A case of acute deterioration in asthma symptoms induced by isoniazid prophylaxis

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The present case report describes a 10-year-old boy with clinical history of steroid-dependent asthma who developed severe exacerbation of his respiratory symptoms upon isoniazid administration. Subsequent control of his asthma symptoms was re-established and maintained only after isoniazid withdrawal. This case is the first to emphasize the dangers of isoniazid administration in patients who have asthma.

Introduction

Isoniazid is one of the most useful anti-tuberculosis drugs available and is the drug of choice in the chemoprophylaxis of tuberculosis (1,2). However, a well-recognized adverse effect is its ability to induce hepatotoxicity (3) and to influence the metabolism of a variety of drugs by modulation of the hepatic microsomal enzyme systems (4,5).

The present case report details the findings in a boy with a long-standing clinical history of steroid-dependent asthma who developed severe respiratory distress requiring maximal pharmacological support upon introduction of isoniazid chemoprophylaxis. Subsequent control of asthma symptoms was re-established and maintained only after isoniazid withdrawal. To the authors' knowledge, this is the first reported human case of acute asthma deterioration induced by isoniazid. This case highlights the importance of considering uncommon side-effects when this drug needs to be used in asthmatics who necessitate prevention for tuberculosis.

Case Report

A 10-year-old boy with brittle steroid-dependent asthma was seen with an acute exacerbation of this asthma. A diagnosis of asthma was made when he was 5 years old. At the age of 7 years, the young patient started to develop recurrent asthma attacks which failed to resolve with standard nebulized therapy, for which he required oral prednisone and occasional domiciliary nasal oxygen. He remained well with inhaled salbutamol and beclomethasone dipropionate 250 µg two puffs at least four times a day and a maintenance dose of 2-5 mg prednisone daily. For the last 3 yr, he had had no exacerbation or worsening of his asthma. His father had been recently diagnosed with active cavitary pulmonary tuberculosis and he was started on isoniazid (300 mg day⁻¹) for tuberculosis chemoprophylaxis as his Mantoux test was strongly positive with a normal chest roentgenogram. Acetylator status was not assessed. Ten days later, his asthma worsened and his peak expiratory flow (PEF) dropped to 80 l min⁻¹ (from his best value of 240 l min⁻¹) (Fig. 1). Physical examination revealed a severely dyspneic boy with cyanosis. His weight (29.5 kg) and height (126 cm) were within normal ranges, but there was some abdominal obesity, and he was flabby with poor musculature. His face was plethoric. The pulse rate was 126 beats min⁻¹, blood pressure was 110/80 mmHg, axillary temperature was 36.6°C, and respiratory rate was 36 min⁻¹. Abdominal striae, ankle oedema and lymphadenopathy were not present. Widespread wheezing was noted on auscultation of his chest. Cardiac examination was unremarkable. Routine laboratory investigations were non-contributory (including normal liver function tests). Results of lung function tests were consistent with severe bronchial obstruction.
ASTHMA DETERIORATION AFTER ISONIAZID

Standard nebulized salbutamol (2.5 mg) was administered with immediate improvement in his clinical picture and spirometry. He was sent home with a 10-day course of 12.5 mg prednisone daily.

The following day, his condition deteriorated further with severe respiratory distress and his PEF was unrecordable (Fig. 1). He was immediately treated with hydrocortisone intravenously, nasal oxygen, and continuous nebulization with high-dose salbutamol (10 mg). Prednisone dosage was further increased to 25 mg day$^{-1}$, and isoniazid was withdrawn. His PEF returned to its usual range within 3 days. At that time, it was felt that resolution of this acute exacerbation of his asthma was due to the increase in steroid dosage, and chemoprophylactic therapy with isoniazid was re-introduced 1 week later. Within 6 days from recommencing isoniazid, his asthma deteriorated again and his PEF dropped to 120 1 min$^{-1}$. Isoniazid was again stopped with spontaneous improvement in his asthma, and PEF values returned to their usual range within 24 h. The patients were advised to continue his therapeutic programme with a maintenance dose of 2.5 mg prednisone daily. There were no subsequent problems with his asthma control.

Discussion

Children and young adults with strongly positive Mantoux tests and no BCG history are at risk from developing clinical tuberculosis. These children should be given chemoprophylaxis with isoniazid for 6 months which significantly reduces the likelihood of subsequent clinical tuberculosis (1,2).

This case of a boy with a clinical history of steroid-dependent asthma, who developed severe exacerbations of his symptoms after isoniazid chemoprophylaxis, emphasizes the dangers of isoniazid administration in patients who have asthma. To the best of the authors’ knowledge, this drug-specific response has never been reported in the medical literature. Considering that asthma is a rather common illness and chemoprophylaxis with isoniazid has been prescribed in a large number of individuals, this is surprising. A possible explanation is that either the treating physicians have not been aware of the worsening of asthma in their patients on isoniazid chemoprophylaxis (which may be mild in most cases), or the adverse reaction described is very rare. The authors favour this latter hypothesis, as the occurrence of an idiosyncratic type of reaction against isoniazid is more likely. However, isoniazid-induced neurological toxicity with subsequent unbalance in the bronchomotor tone cannot be ruled out in this child with asthma.

In these circumstances, suspension of the offending drug is the logical approach. In addition, increasing steroids remains useful although the extent of the increase required is not clear. This young patient suffered a severe exacerbation of his asthma requiring large doses of oral prednisone and intravenous hydrocortisone. As suggested for rifampicin (6), the authors would advocate using isoniazid with caution in steroid-dependent asthmatics.

An additional possibility is that the boy might have become sensitized to isoniazid. A recent study has shown that sensitization to oral isoniazid may occur, and that the asthmatic symptoms are caused by an IgE antibody specific to isoniazid as a hapten (7,8). However, this is unlikely in the present case because of the short time of exposure.

Although clinical observation and accurate history taking supported the view that isoniazid was the cause of the asthma exacerbations in this young patient, other possibilities cannot be excluded. Acute exacerbations of steroid-dependent asthma in a previously stable individual are not unusual. This young patient might have been exposed to a flu-like illness. However, although no investigations were made to prove or exclude a viral infection, his clinical and pharmacological history are against this possibility.

References


