SUBTOTAL THYROIDECTOMY IN THE MANAGEMENT OF GRAVE'S DISEASE

Col PJ VINCENT^{*}, Lt Col MK GARG⁺,
Brig Y SINGH[#] VSM, Wg Cdr VP BHALLA^{**},
Sqn Ldr SGS DATTA⁺⁺

Abstract

Treatment options for Grave's disease include radio-iodine ablation, which is the standard treatment in the USA, antithyroid drug therapy, which is popular in Japan, and surgery, which is commonly employed in Europe and India. There are very few reports about the outcome of surgery in Grave's disease in the Indian setting. Surgery for Grave's disease is an attractive option in under developed countries to cut short prolonged drug treatment, costly follow up and avoid the need for radio-isotope facilities for 1311 ablation. Aim of the present study was to assess the result of subtotal thyroidectomy in 32 cases of Grave's Disease referred for surgery by the endocrinologist in a teaching hospital. Patients were prepared for surgery with Lugol's iodine and propranolol. Subtotal thyroidectomy was performed by a standard technique, which included dissection and exposure of recurrent laryngeal nerves and parathyroid glands. Actual estimation of weight of the remnant gland was not part of the study. Duration of follow up ranged from 6 months to 4 years. 13 of 32 cases were males. Age ranged from 20 to 57 years. There was 1 death in the immediate post-operative period. There were no cases of permanent hypoparathyroidism or recurrent laryngeal nerve palsy. 1 patient developed temporary hypoparathyroidism. 1 patient developed recurrence of hyperthyroidism and 3 cases developed hypothyroidism all within 2 years of surgery. The study has demonstrated the safety and effectiveness of surgery for Grave's Disease in comparison to the reported high incidence of hypothyroidism following radio-iodine therapy and high recurrence rate after anti thyroid drug therapy.

MJAFI 2001; 57 : 203-206

Key Words :Grave's Disease; Thyroidectomy.

Introduction

Grave's disease is perhaps the only autoimmune disease associated with hyperplasia and hyperfunction of the target tissue. This disease is currently thought to result from a specific genetic defect in immunologic surveillance. This permits a 'forbidden clone' of a thyroid directed lymphocytes to survive, interact with antigens on thyroid cell membrane and produce a number of thyro-auto-antibodies called TSI (thyroid stimulating immunoglobulin) which cause hyperthyroidism [1].

Radio-iodine therapy has become the treatment of choice in most of the centres in adults because of its simplicity, safety and low cost. It has been used for the last 50 years and it can be considered as the therapy for nearly all patients except newborns and pregnant females. However there is still reluctance to use it in children and women of childbearing age. It is unsuitable for large goitres. Moreover, the reported rate of post treatment hypothyroidism is as high as 80% [2].

In India where patient compliance is low, follow up

difficult and radio-isotope facilities undeveloped; surgery is a better option for Grave's Disease. Advantages of surgery in Grave's disease are that it can be done safely and it is associated with low incidence of recurrence, which is difficult to treat. Euthyroid state can be achieved in up to 95% of cases and the control of hyperthyroidism is immediate unlike in other modalities. Long and costly follow up is not required and surgery in experienced hands is attended by very few complications and practically zero mortality. In fact, the trend now is to do total or near total thyroidectomy for Grave's Disease instead of subtotal thyroidectomy. In Armed Forces radio-isotope facilities are available in only few centres and surgery is the usual option when drug therapy fails. The present study was conducted on patients referred for surgery by the endocrinologist for various reasons.

Material and Methods

37 patients of Grave's Disease underwent subtotal thyroidectomy in a large teaching hospital between 1994 and 1999. These patients were referred to the surgeon by the endocrinologist after various periods of antithyroid drug treatment and radio-iodine therapy. 32 of these patients who could be followed up for various

^{*}Associate Professor (Surgery), Armed Forces Medical College, Pune - 411 040, ⁺Classified Specialist (Medicine) and Endocrinologist, Command Hospital, (Southern Command) Pune - 411 040, [#]Consultant and Head, Department of Surgery, Armed Forces Medical College, Pune-411 040, ^{**}Classified Specialist (Surgery and GI Surgery), Command Hospital (Air Force), Bangalore, ⁺⁺Graded Specialist (Surgery), 7 Air Force Hospital, Kanpur.

