AMERICAN ACADEMY OF PEDIATRICS

Committee on Drugs

Adverse Reactions to Iodide Therapy of Asthma and Other Pulmonary Diseases

Neonatal deaths from tracheal obstruction caused by congenital goiters have been reported from such widely scattered locales as Buffalo, New York, New York City, Philadelphia, Washington, D.C., Seattle, Tokyo, Japan, and Glasgow, Scotland. The mothers of these infants had asthma and were receiving conventional doses of iodides, either as potassium iodide or as mixtures of bronchodilators and iodides. Because of these deaths, the Committee on Drugs of the American Academy of Pediatrics has reviewed the use of iodides in the therapy of asthma and other chronic pulmonary diseases.

Five current textbooks advocate the use of iodides in chronic asthma.5-9 "Iodide compounds have a stimulating effect on bronchial secretions and represent expectorants of major importance in treating asthma and particularly status asthmaticus."5 The AMA Drug Evaluations6 recommends the use of iodides only for short-term medication. Current Pediatric Therapy7 emphasizes careful patient selection because only an occasional patient may benefit.

Dosage recommendations usually are 300 mg of potassium iodide every two hours in adults1 and 60 mg per year of age four times daily in children.4 These dosage recommendations are many times greater than the 65 mg of organic iodine (T4 and T3) which the average human thyroid gland delivers to the circulation per day, or the estimated daily adult iodide requirement of 200 mg of iodide.6 As a matter of fact, these recommended dosages for iodides represent 10 to 30 times the total body content of iodide!

Many preparations—some of which are available on an over-the-counter (nonprescription) basis—contain iodides, including antiasthmatic preparations, expectorants, and preparations whose trade names may not suggest the presence of iodides. The names of preparations which will provide 2 mg or more of iodide (ten times the daily nutritional requirement) per 24 hours when used as recommended are available on request from the Committee.

A warning was published in The Medical Letter8 about drug-induced goiters in fetuses and in children and adults who receive iodides as expectorants for therapy of asthma. Toxicity has also been reported in patients with cystic fibrosis who were receiving long-term iodide therapy.10

EVIDENCE OF EFFICACY AS AN EXPECTORANT

Studies purporting to show effectiveness of iodides are subjective11 and may reflect the unconscious bias of the authors. Iodides have never been evaluated in status asthmaticus and have been studied objectively only once in patients with chronic asthma.12 This study was carried out on children who had chronic, severe asthma and were living in a residential treatment home. The patients received potassium iodide in two different dosages or a placebo in a double-blind crossover. This study is subject to the criticism that a true "double-blind" study of iodides is impossible because they impart a characteristic, "metallic" taste to sputum which is readily recognized by patients. The findings were as follows:

(1) Only 18% of children receiving iodides had "significant improvement" in asthma control, 36% showed no response at all, and the others were benefited only mildly.

(2) There was no meaningful correlation between serum iodide levels and response to therapy or to sputum viscosity.

(3) Toxicity was significant: 18 of 52 children developed goiters while on iodide therapy. Thirteen of 15 adolescents developed or had intensification of acne. One adolescent developed a severe papulovesicular rash which cleared when the iodides were discontinued and reappeared when they were resumed.
TOXICITY OF IODIDES

Adverse effects of iodides may be grouped into three categories: (1) direct effects on the thyroid, (2) hypersensitivity reactions, and (3) other effects.

Effects on the Thyroid

Iodides can induce goiter and hypothyroidism in normal children and adults as well as in those with asthma and cystic fibrosis. The mechanism of how this effect occurs is not certain. Excess iodide may impair release of T4 and block uptake of iodine by the thyroid; this could result in formation of a goiter because of overproduction of the thyroid stimulating hormone (TSH) by the pituitary. The fact that not everyone at risk develops goiter or hypothyroidism suggests that those who do develop these ailments have a failure of the normal adaptive mechanism to excess iodides.

Martin and Rento studied two infants with goiter whose mothers had received iodide-containing medication during pregnancy. These infants appeared to have suppression of organic iodine binding in utero with depression of thyroid hormone synthesis. Galina et al. reported two neonatal deaths resulting from tracheal obstruction secondary to congenital goiters. Carswell et al. reported eight additional cases, four of whom died from upper airway obstruction. Another case in which the patient died has recently been reported from Japan. Iodides are also excreted in breast milk and may constitute a hazard to nursing infants.

Thyrotoxicosis has recently been shown to be a further complication of iodide treatment, particularly in patients with preexisting goiter, and can be induced by as little as 500 mg of iodide per day.

Hypersensitivity Reactions

The following hypersensitivity reactions attributable to iodide ingestion have been reported: erythema nodosum, iododerma with necrotizing skin lesions, urticaria, bullous eruptions, drug fever, and hypersensitivity angiitis. Although anaphylactoid or anaphylactic reactions have been reported with the use of iodinated contrast media, such reactions have not been reported when sodium or potassium iodide solutions were administered orally.

Other Reactions

Acneiform skin eruptions, parotid gland swelling ("iodide mumps"), and rhinitis are further complications of iodide therapy. Of these, acneiform eruption poses the most serious threat to the adolescent because permanent facial scarring may result if the relationship to iodide therapy is not recognized and the drug discontinued promptly.

RECOMMENDATIONS

The Committee recommends the following:

1. Iodides should be used as expectorants only in patients with chronic disease who have a reproducible, clearcut amelioration which cannot be obtained with a less toxic agent. The dosage should be as low as possible, and the drug should be used for the shortest time possible.

2. Iodides should never be used as expectorants during pregnancy and should be discontinued or decreased during breast-feeding.

3. Iodides should not be prescribed as expectorants during adolescence because of their potential to induce acneiform eruptions, exacerbate existing lesions, and adversely affect the thyroid.

4. Iodides should never be prescribed as expectorants for patients with goiter.

5. All preparations containing iodides should be clearly labeled as to their iodide content, with the warning that they are contraindicated in pregnancy.

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