Rapid preparation of severe uncontrolled thyrotoxicosis due to Graves' disease with Iopanoic acid - a case report

[La préparation rapide, avec de l'acide iopanoïque, pour une thyrotoxicose sévère non contrôlée causée par une maladie de Graves - une étude de cas]

Chandra Kant Pandey MD, Mehdi Raza MD, Sanjay Dhiraaj MD, Anil Agarwal MD, Prabhat Kumar Singh MD

Purpose: To report the rapid preoperative preparation of a case of thyrotoxicosis due to Graves' disease resistant to medical treatment.

Clinical features: A 14-yr-old boy presented with a history of progressive swelling in the neck. Signs and symptoms were compatible with hyperthyroidism. Thyroid function tests revealed: serum T_4 296.5 nmol·L^{-1}, serum T_3 6.06 nmol·L^{-1} and serum thyroid-stimulating hormone < 0.15 mIU·L^{-1}. The diagnosis of thyrotoxicosis due to Graves' disease was made. Therapy was instituted with carbimazole 30 mg·day^{-1} and propranolol 80 mg·day^{-1}, which were gradually increased to carbimazole 80 mg·day^{-1} and propranolol 120 mg·day^{-1}, without response. Preparation was attempted by adding Iopanoic acid 500 mg four times a day and dexamethasone 0.5 mg four times a day in addition to the above drugs for five days. T_3 levels declined to 1.8 nmol·L^{-1}, but the serum T_4 remained elevated. Symptoms of hyperthyroidism persisted but with decreased intensity. As the patient could not be made euthyroid, surgery was planned to relieve the symptoms. Anesthesia was uneventful except for intraoperative and postoperative tachycardia, which was managed successfully with esmolol.

Conclusion: In life threatening thyrotoxicosis refractory to medical treatment, Iopanoic acid may be used as an adjuvant to antithyroid drugs for rapid preparation of the patient prior to surgery.

Objectif : *Présenter la préparation préopératoire rapide d'un cas de thyrotoxicose engendrée par une maladie de Graves résistante au traitement médical.*

Éléments cliniques : *Un garçon de 14 ans a consulté pour une tuméfaction progressive au cou. Les signes et les symptômes étaient compatibles avec l'hyperthyroïdie. L'étude de la fonction thyroïdienne a révélé : une T_4 sérique de 296,5 nmol·L^{-1}, une T_3 sérique de 6,06 nmol·L^{-1} un taux d'hormone thyréostimuline < 0,15 mUI·L^{-1}. Le diagnostic de thyrotoxicose causée par une maladie de Graves a été établi. Le traitement, amorcé avec 30 mg·jour^{-1} de carbimazole et 80 mg·jour^{-1} de propranolol, a été graduellement augmenté à 80 mg·jour^{-1} de carbimazole et à 120 mg·jour^{-1} de propranolol, sans résultat. La préparation préopératoire a été tentée avec l'addition, pendant cinq jours, de 500 mg d'acide iopanoïque quatre fois par jour et de 0,5 mg de dexaméthasone quatre fois par jour, en plus des médicaments déjà prescrits. Les niveaux de T_3 ont baissé à 1,8 nmol·L^{-1}, mais la T_4 sérique est demeurée élevée. Les symptômes d'hyperthyroïdie ont persisté, mais réduits en intensité. Étant donné l'échec à rétablir l'état euthyroïdien du patient, une opération a été planifiée pour soulager les symptômes. L'anesthésie s'est bien déroulée, sauf pour une tachycardie peropératoire et postopératoire traitée à l'esmolol.*

Conclusion : *Dans un cas de thyrotoxicose réfractaire au traitement médical, l'acide iopanoïque peut compléter le traitement antithyroïdien pour la préparation préopératoire rapide d'un patient.*

THYROIDECTOMY is the definitive treatment for thyrotoxicosis, especially in patients resistant to medical treatment, but it should preferably be performed when the patient is euthyroid to decrease perioperative cardiac risks.[1] Pharmacological restoration of a euthyroid state may take several weeks or months, whereas preoperative prompt control of thyrotoxicosis is a major goal in these patients. We describe the use of Iopanoic acid, an oral cholecystographic agent, for rapid preoperative preparation of uncontrolled severe thyrotoxicosis in a patient who underwent surgery for excision of a toxic goiter due to Graves' disease refractory to propranolol and antithyroid drugs.