periods up to 4 years constituted the subjects of this study (follow up rate of 86.5%; range of follow up : 6 months to 4 years; median follow up : 26 months). Patients were taken up for subtotal thyroidectomy after being made euthyroid with antithyroid drugs. Lugol's iodine was administered for 10 days preoperatively and tablet propranolol for 5 days preoperatively continuing into the post-op period. Pre-op evaluation included goitre size, indirect laryngoscopy, estimation of T3, T4, TSH and FNAC of the goitre.

Operation Technique

Bilateral subtotal thyroidectomy was performed by a standard technique under endotracheal anaesthesia. The recurrent laryngeal nerves were demonstrated. The parathyroid glands were identified and safeguarded. The branches of the inferior thyroid artery were ligated and cut close to the thyroid gland; the main trunk of the artery was spared, thus safeguarding the blood supply to the parathyroid glands. Thyroid remnant of about 6gms was left behind though actual estimation of the remnant was not part of the study. Post op follow up was done at intervals of 1 month, 3 months, 6 months, 9 months, 1 year and there after at yearly intervals.

Evaluation of Thyroid Function

Pre and postoperative thyroid function was evaluated by estimation of T3, T4 and TSH by radioimmunoassay. The kits used were :

Hormone	Kit	Normal values
T3	RIAK-4	0.8 to 2.2 ng/ml
T4	RIAK-5	5.5 to 13.5 mg/ml
TSH	IRMA-9	0.5 to 6.5 m.u/ml

Patients were divided into three groups according to their TSH levels after surgery.

1. Patients with suppressed TSH levels indicating recurrence of hyperthyroidism.
2. Patients with normal TSH were the euthyroid group.
3. Patients with elevated TSH were the hypothyroid group.

Levels of T3 and T4 were examined simultaneously to exclude errors and corroborating the thyroid status. Indirect laryngoscopy was done one-month post operatively.

Results

13 out of 32 cases were male. Age ranged from 20 to 57 years (Table-1). Period of anti thyroid drug therapy prior to surgery ranged between 1-4 years (Table-2). Reason for surgery was failure of antithyroid drug therapy in the majority of cases but there were also other reasons for surgical referral (Table-3).

Surgical Complications

Death	- 1
Temporary hypoparathyroidism	- 1
Permanent hypoparathyroidism	- nil
Recurrent laryngeal nerve palsy	- nil
Wound haematoma	- nil
Wound infection	- 1

Outcome of Surgery

According to the hormonal evaluation criteria there was 1 case of recurrent hyperthyroidism (TSH level :0.2 m.u/ml) (3.1%) and 3 cases of hypothyroidism (9.4%). TSH levels of the 3 cases labelled as hypothyroidism were 18.5 m.u/ml, 11.4 m.u/ml and 13.8 m.u/ml. The rest of the cases remained euthyroid after surgery (87.5%). The only instance of recurrence occurred within 6

TABLE 1

Reasons for surgery

	No.	Percentage
Failure of anti thyroid drugs	23	71.87
Large size goitre	4	12.50
Patient's choice	2	6.25
Adverse effect of drug therapy	1	3.12
Failure of radio-iodine	2	6.25

TABLE 2

Complications of subtotal thyroidectomy

Series	Hypoparathyroidism (%)	Recurrent laryngeal nerve palsy.(%)
Linos DA [6]	1.6	1.6
Razack MS [7]	1.4	1.4
Campana FP [9]	2.5	3.8
Shaha AR [11]	0.5	0.5
Present series	3.13	0

TABLE 3

Outcome of surgery : Hypothyroidism and recurrence

Series	Total no. of patients optd	Hypothyroidism (%)	Recurrence (%)
Nicolsi A [14]	70	31	31
Chiu MT [15]	41	8	8
Kasuaga [16]	179	16.5	-
Kiminori [12]	728	-	14.6
Torrango [13]	179	-	5.5
Present series	32	9.4	3.1

months after surgery. 1 case of postoperative hypothyroidism was detected within 9 months and the other 2 cases within 2 years after surgery.

