Outcome of thyrotoxicosis treatment with 3 different modalities

Faiza A. Qari, FRCP, ABIM, *Tariq A. Naser,* ABIM, *Ibrahim M. Hashim,* FRCP, PhD, *Gerald J. Tevaarwerk,* BA, MD.

ABSTRACT

Objective: To assess the efficacy of 3 different treatment modalities for thyrotoxicosis and a comparison of their cost effectiveness.

Methods: The case records of 100 patients treated for thyrotoxicosis at King Khalid National Guard Hospital in Jeddah were reviewed, during the period January 1992 through to January 2000. Their various treatments and responses were recorded as well as their thyriometabolic status, one year following the last treatment. The treatment consisted of an average of 9 months of antithyroid medication, thyroidectomy or treatment with radioactive iodide. Cure was defined as a patient being euthyroid or hypothyroid for a minimum period of at least one year. Cost-effectiveness was calculated as the total cost of treating the patient in a specific treatment modality, divided by those who were considered to be cured.

Results: For the remainder, the cost could not be definitively determined. The mean age was 41±15.7 years, with female to male ratio of 6:1. Grave's disease was the underlying cause in 76% of cases, toxic multinodular goiter in 13% and toxic nodule in 1%. Ninety-one patients, who were treated with anti-thyroid medication for an average of 9 months, had a success rate of 11%. The success rate with surgery was 54.5%, while of 68 patients treated with radioactive iodide 65 (96%) were cured. Radioactive iodide was the most cost effective modality of treatment costing 1700 Saudi Riyals, followed by surgery at 40,000 Saudi Riyals. Medical treatment was the most expensive at 135,000 Saudi Riyals per cure.

Conclusion: A treatment of thyrotoxicosis with radioactive iodine is much more efficacious than medical or surgical modalities. Furthermore, it is by far the most cost effective and has no harmful effects.

Keywords: Thyrotoxicosis, hyperthyroidism, grave's disease, radioiodine treatment.

Saudi Med J 2001; Vol. 22 (10): 907-909

Hyperthyroidism is a common endocrine disorder worldwide, with a prevalence of 2 in 1000 in iodine sufficient areas.[1] Several different disorders can cause hyperthyroidism.[2] The most frequent cause is Grave's disease, an autoimmune disorder characterized by diffuse enlargement of the thyroid gland, sometimes associated with exophthalmopathy. Radioactive iodide (RAI) has been used to treat hyperthyroidism for the last 50 years. The efficacy, safety and low cost of this therapy have made this the preferred definitive treatment in most patients with this disorder. We report a series of 100 patients with hyperthyroidism, the aetiology and clinical manifestations, and the efficacy and cost effectiveness of different modalities of treatment as observed at the King Khalid National Guard Hospital, Jeddah, Kingdom of Saudi Arabia.

Methods. *Patients.* The case records of 100 thyrotoxic patients consecutively treated at the King Khalid National Guard Hospital were reviewed,

From the Department of Medicine (Naser & Tevaarwerk), Clinical Biochemistry (Hashim), King Khalid National Guard Hospital, and the Department of Medicine (Endocrinology & Metabolism) (Qari), King Khalid Abdulaziz Medical College, Jeddah, Kingdom of Saudi Arabia.

Received 23rd December 2000. Accepted for publication in final form 7th April 2001.

Address correspondence and reprint request to: Dr. Faiza A. Qari, Assistant Professor, Department of Medicine (Endocrinology & Metabolism), King Khalid Abdulaziz Medical College, PO Box 13042, Jeddah 21943, Kingdom of Saudi Arabia. Fax. +966 (2) 6743781. E-mail: karifaiza@hotmail.com

during the period January 1992 through to January 2000. The patients were Saudis. All patients were subjected to a full history and physical examination, including a detailed examination of the thyroid gland. All patients had thyroid function tests, free of T4, free of T3, thyroid stimulating hormone (TSH), which were carried out by radioimmunassay method using commercial kits. Relevant data such as the patients age, sex, cause of thyrotoxicosis (Grave's disease, toxic multinodular goiter, toxic adenoma, sub-acute thyroiditis or other), which depends on clinical presentation, thyroid scan, and ultrasound of goiter and thyroid antibodies, antimicrosomal and antithyroglobulin antibodies. The mode of therapy medical, subtotal thyroidectomy, radioactive iodide was reported as medical with antithyroid medications for at least 9 months duration. Outcome of treatment was noted. Unsuccessful treatment was defined as a recurrence (relapse) of thyrotoxicosis within one year of the end of the previous treatment. A patient was considered cured if euthyroid, or hypothyroid requiring replacement therapy, for more than one year after the cessation of the last treatment.

