Propranolol in the Surgical Management of Thyrotoxicosis

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Forty-nine thyrotoxic patients prepared for partial thyroidectomy with the β-adrenoceptor blocking drug, propranolol, and iodine are compared with 42 patients prepared with carbimazole and iodine. The age and sex distribution of the two groups were comparable, but patients with obstructive airways disease and possible cardiac insufficiency were excluded from preparation with propranolol. The mean duration of preoperative treatment with propranolol was 40 days, compared with 89 days for carbimazole. Propranolol treated patients had lower pulse rates before and after operation. The serum PB^{127}I values immediately before and after operation were higher in the propranolol group than in the carbimazole group, but were the same in both groups one and four months after operation. The incidence of hypothyroidism at one year after operation was 30% in the carbimazole prepared patients and 31% in the propranolol patients. Serum calcium levels were higher in the propranolol group at the time of operation. No adverse effects from the use of propranolol and at operation the thyroid gland prepared with propranolol was firmer, less friable, more easily mobilised and less likely to bleed than the gland prepared with carbimazole. There is, consequently, less risk of damage to the parathyroid glands and recurrent laryngeal nerves. However, the basal metabolic rate remains high on propranolol therapy and very careful supervision is advised.

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INITIAL ATTEMPTS at producing sympathetic blockade in the management of thyrotoxicosis were surgical[2,5] but recently various pharmacological agents, including reserpine,[1] guanethidine[12] and alpha-methyldopa,[11] have been introduced in an attempt to reduce the excessive adrenergic activity which contributes to the clinical features of this condition. Following the introduction of propranolol, beta-adrenoceptor blockade has been shown to modify many of the features of thyrotoxicosis, and though the place of beta-blockade in the management of this condition has not yet been clearly defined, propranolol is used successfully in the treatment of thyroid crisis[9] and as an adjuvant to radio-iodine therapy.[3]

Patients with thyrotoxicosis are usually prepared for surgery with conventional thiourea derivates but recently Lee *et al.*[6] have described their experience with propranolol in this situation. The mechanisms of action of these drugs are dissimilar and it is unlikely that either influences the natural history of the disease.[7] In this paper we compare the use of these drugs in the preparation of thyrotoxic patients for surgery and try to determine whether patients prepared with propranolol differ in any respect before, during or after operation from those prepared with carbimazole.

Patients and Methods

In a study commencing in July 1970, 132 patients underwent thyroidectomy for thyrotoxicosis. Our usual method of preoperative preparation was to make the patient euthyroid with carbimazole and then give iodine for up to ten days before operation. In our early experience with propranolol, this drug was prescribed in addition to carbimazole before operation, but with increasing knowledge of the effects of β-blockade in this situation, it eventually became possible to omit carbimazole

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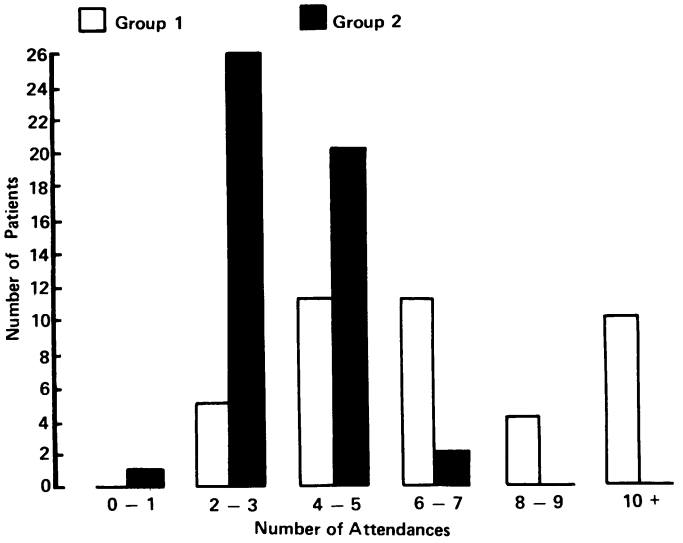

FIG. 1. The number of out-patient visits by patients prepared for thyroidectomy with carbimazole (Group 1) and with propranolol (Group 2).

therapy. Apart from excluding patients with possible cardiac or obstructive airways disease from propranolol treatment, no attempt was made to select patients for any particular preoperative regime. Forty-one patients had combined therapy with carbimazole and propranolol and are not discussed further. Forty-two patients (seven men) were prepared with carbimazole (Group 1) and 49 patients (seven men) with propranolol (Group 2). The age range of the patients prepared with carbimazole was 15–60 years. Six patients were 20 years old or less and three were 50 years or older. In the propranolol group, the age range was 15–64 years. Six patients were aged 20 years or less and five were 50 years or more. All were given iodine preoperatively for periods varying between three and ten days. Patients in Group 1 received varying doses of carbimazole and in each case the dose was the minimum necessary to make the patient clinically and biochemically euthyroid. The initial dose was 40 mg or 60 mg daily given in four divided doses. The maintenance dose before operation varied from 2.5 mg twice daily to 5 mg thrice daily. The total daily dose of propranolol, except for two patients, was 120 mg daily given as 40 mg eight-hourly. The two remaining patients were prescribed 40 mg six-hourly, and we have continued to use this latter dose for subsequent patients.