Discussion

The large number of male patients (M:F=13:19) in this study was due to the predominant military population under treatment. The reported male:female ratio for Grave's Disease in the general population is 2:9 [2].

Treatment of Grave's Disease continues to be highly controversial. Radio-iodine therapy is the treatment of choice in many centres especially in the United States [3]. An opinion survey conducted among members of Japan Thyroid Association in 1997 revealed that antithyroid drug therapy is the treatment of choice among 98.6% of the members [4]. However, surgery in Grave's Disease is still the primary and preferred modality of treatment in many institutions [5-9].

Aim of this study was to assess the safety and efficacy of subtotal thyroidectomy for Grave's Disease.

Advantages of surgical treatment of Grave's Disease are that it can be done safely and is associated with a low incidence of recurrence. We prepare the patients with Lugol's iodine to reduce vascularity. This is the current trend advocated by Vittal S [10]. Sparing the main trunk and ligating only the branches of the inferior thyroid artery close to the gland preserves the blood supply of the parathyroid gland [11]. By using this technique only 1 patient developed temporary hypoparathyroidism and none developed permanent hypoparathyroidism. This is comparable to results of published series [7,8,12,13] (Table-2). 1 death in this series occurred in the immediate postoperative period; the only positive finding was hyperkalaemia and it was probably not related to thyroid surgery itself.

The main goal of surgery is to avoid recurrence of hyperthyroidism and to achieve this the remnant size should be extremely small. At the same time, the smaller the remnant higher the incidence of hypothyroidism. In our cases the size of the remnant, though not weighed, was sought to be kept at about 6 gm resulting in a recurrence rate of 3.1% and hypothyroidism in 9.3% of cases. This is well within the range reported in literature [14-18] (Table-3). If the aim of surgery is a long standing euthyroid state an adequate thyroid remnant should be left in place. Many reports regarding factors related to post operative thyroid dysfunction have been published. Endocrine surgeons need to know which patients need to retain a small or large thyroid remnant. A useful guideline for the surgeon to avoid recurrence is provided by high preoperative levels of TBH (TSH inhibitory immunoglobulin) and MCHA (antimicrosomal antibody measured by haemagglutination assay). If these levels are high a small remnant less than 4 gm will prevent recurrence [14].

In contradiction to gradual, progressive and cumulative increase in the incidence of post treatment hypothyroidism following radio-iodine therapy, the vast majority of cases of hypothyroidism developing after subtotal thyroidectomy occur within the first 6-12 months [19]. This early onset is cited as a definite advantage of surgery. This was so in our cases. Also, 70% of cases of postoperative hypothyroidism after surgery are temporary with thyroid function returning to normal 6 to 12 months after surgery [20]. However, our cases did not display this pattern.

The current trend in surgery for Grave's disease is total or near-total thyroidectomy as opposed to subtotal thyroidectomy [6-9,12]. This has led to renewed interest in surgery, as recurrent hyperthyroidism can be totally eliminated. This radical surgery is not suit-

able for Indian patients as it will result in permanent hypothyroidism and life long hormone replacement therapy and follow up. For similar reasons radio-iodine therapy is not the ideal choice in our country. Radio-iodine therapy also aggravates ophthalmopathy of Grave's Disease [5]. 2 patients in our study had opted for surgery in lieu of radio-iodine therapy by own choice.

In conclusion it can be stated that subtotal thyroidectomy is an attractive option for treatment of Grave's Disease. It is safe, quick, effective and results in acceptable rates of recurrence and hypothyroidism. It is especially suited for a developing country like India.

