The Use of a Selective Beta-adrenergic Receptor Blocker for the Preoperative Preparation of Thyrotoxic Patients

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Metoprolol, a cardioselective beta-blocker, was used in two asthmatic, thyrotoxic patients in preparation for thyroidectomy. Adequate reduction in resting heart rate was achieved in both individuals without inducing clinically significant airway obstruction. Beta-1-blockade can be selectively employed in this clinical setting, but patients should be hospitalized and closely monitored for adverse effects on pulmonary function. Metoprolol therapy in patients with reversible airway obstruction is discussed with reference to recent studies on relative cardioselectivity.

PROPRANOLOL, A BETA-ADRENERGIC receptor blocking agent, is effective for the preoperative preparation of selected thyrotoxic patients. The systemic manifestations of hyperthyroidism such as tachycardia, tremor, and perspiration can be controlled in a matter of hours. The traditional preoperative management with thionamides and iodine sometimes requires weeks to achieve symptomatic relief and the production of a euthyroid state. It is occasionally unsuccessful. The administration of nonselective beta-adrenergic agents to patients with reversible airway disease has been limited by adverse effects on pulmonary function. Recently, metoprolol, a beta-adrenergic blocker with beta-1-selectivity, has been introduced and shown to have less adverse effect on pulmonary function than propranolol.[1-3] The opportunity recently arose to employ metoprolol in the preoperative preparation of two patients in whom bronchospastic disease complicated the management of their thyrotoxicosis.

Patient Material

Case 1

I.S., a 76-year-old female, was admitted for repair of an acutely incarcerated, symptomatic umbilical hernia. Past medical history included asthma controlled with oral aminophylline. Review of systems revealed a 40-lb weight loss over the preceding six months. Physical examination revealed a 4 by 4 cm firm nodule in the left lobe of the thyroid and a pulse of 120. T3 uptake and T4 were 33.9% and 14.0 ug/dl, respectively. TSH was less than 2.5 uU/ml. A thyroid scan demonstrated a "hot" nodule in the left lobe of the thyroid, and ultrasound examination showed the nodule to be solid. Preoperation preparation consisted of five days of propythiouracil 100 mg tid, saturated iodine solution, and metoprolol 100 mg bid. Pulmonary function studies prior to metoprolol therapy demonstrated small airway obstruction, improved by bronchodilators.

On the day prior to surgery, the patient's pulse rate was 70 per minute, and no wheezing or tachypnea was noted. The patient underwent a left thyroid lobectomy, isthmusectomy, and umbilical herniorrhaphy without complications. The patient was maintained on metoprolol for seven days after operation. Pathology revealed benign colloid nodules with focal residual hyperplasia.

Case 2

Y.G., a 15-year-old girl, presented with complaints of nervousness, heat intolerance, and weight loss. Past medical history revealed asthma since age 4 currently controlled with oral aminophylline. Physical examination revealed exopthalmos, a diffusely enlarged thyroid gland, fine tremors, and a resting pulse of 96. T3 uptake and T4 were 60% and 17.4 ug/dl, respectively. The patient was placed on prophythiouracil (PTU) 450 mg per day in divided doses (Fig. 1). T3 uptake and T4 remained elevated two months later. PTU was increased to 600 mg per day. Three months later thyroid function studies remained elevated, and the patient was symptomatically unchanged. Subtotal thyroidectomy was planned, and the patient was started on saturated iodine solution in addition to PTU. Her resting pulse rate remained 90 per minute. Three days before operation, propranolol was started (60 mg per day in divided doses), but was subsequently withdrawn after wheezing and tachypnea developed. Improvement in her respiratory status was noted after inhalation therapy with beclomethasone dipropionate. Three days later subtotal thyroidectomy was attempted, but upon induction of general anesthesia, her pulse rose to 160. Anesthesia was terminated, and her pulse slowly returned to preoperative levels. Two days later the patient was started on metoprolol 25 mg tid. Resting pulse rate was 90. The following day, metoprolol was increased to 50 mg tid with a subsequent drop in pulse to 76 per minute. No wheezing developed, and her FEV_1 measured 60% of predicted with improvement to 71% with bronchodilators. An uncomplicated subtotal thyroidectomy was performed the next day. Her pulse rate remained below 90 throughout the procedure. The patient was maintained on metoprolol 25 mg tid for five days after operation. Her

