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## CASE REPORT

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# Hypothyroidism Secondary to Iodinated Glycerol

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### INTRODUCTION

Iodinated glycerol (Organidin®), a mucolytic used in the treatment of respiratory disorders, has recently been the subject of a national study which demonstrated the drug's effectiveness and safety. Though infrequently reported, hypothyroidism has occurred in patients treated with this drug. We report the case of a male patient who developed hypothyroidism after long term use of the drug.

### CASE

A 51 year-old male with a long history of emphysema secondary to alpha<sub>1</sub> antitrypsin deficiency was admitted to hospital with a chief complaint of increased shortness of breath accompanied by a productive cough of one week's duration. Three days prior to admission, because of increasing dyspnea, he increased his prednisone dosage from 20 to 30 mg daily, increased the frequency of his salbutamol usage, and started himself on trimethoprim/sulfamethoxazole. Despite this, his dyspnea worsened and he was admitted to hospital.

His past medical history was re-

markable for cataracts in both eyes, with implants in 1984 and 1986, an inguinal hernia repair 30 years prior and hemorrhoids. Medications on admission were theophylline sustained release 150 mg po tid, iodinated glycerol 60 mg po qid, ipratropium bromide inhalations prn, salbutamol by rotohaler inhalations prn, lorazepam 2.5 mg po daily, and cotrimoxazole double strength po bid. As well, the patient was receiving long term home oxygen therapy. The patient was reported to be allergic to codeine and tetanus toxoid.

His family history was positive for emphysema. The patient was on disability pension and lived at home with his wife and children. He had smoked for many years, but quit eight years prior to admission. The patient complained of dyspnea, recent sleeplessness, dysphagia from solids, loss of appetite, muscle fasciculations, and cold intolerance.

Upon physical examination, the patient appeared to be his stated age. The patient's vital signs were: pulse rate 100 beats per minute; respiratory rate 22 per minute; and blood pressure 140/100 mmHg with no pulsus paradoxus. The patient was afebrile.

A chest X-ray showed hyperinflation, decreased lung markings especially at the bases and no pneumothorax. Blood gases on 4L oxygen by nasal prongs were PO<sub>2</sub> of 79 mmHg, pH 7.43, PCO<sub>2</sub> of 43 mmHg and bicarbonate of 28 mmol/L. Other lab values were unremarkable. A theophylline level of 50 µmol/L (N 55 - 110 µmol/L) was reported. Examination of the head and neck revealed normal conjunctiva and normal oral mucosa. There was no cervical lymphadenopathy and the neck was supple. Chest examination revealed a barrel chest, with mild use of accessory muscles and indrawing. There was no tracheal tug or deviation. The chest was noted to be hyperinflated. Breath sounds were poor bilaterally and scattered crackles could be heard. Fine wheezes were audible on forced expiration. Cardiovascular examination revealed good peripheral pulses and jugular venous distention was noted.

The patient was admitted to hospital for treatment of his exacerbation of COPD and the following therapies were initiated. The prednisone was tapered to 20 mg daily on the third day in hospital and 15 mg on the sixth day. The patient was started on

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ranitidine 150 mg po bid for symptoms of gastroesophageal reflux. In reviewing the patient's drug history with him, it was discovered that he had been prescribed iodinated glycerol 5 mL qid approximately one year earlier and had noted some subjective response to this therapy. With time however, the patient reported diminishing effectiveness and the physician caring for him had suggested that the patient discontinue the iodinated glycerol. Despite this recommendation, the patient continued to take the medication up until his admission to hospital. In hospital, because of this lack of response and complaints from the patient regarding dyspepsia and bad taste, the drug was discontinued. In light of complaints of cold extremities in a patient who was receiving a drug of known hypothyroid potential, a TSH test was ordered and subsequently reported as 50 mU/L (N 0.45-9.2 mU/L). Because of this, levothyroxine was begun on the sixth day in hospital.

The patient remained in hospital for several days and was discharged home on the levothyroxine 0.1 mg daily as well as his respiratory medications.

## DISCUSSION

Organically bound iodine such as iodinated glycerol is metabolized into free iodide after absorption.<sup>1</sup> Iodide inhibits the binding of iodine to the tyrosine residue of the thyroglobin molecule inhibiting the synthesis of the thyroid hormones, thyroxine and tri-iodothyronine. In a normal individual, this inhibition is prevented by a decrease in iodide transport through

an autoregulation mechanism. However, in patients with iodide induced goitre, there is an increase in iodide transport further reducing thyroid hormone synthesis and causing hyperplasia of the gland.<sup>1</sup>

Drinka et al reported reversible hypothyroidism in nursing home residents using iodinated glycerol as an expectorant.<sup>2</sup> Five patients who had been on iodinated glycerol 70 - 150 mg daily for periods of 24 - 610 days, with no past history of thyroid disease, were identified. The mean TSH of the group was elevated at  $13.1 \pm 3.8$  mU/L. After discontinuation of iodinated glycerol the TSH levels fell toward the normal range in all subjects. Gomolin described a case report of a patient who experienced marked hypothyroidism while receiving a saturated potassium iodine solution.<sup>3</sup> This was stopped with improvement but a few months later the patient received iodinated glycerol, and hypothyroidism was again induced. Within a month of discontinuing the iodinated glycerol, recovery was noted. As well, the development of a goitre has been described in a 14 year old girl who received 30 mg iodinated glycerol three times daily for one month. The goitre resolved when the drug was discontinued.<sup>4</sup> In our case, levothyroxine was prescribed in part because of the markedly elevated TSH test. In all likelihood, as in other cases, simply discontinuing the drug would result in improvement although there may be some delay in returning to the euthyroid state.

The national mucolytic study had a primary goal of assessing the safety and efficacy of orally administered

iodinated glycerol tablets in the management of patients with stable bronchitis.<sup>5</sup> It was concluded from the study that iodinated glycerol 60 mg qid is clinically effective and safe as adjunctive therapy in chronic obstructive bronchitis. There were no adverse endocrinologic effects reported. However, this two month study did not measure TSH nor was it of sufficient length to consider the long term effects of iodinated glycerol. Our case and those reported previously in the literature illustrate the need to consider the long term effects of iodinated glycerol in the assessment of its effectiveness, and the necessity of weighing the risks versus the benefits.

These few case reports indicate that pharmacists and other health care professionals must be aware of the potential for adverse effects on the thyroid of prolonged iodinated glycerol therapy. ☒

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