References

1. Rappoport B, Greenspan FS, Filltti S. Clinical experience with a human thyroid bio-assay for thyroid stimulating immunoglobulin. *J Clin Endocrinol Metab* 1984;58:332-8.
2. Lysterly HK. Hyperthyroidism. In Sabiston DC, Lysterly HK, editors. *Textbook of Surgery The biological basis of modern surgical practice*. 15thed. Philadelphia : WB Saunders Co. 1996;611-21.
3. Robert DU. The Thyroid: physiology, hypothyroidism, thyrotoxicosis and painful thyroid. In Philip F, John DB, Lawrence AF, editors. *Endocrinology and metabolism*, 3rd ed. New York: McGraw-Hill Inc., 1995;435-519.
4. Mori T, Sugawa H, Kosugi S, Ueda M, Hai N, Matsuda A. Recent trends in the management of Grave's hyperthyroidism in Japan. *Endocr J* 1997;44(4):509-17.
5. Abe Y, Sato H, Noguchi M, Mimura T, Sugino K, Ozaki O, Yoshimura H, Ito K. Effect of subtotal thyroidectomy on natural history of ophthalmopathy in Grave's Disease. *World J Surg* 1998;22(7):714-7.
6. Linos DA, Karakitsosis D, Papademetriou J. Should the primary treatment of thyrotoxicosis be surgical? *Eur J Surg* 1997;163(9):651-7.
7. Razack MS, Lore JM, Lippes HA, Schaefer DP, Rassael H. Total thyroidectomy for Grave's Disease. *Head Neck*. 1997;19(5):378-83.
8. Vittal S. Thyrotoxicosis : a brief review. In Roshan Lall Gupta editor. *Recent Advances in Surgery*. 5th ed. New Delhi: Jaypee Brothers, 1996;272-9.
9. Campana FP, Marchesi M, Biffoni M, Tartaglia F, Nuccio G, Stocco F et al. Total thyroidectomy technique: suggestions and proposals in surgical practice. *Ann Ital Chir* 1996;67(5):627-35.
10. Piccolo P, Vitti P, Rago T, Iacconi P, Bartalena L, Bogazzi F. et al. Surgical treatment of Grave's Disease: subtotal or total thyroidectomy? *Surgery*. 1996;120(6):1020-4.
11. Saha AR, Jaffe BM. Parathyroid preservation during thyroid surgery. *Am J Otolaryngol*. 1998;19(2):113-7.
12. Kimimori S, Takashi M, Osamu O, Yoshio K, Hiroyuki I, Nobuyuki W et al. Early recurrence of hyperthyroidism in patients with Grave's Disease treated by subtotal thyroidectomy. *World J Surg* 1995;19:648-52.

13. Torring O, Tollstedt L, Wallin G, Lundell G, Ljunggren JG, Taube A et al. *J Clin Endocrinol Metab.* 1996;81(8):2986-93.
14. Nicolsi A, Meluddu C, Meleddu G, Masidda B, Calo PG, Pinna M et al. Current trends in the treatment of Grave's Disease. *Minerva Chir.* 1995;50:659-65.
15. Chiu MT, Soon PC, Ng BK. Selection for patients for surgery in the management of thyrotoxicosis. *Ann Acad Med Singapore.* 1993;22(4):553-6.
16. Kasuga Y, Kobayashi S, Fujimori M, Shingu K, Asanuma K, Hama Y et al. Changes in thyroid function and immunological parameters long after subtotal thyroidectomy for Grave's Disease. *Eur J Surg* 1998;164(3):173-8.
17. Anthony JE, Clove SG, Richard HE. editors. *Surgery of the thyroid.* In *Manual of endocrine surgery.* 2nded. New York. Springer-Verlag 1984;71-150.
18. Toft AR, Irvine WJ, Mc Intosh D. Temporary hypothyroidism after surgical treatment of Grave's Disease. *Lancet* 1976;2:1135-6.
19. Wilkin TJ, Gunn A, Isles TE. Short-term tri-iodothyronine in prevention of temporary hypothyroidism after subtotal thyroidectomy for Grave's Disease. *Lancet* 1979;2:63-6.
20. Gittoes NJ, Franklyn JA. Hyperthyroidism:current treatment guidelines. *Drugs* 1998;55(4):543-53.

NOTICE

MJAFI is despatched to all officers of AMC and AD Corps (except the non technical officers) as per the addresses and nominal roll forwarded by the units. If you or any officers known to you are not receiving the Journal regularly, please forward their names and address as per format given below for inclusion in the mailing list,

Personal no.	Rank	Name in full (as per Army list)	Appointment (speciality)	Previous unit	Present address with PIN
-----------------	------	------------------------------------	-----------------------------	---------------	-----------------------------