From the Department of Anaesthesiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India.

Address correspondence to: Dr. Chandra Kant Pandey, Department of Anaesthesiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, India. Phone: 0091-522-2668800, ext. 2490; Fax: 0091-522-2668017; E-mail: ckpandey@sgpgi.ac.in

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Case report

A 14-yr-old, 69 kg boy presented with a ten-month history of progressive swelling in the neck and complained of fatigue, generalized weakness, excessive sweating and intolerance to heat, nervousness, decreased sleep, hyperexcitability, palpitation, diarrhea and reduced visual acuity. There were no complaints of dyspnea, dysphagia, and hoarseness of voice or feeling of suffocation. On examination there was exophthalomos, proptosis and lid lag but no diplopia or convergence defect. Extra-ocular muscle movements were normal. Both lobes of the thyroid were diffusely enlarged (7 × 5 cm and 6 × 4 cm), firm, non-tender, and mobile with palpable lower margins. There was bruit over the enlarged gland. Fine tremors of the hands and tongue were also noticed. His blood pressure was 160/70 mmHg. The electrocardiogram revealed sinus tachycardia (heart rate 120 beats·min^{-1}) with no rhythm disturbances. The echocardiogram was normal. His thyroid function tests revealed: serum T_4 296.5 nmol·L^{-1} (normal 50–160 nmol·L^{-1}), serum T_3 6.06 nmol·L^{-1} (normal 1.3–2.8) and serum thyroid-stimulating hormone (TSH) < 0.15 mIU·L^{-1} (normal 0.3–6.0). Based on clinical presentation and laboratory investigation the diagnosis of thyrotoxicosis due to Graves' disease was made. The treatment (Table) instituted was carbimazole 30 mg·day^{-1} and propranolol 80 mg·day^{-1} which was gradually increased to carbimazole 80 mg·day^{-1} and propranolol 120 mg·day^{-1} but the control was unsatisfactory (serum T_3 5.75 nmol·L^{-1} and serum T_4 328 nmol·L^{-1}, heart rate 110 beats·min^{-1}).

Since the patient could not be rendered euthyroid, control was attempted by adding Iopanoic acid 500 mg four times a day and dexamethasone 0.5 mg four times a day in addition to carbimazole and propranolol. Amlodipine 5 mg once daily was added to control hypertension. Within five days of institution of this therapy the serum T_3 levels declined to 1.8 nmol·L^{-1}, but the serum T_4 remained elevated (308.8 nmol·L^{-1}). The symptoms of hyperthyroidism persisted but decreased in intensity. As the patient could not be made euthyroid with medical therapy alone, surgery was planned to relieve the symptoms of hyperthyroidism.

The patient was premedicated with lorazepam 2 mg and ranitidine 150 mg the night before surgery and one hour prior to surgery. He also received his total daily dose of carbimazole 80 mg as a single dose along with Iopanoic acid 500 mg, dexamethasone 0.5 mg and amlodipine 5 mg. Intravenous access, central venous and radial artery cannulation along with standard monitoring were instituted. Anesthesia was induced with fentanyl 200 µg, propofol 200 mg, and vecuronium 8 mg. Esmolol 21 mg (300 µg·kg^{-1}) was administered prior to intubating the trachea with a size 8.0-mm cuffed endotracheal tube and initiating mechanical ventilation. Anesthesia was maintained using isoflurane with 66% N_2O and oxygen, fentanyl and vecuronium along with a propofol and esmolol (200 µg·kg^{-1}·min^{-1}) infusion. Heart rate varied between 70 to 80 beats·min^{-1} and the blood pressure remained stable for the next three hours. Heart rate increased up to 110 beats·min^{-1} during surgical manipulation of the gland and was treated with a 21-mg bolus of esmolol followed by a 300-µg·kg^{-1}·min^{-1} infusion.

