is buttressed, and may mean that such patients desirous of non-surgical cure may

require even higher doses (than 30 mCi) or multi-dosing. Nodular goitre requiring cumulative dose of up to 46 mCi has been described.[20]

Gender

The male-to-female ratios of patients treated at NCRNM and UCH: 1:4 and 1:7, respectively, are similar to global figures.[2,21,22] The hyperthyroid male has been described severally as being more resistant to RAI treatment. Those of African descent have further been found to be more prone to treatment failure than their Asian or Caucasian counterparts following RAI.[23-25]

Other studies[21,22,24] had previously indicated age, gender, pretreatment with ATD, and dose of RAI as predictive of outcome of RAI therapy. TAO as a predictor had also been described, and was the only significant finding in this study. A larger prospective, randomized study offering different doses of RAI to hyperthyroid patients is indicated, during which we hope to derive further information predicting outcome of RAI therapy in this part of the world.

Limitations

The problem of missing data/records as is usually seen with retrospective studies was also experienced.

These are tertiary hospital-based data and may not be true reflections of the community.

A high patient default rate was observed and was attributed to the custom of most patients returning to sources of referral after RAI administration.

There was a bias toward prescribing larger doses of RAI for therapy of nodular goitre and recurrent goitres.

Estimation of RAI uptake was only recently instituted at both centers, and thus was omitted from analysis.

Financial and logistic constraints[10] are quite real in this area of the world. The fear of nuclear therapy, which is a novel method of treatment, has been predominantly expressed by medical personnel and passed on to patients, who then perceive it as a dangerous form of treatment.

Conclusion

Our findings suggest that hyperthyroid patients with TAO will benefit from a higher RAI dose than their counterparts without TAO. Accordingly, this information should be considered when assessing patients for RAI therapy while deciding on optimal dose for cure. Both institutions have since incorporated this information into their respective management protocols. Meanwhile, larger prospective studies will be needed to derive more robust information.

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References

1. Ogbera AO, Kuku SF. Epidemiology of thyroid diseases in Africa. Indian J Endocrinol Metab 2011;15(Suppl 2):S82-8.
2. Famuyiwa OO, Bella AF. Thyrotoxicosis in Nigeria. Analysis of a five year experience. Trop Geogr Med 1990;42:248-54.
3. Der EM, Quayson SE, Clegg-Lamptey JN, Wiredu EK, Ephraim RK, Gyasi RK. Thyroid disorders in Accra, Ghana: A retrospective histopathological study at the Korle-Bu Teaching Hospital. J Biomed Sci 2013;2:1-7.
4. Beierwaltes WH. The history of the use of radioactive iodine. Semin Nucl Med 1979:3;151-5.
5. Sawin CT, Becker DV. Radioiodine and the treatment of hyperthyroidism: The early years. Thyroid 1997;7:163-76.
6. Agboola-Abu CF, Kuku S. Experience in the use of radioactive iodine therapy for hyperthyroidism in Nigerian patients. A study of twenty-two patients. West Afr J Med 2003;22:324-8.
7. Shen DH, Kloos RT, Mazzaferri EL, Jhian SM. Sodium iodide symporter in health and disease. Thyroid 2001;11:415-25.
8. Cavalieri RR. Iodine metabolism and thyroid physiology: Current concepts. Thyroid 1997;7:177-81.
9. Dunn JT, Dunn AD. The importance of thyroglobulin structure for thyroid hormone biosynthesis. Biochimie 1999:81;505-9.
10. Adedapo KS, Onimode YA, Ejeh JE, Adepoju AO. Avoidable challenges of a nuclear medicine facility in a developing nation. Indian J Nucl Med 2013;28:195-9.
11. Ogbera AO, Ekpebegh C, Eregie A, Kuku SF. The role of radioactive iodine usage in the management of thyroid disorders with emphasis on sub-Saharan Africa. West Afr J Med 2008;27:211-7.
12. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. Available from: http://www.wma.net/en/30publications/10policies/b3/. [Last accessed 2015 Feb 19].
13. IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY: IBM Corp; 2012.
14. Carstensen B, Plummer M, Laara E, Hills M (2014). Epi: A package for statistical analysis in epidemiology. R package version 1.1.67. Available from: http://www.CRAN.R-project.org/package=Epi. [Last accessed on 2015 Feb 19].
15. Sidibé el H. Thyroid diseases in sub-Saharan Africa. Sante 2007;17:33-9.
16. Lazarus JH. Epidemiology of Graves' orbitopathy (GO) and relationship with thyroid disease. Best Pract Res Clin Endocrinol Metab 2012;26:273-9.
17. Acharya SH, Avenell A, Philip S, Burr J, Bevan JS, Abraham P. Radioiodine therapy (RAI) for Graves' disease (GD) and the effect on ophthalmopathy: A systematic review. Clin Endocrinol (Oxf) 2008;69:943-50.
18. Ekpebegh C, Ogbera A, Odeleye T, Kuku SF. Hypothyroidism at one year following radioactive iodine therapy; incidence and associated factors: Report from a tertiary Nigerian hospital. Internet J Endocrinol 2007;4;2. [Last accessed on 2015 Jan 29].

19. Modebe O. Experience with carbimazole in the drug treatment of the hyperthyroidism of Graves' diseases in Nigerians. East Afr Med J 1992;69:153-6.
20. Sagel J, Epstein S, Kalk J, Van Mieghem W. Radioactive iodine (131I) therapy for thyrotoxicosis at Groote Schuur Hospital over a 6-year period. Postgrad Med J 1972:48:308-13.
21. Brent GA. Clinical practice. Graves' disease. N Engl J Med 2008;358:2594-605.
22. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, *et al*. The spectrum of thyroid disease in a community: The Whickham survey. Clin Endocrinol (Oxf) 1977:7;481-93.
23. Blahd WH, Hays MT. Graves' disease in the male. A review of 241 cases treated with an individually calculated dose of sodium iodide I 131. Arch Intern Med 1972;129:33-40.
24. Ariza MA, Loken WM, Pearce EN, Safer JD. Male sex, African American race or ethnicity, and triiodothyronine levels at diagnosis predict weight gain after antithyroid medication and radioiodine therapy for hyperthyroidism. Endocr Pract 2010;16:609-16.
25. Allahabadia A, Daykin J, Holder RL, Sheppard MC, Gough SC, Franklyn JA. Age and gender predict the outcome of treatment for Graves' hyperthyroidism. J Clin Endocrinol Metab 2000;85:1038-42.

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