TABLE 1. *Mean Pulse Rates in Thyrotoxic Patients Undergoing Partial Thyroidectomy*
(Means ± S.E.M.)

	Beginning of Operation	End of Operation	24 Hours	48 Hours
Group 1 (Carbimazole)	81 ± 2	80 ± 2	89 ± 2	90 ± 2
Group 2 (Propranolol)	70 ± 1	73 ± 1	81 ± 1	80 ± 1

TABLE 2. *Average Blood Pressures in Thyrotoxic Patients Undergoing Partial Thyroidectomy*
(Means ± S.E.M.)

		Beginning of Operation	End of Operation
Group 1 (Carbimazole)	Systolic	130 ± 3	126 ± 3
	Diastolic	78 ± 2	78 ± 1
Group 2 (Propranolol)	Systolic	128 ± 3	118 ± 3
	Diastolic	76 ± 2	78 ± 2

Preoperative medication was with omnopon and either scopolamine or atropine, and atropine was also given intraoperatively if the anaesthetist considered that the pulse rate was falling unduly. Approximately 15 minutes before operation 8–12 ml of lignocaine (0.5%) containing adrenaline (1:200,000) were infiltrated into the wound area to reduce bleeding. Anaesthesia was maintained with halothane, nitrous oxide and oxygen. The pulse rate was measured four-hourly from 24 hours before operation until the time of discharge and hourly for 24 hours after operation. Blood pressure was recorded on admission, at the beginning, during and at the end of operation, and thereafter until the pressure had stabilised. A record was kept of total gland mass, which was calculated from the measured weight of resected thyroid tissue and remnant weight estimated during operation.[4]

Serum levels of protein bound iodine ($PB^{127}I$), calcium, alkaline phosphatase and proteins were estimated at the patient's first appearance, during drug therapy, immediately before and after operation, at 24 and 48 hours, and at one month and four months after operation.

Where propranolol was used in preoperative preparation, the patients early in the series were retained for an extra day, but later we reverted to our customary practice of discharge on the second or third day after operation. Propranolol therapy was maintained until the seventh postoperative day.

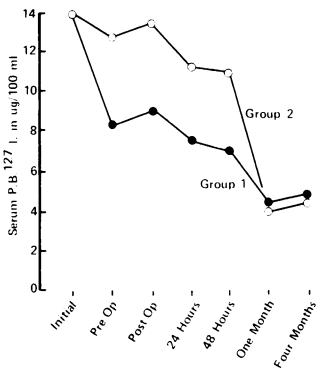

FIG. 2. The serum $PB^{127}I$ values in patients prepared for thyroidectomy with carbimazole (Group 1) and with propranolol (Group 2).

Results

The mean duration of treatment was 40 days for patients prepared with propranolol compared with 89 with carbimazole. The number of outpatient attendances from initial visit to the time of operation is given in Fig. 1.

At the beginning of operation, the mean pulse rate in Group 2 was significantly lower than in Group 1 ($p < 0.001$). The propranolol treated patients had also significantly lower pulse rates at 24 hours ($p < 0.005$) and 48 hours ($p < 0.001$) after operation (Table 1). Average systolic and diastolic blood pressures at the beginning and end of operation were similar in both groups, although the systolic pressure at the end of operation was lower in Group 2 ($p < 0.05$) than in Group 1 (Table 2).

The mean serum $PB^{127}I$ values were the same at the time of initial examination (Fig. 2) but were significantly higher ($p < 0.001$) in the propranolol prepared patients immediately pre- and postoperatively and at 24 and 48 hours after operation. At one month and four months after operation, there were no significant differences.

Serum calcium levels corrected for serum protein concentration were similar when the patients were first seen (Fig. 3), but were higher in the propranolol treated patients preoperatively, postoperatively and at 24 hours after operation ($p < 0.001$), and at 48 hours after operation ($p < 0.005$). These differences were not evident at one and four months after operation. In general there appeared to be a parallel reduction in the serum alkaline phosphatase levels in the two groups (Fig. 4) with the exception of the estimation at one month after operation which was higher in patients prepared with propranolol ($p < 0.05$).

Using the criteria we employ for assessing postoperative thyroid status,[8] the incidence of hypothyroidism following operation was 30% in the carbimazole prepared patients and 31% in the propranolol group.

Mean total gland mass was 51.0 g for the carbimazole prepared patients and 50.3 g for the propranolol group.

