



Treatment of juvenile thyrotoxicosis: A review with emphasis on radioiodine treatment

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Abstract

Objective: The aim of the present study was to evaluate the utility of radioiodine treatment for thyrotoxicosis in childhood and adolescence and to evaluate its outcomes.

Methods: This was a retrospective monocentric study of 15 patients (ages 7- 18 years) with a diagnosis of thyrotoxicosis who received iodine-131 (I-131) treatment from January 2015 to July 2019 in the Nuclear Medicine department of King Fahd Medical city. Age, gender, duration of antithyroid drug (ATD) treatment, thyroid uptake, total dose and number of treatments with I-131, and thyroid status at 6 months after treatment were recorded.

Results: The outcomes of 15 patients (100% female) treated with radioactive iodine were analyzed to assess the effectiveness of therapy by iodine 131. All children and adolescents underwent 99m technetium thyroid scan with uptake before the procedure. There was no pre-existing ophthalmopathy. Thyroid uptake value was calculated using Sodium Perchnetate. The average of the treatment activity of iodine 131 was 340.4 MBq (247.9-555). There was no vomiting in all cases. Six 6 months after treatment, 7/15 were euthyroid, and 8/15 were hypothyroid. There was no hyperthyroid. All the patients received single radioiodine treatment.

Conclusions: Radioiodine treatment is safe and effective for thyrotoxicosis in childhood and adolescence. The results of this present study support the use of radio dine 131 in treating hyperthyroidism in this particular population. It is suitable as a good Second-line therapy for patients who fail to respond to ATD treatment. Although special treatment precautions may be required in this age group, the ease of administration, effectiveness and safety of radio dine 131 continue to make it more and more attractive for initial treatment of hyperthyroidism, especially when the appropriate treatment activity is prescribed.

Keywords: radioiodine treatment, thyrotoxicosis, children, adolescence, outcome

Introduction

Thyrotoxicosis is a rare endocrinopathy in childhood and adolescence, affecting only 0.02% of all children [1]. The most common cause of thyrotoxicosis in patients younger than 18 years of age remains Graves' disease (GD), which accounts for 10-15% of all paediatric thyroid diseases [2]. GD is rare under the age of 5 years; it has a peak incidence at age 10-15 years, with female predominance [2, 3]. The management of thyrotoxicosis in children and adolescents remains controversial until now. The current therapeutic methods of thyrotoxicosis include the treatment with antithyroid drugs (ATD) as a first line followed by definitive therapy including both radioactive iodine (RAI) therapy and thyroidectomy [4], which usually considered in cases of relapse, ATD toxicity, or lack of compliance.

However, medical treatment by ATD is generally associated with a high relapse rate, risk of side effects including hepatic failure and bone marrow suppression, and low compliance associated with prolonged ATD therapy. Several studies reported that after ATD medications are discontinued, 35-60% of patients may experience relapse [3]. Therefore, definitive therapy is favored as the first-line

treatment in several countries [4].

Radioactive iodine was introduced for the treatment of Graves' disease in children more than 60 years ago [5]. In the years since, the use of radioactive iodine to treat Graves' disease has been reported for 1000 children, with administered iodine-131 doses ranging from 1.85 to 14.5 Mbq/g [6, 7-14]. Follow-up studies have not revealed increases in rates of thyroid cancer or genetic abnormalities in children or in the offspring of such children treated with moderate or high doses of radioactive iodine [15]. These observations coupled with saddening results associated with medical therapy for most patients conduct to the increased use of radioactive iodine for treating Graves' disease in children [7, 13].

In fact, there is an increasing tendency to recommend RAI treatment as the first therapeutic modality in children and adolescents, mainly due to its very high cure rate (exceeding 95%) [16]. When RAI is used at appropriate doses, most patients can be successfully treated with a single oral dose and rare complications [16]. The treatment effect is due to radioiodine-mediated destruction and also a particular effect on thyroid autoimmunity.

The present study reviews our local experience in the treatment of infants and adolescent patients with hyperthyroidism and evaluates the effectiveness and the outcome of this simple radical treatment. Emphasis was placed on the reasons for a change in medical treatment, utility of treatment, need for treatment and development of hypothyroidism, thus encourage to prefer the radioiodine as first line in the treatment of hyperthyroidism in children and adolescents.