TABLE Summary of the treatment given to the patient for preparation for thyroidectomy

Drug	*Rationale*	*Order of administration*
Carbimazole (30–80 mg)	Antithyroid effects, converts hyperthyroid state to euthyroid	Initial drug of therapy
Propranolol (80–120 mg)	To inhibit the peripheral conversion of T_4 to T_3, control tachycardia and hypertension, block the peripheral effects of thyroid hormones	Along with carbimazole
Amlodipine (5 mg)	To control hypertension	Along with carbimazole and propranolol
Iopanoic acid (500 mg four times a day)	To inhibit the conversion of T_4 to T_3, reduce tissue uptake of thyroid hormones, decrease thyroid hormone synthesis, decrease thyroid response to TSH, and decrease the release of thyroid hormones from the thyroid gland	Added when above drugs could not control hyperthyroidism
Dexamethasone (0.5 mg four times a day)	To inhibit thyroid hormone secretion	Administered along with Iopanoic acid

TSH = thyroid-stimulating hormone.

At the end of surgery, after extubating the trachea, the heart rate increased to 125 beats·min^{-1} and a bolus of 21 mg *iv* esmolol was repeated. The patient was moved to the postanesthesia care unit with the esmolol infusion at the rate of 300 μg·kg^{-1}·min^{-1}. The esmolol infusion was continued for the next 12 hr and gradually tapered. Meanwhile propranolol 40 mg was restarted orally. The heart rate remained stable thereafter and ranged between 70 to 80 beats·min^{-1}. The postoperative course was uneventful and the patient was discharged from the hospital after three days.

Discussion

The tree major forms of treatment for hyperthyroidism are antithyroid drugs, radioactive iodine and thyroidectomy.[2,3] In order to perform thyroidectomy, patients should be rendered euthyroid. Conventional preoperative preparation includes antithyroid drugs, and iodine administration for at least four to six weeks.[2] Corticosteroids, as well as iodine-containing compounds, when used as single therapy have been able to reverse clinical manifestations of thyrotoxicosis. However, a pharmacological combination which acts at three levels: inhibition of thyroid hormone secretion (betamethasone and Iopanoic acid), inhibition of the peripheral conversion of T_4 to T_3 (Iopanoic acid, betamethasone and, to a lesser degree, propranolol) and blockade of the peripheral effects of thyroid hormones (propranolol) is useful.[2]

Iopanoic acid may improve hyperthyroidism by several mechanisms in addition to its ability to inhibit the conversion of T_4 to T_3.[4] It reduces tissue uptake of thyroid hormone.[4] It is also known to inhibit the nuclear binding of T_3. Its effects on the thyroid gland include reduced thyroid hormone synthesis; decreased proteolysis of thyroglobulin; decreased thyroidal response to TSH; and decreased release of thyroid hormones from the thyroid gland.[4] Yet, long-term treatment with Iopanoic acid is not feasible because of the recurrence of hyperthyroidism as a result of an escape phenomenon.[1]

Thyroidectomy is one of the definitive treatments for thyrotoxicosis especially in patients resistant to medical treatment.[1] Surgery is indicated in pregnant hyperthyroid patients intolerant to antithyroid drugs, breast feeding patients, non-pregnant patients who refuse radioactive iodine therapy, children with Graves' disease, patients resistant or allergic to radioactive iodine or antithyroid drugs, and patients with large or nodular goiter or with a cold nodule in active progressive ophthalmopathy.[3] Radioactive iodine could not be used in this case because of patient's young age and ophthalmopathy.[5] Surgery was also favoured over radioactive iodine because the ophthalmic findings do better with surgery and it may be life saving in these patients.[3,5–8] Because of unresponsiveness to conventional therapy and the urgent need of a rapid control of thyrotoxicosis, Iopanoic acid (circulating thyroid hormone levels decreased in three days), was preferred over Lugol's solution in this case.[3]

Based on our experience with this patient we conclude that, in cases of life threatening thyrotoxicosis refractory to medical treatment, Iopanoic acid may be an adjuvant to antithyroid drugs for the rapid preparation of patients prior to thyroidectomy when surgery cannot be delayed.

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