Statistical Analysis. Treatment success rates were compared statistically using the Chi-square test. Cost effectiveness was calculated by adding the total cost of the treatment per patient, the time spent in hospital and the time lost at work for all patients treated by one of the modalities, divided by the number of patients that were considered to be cured.

Results. The mean age was 41±15.7 years, with a female to male ratio of 86:14 (6:1). Out of the 100 patients 76% had Grave's disease, 13% had toxic multinodular goiter and others T3 toxicosis, toxic adenoma and persistent postpartum thyrotoxicosis occurred in 4 patients only. The exact etiology was not evident in 7 patients due to the lack of data. (Table 1). Table 2 shows the symptoms and signs in the patients studied. Atrial fibrillation was the main clinical presentation in 11 patients, 80% of them were above 50 years of age. The mean FT4 was 42±21.7 μmol/L (normal range, 9.1-23.8 μmol/L) and FT3 was 18.9±11.7 μmol/L (normal range 2.3-6.3 μmol/L). Out of the 91 patients treated medically 10, 11% were in remission for more than one year after the cessation of treatment, while 81 patients 89% relapsed and were given an alternate treatment. This can be explained due to poor compliance on medical treatment for 9 months duration. Eighty-one patients received RAI treatment, and 20 were subjected to surgery. Twenty-two patients underwent sub-total thyroidectomy or near total thyroidectomy for a big goiter with pressure symptoms or failure of medical therapy. Of those treated with thyroidectomy 12 of them (54.5%) were in remission, whereas 10 (45%) had a relapse and needed secondary treatment

Table 1 - Causes of thyrotoxicosis.

Causes	n of cases	%
Grave's disease	76	(76)
Toxic multinodular goiter	13	(13)
No cause	7	(7)
Others	4	(4)
Total	**100**	**(100)**

n=number

Table 2 - Clinical manifestation of 100 patients with thyrotoxicosis.

Symptom	Cases	%	Signs	Cases	%
Palpitation	81	(81)	Diffuse goiter	76	(76)
Tremor	72	(72)	Multinodular goiter	13	(13)
Weight loss	72	(72)	Thyroid nodule	1	(1)
Nervousness	66	(66)	Tremor	19	(19)
Fatigue	45	(45)	Exophthalmous	38	(38)
Heat Intolerance	33	(33)	Lid lag	40	(40)
Increased appetite	12	(12)	Lid retraction	33	(33)
Dyspnea	7	(7)	Ophthalmoplegia	14	(14)
Irregular period	6	(6)	Atrial fibrillation	11	(11)
Diarrhea	3	(3)			
Proximal myopathy	3	(3)			
Thyroid storm	1	(1)			

Table 3 - Outcome of the 3 different treatments of hyperthyroidism.

Modality treatment	n of patients	n of patients in remission	%	n of patients in relapse	%	Cost per patient
Medical	91	10	(10)	81	(89)	20,400 SR
Surgery	22	12	(54.5)	10	(45)	27,000 SR
Radioactive iodine	68	65	(96)	3	(4)	1,600 SR

n=number, SR=saudi riyal

with radioactive iodine. Sixty-eight patients were treated with radioactive iodine. Seven of them as a first time of treatment, whereas 61 as a second line of treatment for failure of medical or surgical treatment. However 10 patients who received medical treatment initially, lost follow up. From 68 patients who were treated with RAI, 65 (96%) had remission, and only 3 needed second dose of radioactive as the initial dose was small 6 mCi. (Chi Square v radioactive iodine remission is p value 0 .001288) which is significant. (Table 3).