Methods

Between January 2015 and July 2019, all children and adolescent patients who received iodine-131 (I-131) treatment for hyperthyroidism at the Nuclear Medicine Department of King Fahd Medical City, Riyadh, Kingdom of Saudi Arabia, were included in this retrospective study. All patients were diagnosed by endocrinologists on the basis of their clinical and laboratory findings. Age, gender, duration of antithyroid drug (ATD) treatment, thyroid uptake, the total dose and number of treatments with I-131, and disease status at 6 months after treatment were recorded. The primary indication for I-131 treatment among all patients was failure of the medical treatment (100%).

All patient was performed Technetium-99m Pertechnetate scintigraphy to calculate the thyroid uptake value. Approximately 185 MBq of 99mTc-pertechnetate was administrated to the patient intravenously. Fifteen minutes after the administration, anterior planar images of the neck and chest were acquired using a gamma-camera equipped with high-resolution parallel-hole collimator (Bright view,

Philips, USA) with an acquisition time of 10 minutes, using a 20% window centered Around the 140 KeV peak of 99mTc and a 128×128 computer matrix. Thyroid uptake value was calculated using Sodium Pertechnetate. The normal range was between 0.5% to 3.5%.

Images were analyzed by an experienced board-certified nuclear medicine physician.

All patients were treated with a fixed dose of I-131. All patients were assessed for treatment outcome at 6 months after I-131 treatment. The patients were classified into 2 groups according to treatment success (euthyroid and hypothyroid) and treatment failure (hyperthyroid). The rate of treatment success was calculated.

Results

During the study period, 15 patients (100% female) with a mean age of 14.6 years (range, 7-18 years) received I-131 treatment for hyperthyroidism at our institution. All patients had been treated medically by ATD before receiving RAI. There was no pre-existing ophthalmopathy. The outcomes of 15 patients treated with RAI were analyzed to assess the effectiveness of therapy. The thyroid scintigraphy showed in all cases enlarged thyroid gland with markedly increased radiotracer trapping with homogenous distribution (figure). The thyroid uptake Thyroid uptake value was calculated using Sodium Pertechnetate was high with an average of 20% (range, 19-35 %) (Figure). The average of the treatment activity of iodine 131 was 340.4 MBq (247.9-555). There was no vomiting in all cases.

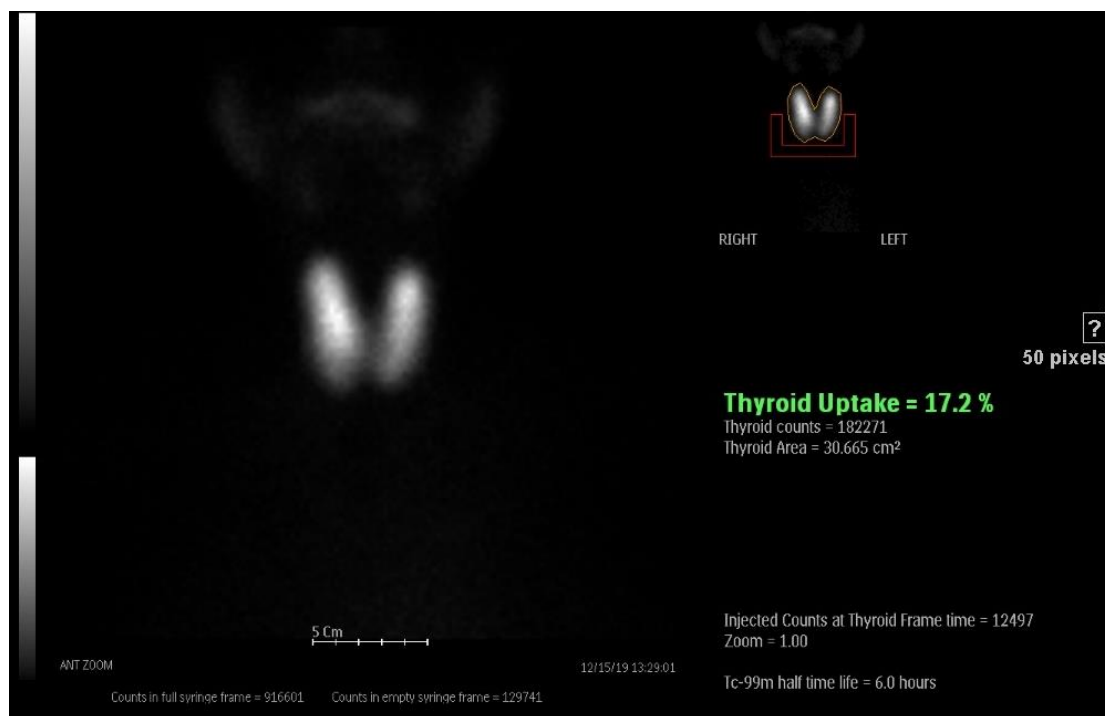


Fig 1: Technetium-99m pertechnetate scintigraphy showed enlargement thyroid gland, with increased homogeneous radiotracer uptake. There is a decrease in background activity. Thyroid uptake value: 17.2 % (normal range between 0.5% to 3.5%). The findings are consistent with Diffuse Toxic Goiter (Graves' disease).

The analysis showed that at 6 months after treatment 7/15 were euthyroid, and 7/15 were hypothyroid. There was no hyperthyroid. As the patients were classified into 2 groups according to treatment success (euthyroid and hypothyroid) and treatment failure (hyperthyroid). The treatment success was 15/15. All the patients received single radioiodine

treatment.

Discussion

The treatment of thyrotoxicosis with RAI was introduced more than 60 years ago and was initially limited to adult patients. However, this treatment has lately become more

and more popular in many countries for treating thyrotoxicosis in children and adolescents [4, 16-19]. The objective of RAI treatment in hyperthyroidism is to achieve the hypothyroid state. Until now, there is no clear consensus guideline on RAI treatment for hyperthyroidism in children and adolescents. The dose used for treatment in this population varies among investigators [16-25]. RAI dose is typically calculated based on thyroid gland volume and I-131 uptake. Some factors, including thyroid gland size and I-131 delivered dose to thyroid tissue, have been reported to influence treatment outcome [4, 21, 26].

Several studies have reported a very high remission rate (>95%) with doses >150 $\mu\text{Ci/g}$ [16, 20, 28]. In the present study, we observed that 55.6% of our patients achieved the euthyroid and hypothyroid state after a single dose, which is a much lower rate than reported by other studies. Male sex, high free thyroxine at diagnosis, a palpable goiter, use of ATD, time elapsed before RAI treatment, and pre-existing ophthalmopathy have been reported as the predictors of poor treatment outcome [25, 29]. This could explain the high success rate in the current study.

Conclusions

Radioiodine treatment is safe and effective for thyrotoxicosis in childhood and adolescence. The results of this present study support the use of radio iodine 131 in treating hyperthyroidism in this particular population. It is suitable as a good second-line therapy for patients who fail to respond to ATD treatment. Although special treatment precautions may be required in this age group, the ease of administration, effectiveness and safety of radio iodine 131 continue to make it more and more attractive for initial treatment of hyperthyroidism, especially when the appropriate treatment activity is prescribed.