Discussion

Many of the features of hyperthyroidism are mediated through the autonomic nervous system and the beneficial effects of propranolol are the result of β-adrenoceptor blockade and suppression of those symptoms and signs related to increased sympathetic activity. Propranolol does not interfere with thyroidal iodine uptake, and thyroid hormone synthesis and release are unchanged. This contrasts with the action of carbimazole, which inhibits, at least, the iodide oxidation and organification steps of thyroxine synthesis, leading to reduced production of thyroid hormones.

Our use of propranolol in the preparation of the thyrotoxic patient for surgery has been cautious, and initially we employed it in conjunction with carbimazole. Recognizing the risks of precipitating heart failure and bronchospasm, we were careful to exclude patients with a history of cardiac insufficiency or obstructive airways disease and none of the patients had any significant associated disease. In the event we did not find it necessary to stop propranolol or reduce its dosage because of side effects.

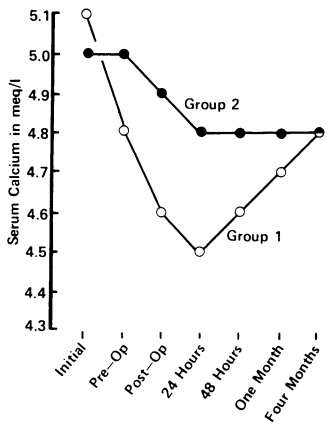

FIG. 3. The serum calcium levels in patients prepared for thyroidectomy with carbimazole (Group 1) and with propranolol (Group 2).

The difference in blood pressure between the two groups was small, but the pulse rate in the propranolol prepared patients was significantly lower both before and after operation. Reduction of pulse rate is of subjective benefit to the thyrotoxic patient, though the absence of reflex tachycardia is a potential hazard if the patient is exposed to shock from any cause. On seven occasions the anaesthetist gave intraoperative atropine as a prophylactic measure, but in no patient has bradycardia or hypotension been a problem.

We have confirmed that patients treated with propranolol were biochemically thyrotoxic at the time of operation. Serum $PB^{127}I$ levels were still elevated at 48 hours after operation, and for this reason propranolol therapy was maintained for the first postoperative week. It is perhaps too early to compare the effect of the two forms of preoperative management on the incidence of postoperative hypothyroidism, but the results at four months after operation indicate that there is no difference between the groups in this respect.

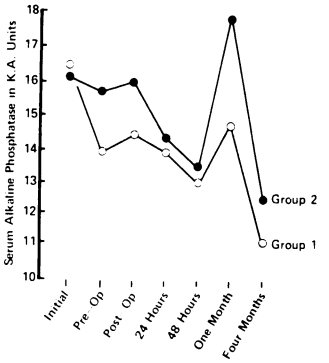

FIG. 4. The serum alkaline phosphatase levels in patients prepared for thyroidectomy with carbimazole (Group 1) and with propranolol (Group 2).

The values for serum calcium and serum alkaline phosphatase are consistent with the bone disease which occurs in thyrotoxicosis, and which is presumed to relate high circulating levels of thyroid hormone. Except for the initial estimation when the patient was first seen, serum calcium values were higher in Group 2 than in Group 1 until 48 hours after operation. We would postulate that whereas thyrotoxic osteodystrophy may heal if the patient is made biochemically euthyroid with carbimazole, it is less likely that healing will occur with propranolol in the dose we have employed. Fears have been expressed that prolonged propranolol therapy might induce a progressive osteodystrophy,[7] and that short term therapy might precipitate dangerous hypocalcaemia.[10] Of the former we have no experience; of the latter we have no evidence.

If a new form of treatment is to merit consideration, it must offer significant advantages over previous methods of treatment. Propranolol administration does not interfere with biochemical or isotopic tests of thyroid activity, and therapy need not be delayed until diagnostic tests are completed. In contrast with carbimazole therapy, where symptomatic relief may not be achieved for several days or weeks, subjective improvement or propranolol may occur within a matter of hours. In this study, the average duration of preoperative therapy with propranolol was 40 days, which was less than half for the carbimazole patients. Latterly preoperative preparation has been reduced in several patients to approximately 14 days, and two patients were operated upon after preparation for five and three days respectively. The number of clinic attendances can be greatly reduced, and when a satisfactory response to propranolol has been confirmed—and this is not unusual at the patient's second visit to the clinic—it is possible to predict and arrange the date of operation.

Technical surgical advantages are difficult to quantify. Though total gland mass was the same in both groups, the thyroid gland prepared with propranolol is of firmer consistence, is less friable and has a reduced risk of tearing when compared with the gland prepared with carbimazole. These differences have been mentioned recently by Lee *et al.*[6] Mobilisation of the gland and resection of the lobes are easier and haemorrhage is less. In consequence there is less risk of interference with the parathyroid glands and recurrent laryngeal nerves. These benefits, added to easier and more rapid control of symptoms, suggest that preparation for partial thyroidectomy with propranolol should be considered in the management of the thyrotoxic patient. However, it should be remembered that propranolol does not affect all the features of hyperthyroidism and in particular has little effect on the basal metabolic rate. Until more information is available we would suggest that this use of propranolol should be carefully supervised.

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