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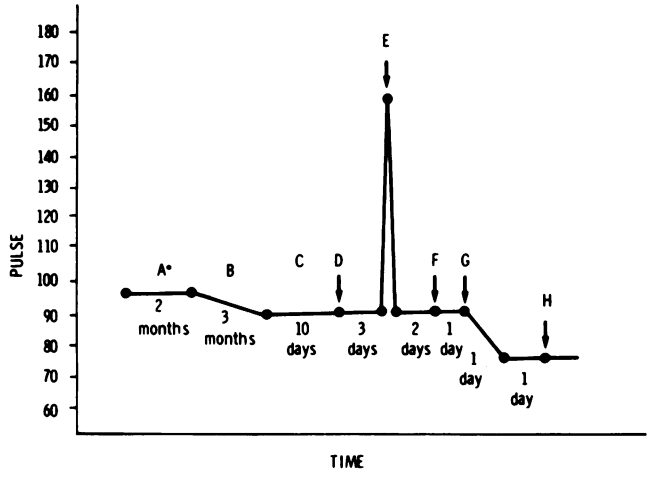

*A. PTU-450 mgm/day (divided doses)
B. PTU-600 mgm/day (divided doses)
C. Saturated iodine added
D. Propanolol-60 mgm/day (stopped because of wheezing)
E. Induction of general anesthesia
F. Metoprolol-75 mgm/day (divided doses)
G. Metoprolol-150 mgm/day (divided doses)
H. Uncomplicated thyroidectomy

FIG. 1. Clinical course—Case 2.

asthma was well controlled with beclomethasone diproprionate inhalent.

Discussion

Early investigators related many of the systemic manifestations of hyperthyroidism to overactivity of the sympathetic nervous system. Initial attempts at symptomatic control included sympathectomy[4] and spinal anesthesia.[6,7] Later, with the development of sympathetic blocking agents, reserpine[8] and guanethidine[9] were administered not only for symptomatic control, but also for primary therapy for thyroid storm.[10]

The introduction of beta-adrenergic receptor blocking agents resulted in more specific control of the systemic manifestations of hyperthyroidism without the side effects of total sympathetic blockade. Beta-blocking agents have also been proposed as important adjuncts in the preoperative preparation of these patients.[11-13] Propranolol has been shown to reduce significantly resting heart rate, tremor, and sweating[14,15] and has become invaluable in the treatment of thyroid storm.[16] Although usually used in conjunction with a thionamide and iodine, propranolol has been employed as the sole preoperative agent.[12] The combination of thyrotoxicosis and obstructive pulmonary disease may be a contraindication to the administration of a noncardioselective agent such as propranolol. Propranolol acts on cardiac (beta-1) and bronchial (beta-2) receptors and may cause severe bronchoconstriction in patients with obstructive pulmonary disease.[17,18]

Cardioselective beta-blockers were introduced primarily to avoid adverse pulmonary effects while effectively controlling angina,[19] arrhythmias,[20] and hypertension.[21] Cardioselectivity has been shown to be dose related, being lost at higher plasma levels.[2,22,23] At the commonly employed dosages, cardioselective agents have been demonstrated to produce significantly less airway obstruction in hypertensive asthmatics.[24]

Metoprolol, a beta-adrenergic receptor blocker with beta-1-selectivity, was recently judged as effective as propranolol in controlling the signs and symptoms of hyperthyroidism.[25] Individual response to equivalent doses of metoprolol has varied when resting heart rates were compared.[25] Patient response to identical dosages has also varied on separate days in asthmatics when daily FEV_1 determinations were made.[27] A diurnal variation in peak flow rates has also been described in some asthmatic individuals.[28]

Newer cardioselective agents are currently in use in European centers and recent evidence indicates more specific beta-blocking activity.[23] Atenolol has recently been approved for use in the United States and has been shown to be as effective as propranolol in controlling the peripheral manifestations of thyrotoxicosis.[31]

The incidence of either asthma or hyperthyroidism in the general population is such that occasional coincidental occurrences would be expected.[29] Although asthma and thyroid dysfunction have not been causally linked, exacerbations of severe asthma have been reported with the development of thyrotoxicosis.[30] Thionamides should be used initially and will produce euthyroidism in the majority of cases. Metoprolol should be reserved for patients requiring rapid control of thyrotoxicosis (Case 1) or for patients refractory to thionamide therapy (Case 2) in the presence of reversible airway disease.

Until more experience is gained with the use of selective beta blockers, it is recommended that the preoperative preparation of patients with combined hyperthyroidism and reversible airway disease be performed in the hospital. Response to beta-blockade should be apparent within 24 hours of initiation of therapy. Patients should be maintained on the lowest effective dose as judged by appropriate reduction in pulse rate. Pulmonary function studies should be performed on admission and before surgery to detect any significant deterioration in FEV_1. A decrease in FEV_1 of approximately 15% may be expected.[27] Arterial blood gases have not been shown to be sensitive indicators of significant

metoprolol induced bronchospasm.[27] Patients can be administered bronchodilators as needed as metoprolol will permit bronchodilator response whereas nonselective beta-blockers do not.[18]

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