References

1. Gruneiro-Papendieck L, Chiesa A, Finkielstain G, Heinrich JJ. Pediatric Graves' disease: outcome and treatment. *J Pediatr Endocrinol Metab*,2003;16:1249-1255.
2. Zimmerman D, Lteif AN. Thyrotoxicosis in children. *Endocrinol Metab Clin North Am*,1998;27:109-126.
3. Kagueidou F, Alberti C, Castanet M, Guitteny MA, Czernichow P, Leger J. French Childhood Graves' Disease Study Group. Predictors of auto immune hyper thyroid is mrelapse in children after discontinuation of antithyroid drugtreatment. *J Clin Endocrinol Metab*,2008;93:3817-3826.
4. Namwongprom S, Unachak K, Dejkhamron P, Ua-apisitwong S, Ekmahachai M. Radioactive iodine for thyrotoxicosis in childhood and adolescence: treatment and outcomes. *Journal of clinical research in pediatric endocrinology*,2013;5(2):95.
5. Chapman EM. History of the discovery and early use of radioactive iodine. *JAMA*,1983;250:2042-2044.
6. Hamburger JI. Management of hyperthyroidism in children and adolescents. *J Clin Endocrinol Metab*. 1985;60:1019-1024
5. Lazar L, Kalter-Leibovici O, Pertzalan A, Weintrob N, Josefsberg Z, Phillip M. Thyrotoxicosis in prepubertal children compared with pubertal and postpubertal patients. *J Clin Endocrinol Metab*,2000;85:3678-3682
7. Starr P, Jaffe HL, Oettinger L Jr. Later results of 131-I treatment of hyperthyroidism in 73 children and adolescence: 1967 follow-up. *J Nucl Med*,1969;10:586-590.
8. Kogut MD, Kaplan SA, Collipp PJ, Tiamsic T, Boyle D. Treatment of hyperthyroidism in children: analysis of forty-five patients. *N Engl J Med*,1965;272:217-222.
9. Crile G, Schumacher OP. Radioactive iodine treatment of Graves' disease: results in 32 children under 16 years of age. *Am J Dis Child*,1965;110:501-504.
10. Hayek A, Chapman EM, Crawford JD. Long term results of treatment of thyrotoxicosis in children and adolescents with radioactive iodine (131I) for hyperthyroidism. *N Engl J Med*,1970;283:949-953.
11. Safa AM. Treatment of hyperthyroidism with a large initial dose of sodium iodine I 131. *Arch Intern Med*,1975;135:673-675.
12. Safa AM, Schumacher OP, Rodriguez-Antunez A. Long-term follow-up results in children and adolescents treated with radioactive iodine (131I) for hyperthyroidism. *N Engl J Med*,1975;292:167-171.
13. Levy WM, Schumacher OP, Gupta M. Treatment of Childhood Graves' disease: a review with emphasis on radioiodine treatment. *Cleve Clin J Med*,1988;55:373-382.
14. Clark JD, Gelfand MJ, Elgazzar AH. Iodine-131 therapy of hyperthyroidism in pediatric patients. *J Nucl Med*,1995;36:442-445.
15. Freitas JE, Swanson DP, Gross MD, Sisson JC. Iodine131-I: optimal therapy for thyroidism in children and adolescents? *J Nucl Med*,1979;20:847-850.
16. Levy WJ, Schumacher OP, Gupta M. Treatment of Childhood Graves' disease. A review with emphasis on, radioiodine Etreatment. *Cleve Clin J Med*,1988;55:373-38.
17. Birrell G, Cheetham T. Juvenile thyrotoxicosis; can we do better?. *Archives of disease in childhood*,2004;89(8):745-50.
18. Rivkees SA, Dinauer C. An optimal treatment for pediatric Graves' disease is radioiodine. *J Clin Endocrinol Metab*,2007;92:797-800.
19. Pinto T, Cummings EA, Barnes D, Salisbury S. Clinical course of pediatric and adolescent Graves' disease treated with radioactive iodine. *J Pediatr Endocrinol Metab*,2007;20:973-980.
20. Rivkees SA, Sklar C, Freemark M. Clinical review99: The management of Graves' disease in children, with special emphasis on radioiodine treatment. *J Clin Endocrinol Metab*,1998;83:3767-3776.
21. Rivkees SA, Cornelius EA. Influence of iodine-131dose on the outcome of hyperthyroidism in children. *Pediatrics*,2003;111:745-749.
22. Hernandez-Jimenez S, Pachon-Burgos A, Aguilar-Salinas CA, Andrade V, Reynoso R, Rios A, Reza-Albarran AA, Mehta R, Gonzalez-Trevino O, Gomez-Perez FJ, Perez-Enriquezi B, Rull JA. Radio iodin etreatment in auto immunehy perthyroidism: analysis of outcomes in relation to dosage. *Arch Med Res*,2007;38:185-189.
23. Nebesio TD, Siddiqui AR, Pescovitz OH, Eugster EA. Timecourse to hypothyroid is m after fixed-doseradioablationtherapy of Graves' disease in children. *J Pediatr*,2002;141:99-103.
24. Rivkees SA. Pediatric Graves' disease: controversies in management. *Hormone research in paediatrics*,2010;74(5):305-11.

25. McCormack S, Mitchell DM, Woo M, Levitsky LL, Ross DS, Misra M. Radioactive iodine for hyperthyroidism in children and adolescents: referral rate and response to treatment. *Clin Endocrinol (Oxf)*,2009;71:884-891.
26. Peters H, Fischer C, Bogner U, Reiners C, Schleusener H. Reduction in thyroid volume after radioiodine therapy of Graves' hyperthyroidism: results of a prospective, randomized, multicentre study. *Eur J Clin Invest*,1996;26:59-63.
27. Franklyn JA, Boelaert K. Thyrotoxicosis. *Lancet*,2012;379:1155-1166.
28. Read CH Jr, Tansey MJ, Menda Y. A 36-year retrospective analysis of the efficacy and safety of radioactive iodine in treating young Graves' patients. *J Clin Endocrinol Metab*,2004;89:4229-4233.
29. Boelaert K, Syed AA, Manji N, Sheppard MC, Holder RL, Gough SC, Franklyn JA. Prediction of cure and risk of hypothyroidism in patients receiving ¹³¹I for hyperthyroidism. *Clin Endocrinol (Oxf)*,2009;70:129-138.