Discussion. Thyrotoxicosis is a common endocrine disorder that predominantly affects females.[1,2] Studies from various parts throughout the Kingdom of Saudi Arabia showed an increase in incidence of hyperthyroidism in females (1.7, 1.4, 3.8).[3,4] Our study showed similar preponderance of the disease in females. Grave's disease is the most frequent cause of hyperthyroidism followed by toxic multinodular goiter, findings similar to other published studies in the Kingdom of Saudi Arabia.[5] Clinical manifestations of hyperthyroidism are similar to those which have been reported by Klein et al.[6] The incidence of atrial fibrillation was higher than other studies and was observed after the age of 50 years, in whom, it was the only clinical presentation.[7-9] Antithyroid drugs, surgery, and radioactive iodine (131-I) are all effective treatments of hyperthyroidism.[10] Radioiodine has been used for almost 40 years.[11] Large follow up studies have failed to reveal any increase in the risk of leukemia or thyroid cancer, nor the potential genetic risk in the treated group. Radioactive iodine treatment is absolute contraindicated during pregnancy.[12] Radioactive iodide treatment has been available at King Khalid National Guard Hospital since 1993. Higher doses of RAI of 15-20 mCi is used to counteract secondary failure associated with a low dose.[13] A major problem encountered with a high-dose radioidine treatment is the rapid onset of hypothyroidism, as demonstrated in previous studies using an approach similar to our study.[14] The other advantage of using radioactive iodine treatment in treating hyperthyroidism is cost effectiveness and the frequent use of medical services. The total cost of surgery alone in the Kingdom is about 20,400 Saudi Riyals (SR), if you add the cost of admission, investigations and follow-up as well as time loss from work of at least one month the total cost will rise to about 40,000 SR. While the cost of medical treatment is 27,000 SR. The success of medical treatment is one in 5, so the total cost will be 135,000 SR to have successful treatment in one patient. Radioactive iodide will cost only 1700 SR. As the success rate is 96%, hence it is the most cost effective modality of treatment. (Table 4).

In conclusion, a treatment of thyrotoxicosis with radioactive iodine is much more efficacious than medical or surgical modalities. Furthermore, it is by far the most cost-effective and has no harmful effects. Permanent hypothyroidism occurs earlier and is much more common with this modality. However, treatment of hypothyroidism is highly effective, easy and inexpensive. Most patients would eventually go on to hypothyroidism regardless of the modality of treatment. For it to occur early has the added benefit of ensuring that it is treated when it occurs. In society where medical care is still in the devolving phase in some area the chance of treatment being delayed is significant. Based on these considerations we recommend hat radioactive iodine treatment be the first modality for thyrotoxicosis.

References

1. Leary AC, Grealy G, Higgins TM, Buckley N, Barrey DG, Murphy D et al. Long-term outcomes of treatment of hyperthyroidism in Ireland. Ir J Med Sci 1999; 168: 47-52.
2. Klein I, Becker DV, Levey GS. Treatment of hyperthyroid disease. Annals of Internal Medicine 1994; 121: 281-288.
3. Johansen K, Khan M, Nicholas JY, Woodhouse JA. High-dose iodine 131 treatment of hyperthyroidism: Experience at King Faisal Specialist Hospital and research center. Annals of Saudi Medicine 1988; 6: 466-469.
4. Akaber D, Mushtag M, AL-Sheikh A. Etiology and outcome of thyrotoxicosis at a university hospital. Saudi Med J 2000; 21: 352-354.
5. Sulimani R, Mekki M, Rohinivislam V, Subesinghe N. Thyrotoxiosis: experience from the King Khalid university hospital, Riyadh. Annals of Saudi Medicine 1989; 5: 455-457.
6. Klein I, Trzepacz P, Roberts M, Levey GS. Symptoms rating scale for assessing hyperthyroidism. Arch Intern Med 1988; 148: 387-390.
7. Spaulding SW, Lippes H. Hyperthyroidism: causes, clinical features and diagnosis, Med Clin North Am 1985; 69: 93-96.
8. Halnan K. Radio-iodine treatment of hyperthyroidism a more liberal policy? Clinical Endocrine Metabolism Journal 1985; 14: 476-489.
9. Scott GR, Forfar JC, Toft AD. Grave's disease and atrial fibrillation: the case for even higher doses of therapeutic iodine 131. Br Med J 1984; 289: 399-400.
10. Becker DV. Choice of therapy for Grave's hyperthyroidism, editorial. N Engl J Med 1984; 311: 464-466.
11. Kendall-Tyylor P, Keir MJ, Ross WM. Ablative radio iodine therapy for hyperthyroidism: long term follow up study. Br Med J 1984; 289: 361-363.
12. Nordyke RA, Gillbert FI, Jarada AM. Grave's disease Influence of age on clinical findings. Archive in Internal Medicine Journal 1998; 148: 626-631.
13. Lind P, Langsteger W, Molnar M, Gallowitsh HJ, Mikosch P, Gomez I. Epidemiology of thyroid disease in iodine sufficiency. Thyroid 1998; 8: 1179-1183.
14. Gossage AA, Munro DS. The pathogenesis of Graves disease. Clinical Endocrine Metabolism Journal 1985; 14: