SCD due to the increased basal metabolic requirements of a patient with hemolysis.[4] The hypermetabolic state will require greater dietary energy compared with Hb AA. In this study patients with growth retardation tends to have lower mean Hb.

It has been possible to restore normal growth by nutritional supplementation. There have been reports of responses to folic acid, zinc supplementation or regular blood transfusion, but these approaches are not recommended as standard care. A high concentration of fetal Hb in boys with SS disease is associated with greater linear growth. It is postulated that in boys, low concentrations of fetal hemoglobin increase hemolysis and hence metabolic requirements for erythropoiesis, putting them at greater risk of poor growth.[5] In this study patient with higher Hb F tend to have more underweight, and no explanation available for this paradoxical finding, whoever most agree that the relation between HbF level and clinical severity of SCD is not simple.[1]

Received 12th August 2002. Accepted for publication in final form 21st December 2002.

From the Department of Medicine, Basrah Military Hospital, Basrah, Iraq. Address correspondence and reprint requests to Dr. Abbas A. Mansour, Hattin Post Office, PO Box 142, Basrah 42002, Iraq. Tel. +964 (40) 420388. Fax. +001 (775) 2691705/2541726. E-mail: a.a.m.b@uruklink.net

References

1. Embury SH ,Vichinsky EP. Sickle Cell Disease. In: Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE et al editors. Hematology Basic Principles and Practice. Pennsylvania (PA): Churchill Livingstone; 1995. p. 510-554.
2. El-Hazmi MA, Bahakim HM, Al Fawaz I. Endocrine functions in sickle cell anaemia patients. ***J Trop Pediatr*** 1991; 38: 307-313.
3. National center for health statistics: a growth curve for children: birth-18 years, United States. Hyattville (MD): Department of Health Education and Welfare; 1977. p. 78-1650.
4. Badaloo A, Jackson AA, Jahoor F. Whole body protein turnover and resting metabolic rate in homozygous sickle cell disease. ***Clin Sci*** 1989; 77: 93.
5. Singhal A, Morris J, Thomas P, Dover G, Higgs D, Serjeant G. Factors affecting prepubertal growth in homozygous sickle cell disease. ***Arch Dis Child*** 1996; 74: 502-506.

Effect of itraconazole therapy in allergic bronchopulmonary aspergillosis

Raj Kumar, *MD,* ***Pranav Singh,*** *MBBS,*
Rajan Arora, *DTCD,* ***Shailendra N. Gaur,*** *MD.*

Allergic bronchopulmonary aspergillosis (ABPA) is characterized by type I and type III hypersensitivity reactions to *Aspergillus* antigen. Incidence of ABPA among bronchial asthma has been found to vary from 3.7-11% in western countries. Kumar and Gaur[1] has found prevalence of ABPA in patients of chronic bronchial asthma as 16%. It appears that excessive mucus and inflammation may lead to germination and colonization of *Aspergillus* in the airways. This leads to a constant supply of antigen thereby causing inflammation and attracting eosinophils and lymphocytes. Oral corticosteroids are still the mainstay for treating ABPA. These drugs decrease the airway inflammation; increase the body's efficiency in clearing the organism and decreasing the bronchial environment suitability for *Aspergillus* growth. Despite these benefits, it is well known that corticosteroids have a serious long-term adverse effect. Itraconazole is a highly lipophilic triazole derivative active against *Aspergillus* both in vitro and in vivo. The drug blocks the sterol synthesis pathway in the lungs. Itraconazole also seems to have a more benign adverse effect profile than other oral antifungals such as amphotericin B, hamycin and ketoconazole. Most patients can tolerate the drug with few adverse effects. Itraconazole has not been used much in India. Hence, we present 2 cases where Itraconazole was given and the response was good.

A 21-year-old man (height 164 cm, weight 41 kg) with a bronchial asthma since childhood and increasing in severity over times. At the age of 16 years, he complained of high grade fever with evening rise without any cough or hemoptysis. These symptoms persisted for 2-3 weeks, and the patient was diagnosed as having pulmonary tuberculosis based on chest radiograph abnormalities. No other investigations were carried out. He was put on anti-tuberculosis treatment; a Rifampicin based regimen was started which the patient took with good compliance. After 18 months, the treatment was stopped due to poor response. At the age of 20 years, the patient had complaints of cough with hemoptysis (2-3 episodes per day) and anorexia with significant weight loss. There was no fever. The chest radiographs were within the normal limits and sputum was negative for acid fast bacilli (AFB). Antitubercular drugs was started. Patient took Rifampicin, Streptomycine, Pyrazinamide, Ethambutol for 3 months followed by Rifampicin, Pyrazinamide, Ethambutol for next 3 months. Subsequently, he was taking only Rifampicin which he was still continuing at the time of presentation in September 1997 at our Institute (Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India). The hemoptysis had subsided by then. On investigation, the laboratory findings showed eosionophilia in peripheral blood. Sputum samples were repeatedly negative for AFB. The chest radiographs showed consolidation in the right upper zone. The previous x-ray was examined showed fleeting shadows. A cavity was seen in the left upper zone. Spirometry showed an forced vital capacity (FVC) of 45%, forced expiratory volume at one second (FEV1) - 45% and the ratio of FEV1/FVC was 92%. The serum precipitins against *Aspergillus fumigatus* and *Aspergillus flavus* were positive. The total immunoglobulin (Ig) E was raised. Specific IgE and specific IgG against *Aspergillus fumigatus* were detected. Sputum culture was negative for any pathogenic fungus. The skin test was positive (immediate and late) for *Aspergillus fumigatus*. The

computerized tomography scan of the lung showed cavity on left and central bronchiectasis. There was presence of fibrotic lesions and pleural thickening on the left side. Based on these findings; a diagnosis of ABPA was made and patient was given an oral prednisolone (40 mg/day) with a gradual tapering of dose for a total period of 3 months. The patient did not improve. Along with prednisolone, Itraconazole (200 mg once daily) was given for period of one year. Serological improvement was also observed as the serum was negative for precipitins against aspergillus although specific IgG was still detectable. The eosinophilia also subsided. The patient improved symptomatically. The patient is still being followed up and has no fresh complaints.

A 39-year-old female (height 147 cm, weight 67 kg) had complaints of breathlessness with wheeze, cough with expectoration and a history of frequent nasal and eye symptoms for the last 15 years. Her son is an asthmatic patient. During investigation, her peripheral blood showed eosinophilia. Spirometry showed a FVC of 54%, FEV_1 of 53% and the ratio of FEV_1/FVC 97% which improved after a bronchodilator; for example FVC of 65% FEV_1 of 57% and the ratio being FEV_1/ FVC 88%. Serum precipitins against *Aspergillus fumigatus* were detected. Specific IgE and IgG against *Aspergillus fumigatus* were detected. Skin tests against *Aspergillus fumigatus* antigen were positive (immediate and late), x-ray was normal. The patient was given oral prednisolone (40 mg/day) which was gradually tapered off during a total period of 4 months. The patient improved. After approximately one year she again had an exacerbation of symptoms, and serologically she was positive for ABPA. She did not want to take Prednisolone as previously since her weight increased due to Prednisolone. She was given itraconazole (200 mg per day) for 8 months. Patient showed improvement symptomatically. The serological parameters have also reduced. There were no fresh complaints. Oral corticosteroids has been widely used for the treatment of ABPA to prevent acute episodes as well as to decrease the likelihood of irreversible lung damage. These agents suppress the allergic and inflammatory responses associated with the bronchial colonization by *Aspergillus*. The effectiveness of a systemic antifungal treatment of ABPA was shown by Shale et al[2] in using ketoconozole. Itraconazole, a new triazole with less toxicity has more activity against *Aspergillus species* than ketoconazole. Some studies of ABPA being treated with itraconazole have been reported. Denning et al[3] reported a study of 6 patients with ABPA treated with Itraconazole 200 mg twice a day for a mean of 3-9 months.[5] Five out of 6 patients were receiving corticosteroids simultaneously. By 2 months the mean oral corticosteroid dose was reduced; lung function improved and there was a significant decrease in total IgE levels. During 6 months of follow-up after treatment; one patient suffered acute ABPA and another had an asymptomatic rise in IgE.

In another case reported by Pacheco et al[4] a corticosteroid dependent patient with ABPA treated with itraconazole had a steroid sparing effect as well as improved lung function and decreased IgG to Aspergillus.

In a case report by Nikado et al[5] a patient was originally diagnosed with ABPA at the age of 19 and treated successfully with 4 weeks of oral prednisolone. For a relapse approximately 4 years later, the patient refused prednisolone due to secondary weight gain. After 2 weeks of itraconazole (100 mg per day) the patient showed symptomatic and serological improvement and after 6 weeks of treatment there was improvement in chest x-ray. In another study by Salez et al,[6] 14 patients of ABPA were treated with itraconzole for one year (200 mg per day). Clinical, serological and functional improvement was observed as well as the need for corticosteroid treatment was reduced or eliminated. Our study in 2 patients also showed clinical serological and functional improvement with itraconazole. There were no side effects observed with the drug.

In conclusion, we suggest that Itraconazole is useful in the prevention of ABPA exacerbations and treatment with Itraconazole may have a corticosteroid sparing effect leading to reduction or elimination of use of corticosteroids in management of ABPA. However, randomized controlled studies are required to determine the role of Itraconazole in a long term management of ABPA.

Received 30th April 2002. Accepted for publication in final form 7th December 2002.

From the Department of Respiratory Medicine, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India. Address correspondence and reprint requests to Dr. Raj Kumar, Department of Respiratory Medicine, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi - 100007, India. Fax. +91 (11) 7667420. E-mail: rajneel44@rediff.com

References

1. Kumar R, Gaur SN. Prevalence of allergic bronchopulmonary Aspergillosis in patients with bronchial asthma. ***Asian Pac J Allergy Immunol*** 2000; 18: 181-185.
2. Shale DJ, Faux JA, Lane DJ. Trial of Keloconazole in non-invasive pulmonary aspergillosis. ***Thorax*** 1987; 42: 26-31.
3. Denning DW, Van Wye JE, Lewiston NJ, Stevens DA. Adjunctive therapy of ABPA with Itraconazole. ***Chest*** 1991; 100: 813-819.
4. Pacheco A, Martin JA, Cvevas M. Serologic response to itraconazole in Allergic bronchopulmonary Aspergillosis. ***Chest*** 1993; 103: 980-981.
5. Nikado Y, Nagata N, Yamamoto T, Yoshi C, Ohmori H, Kido M. A case of allergic bronchopulmonary Aspergillosis successfully treated with Itraconazole. ***Respir Med*** 1998; 92: 118-124.
6. Salez F, Brichet A, Desurmont S, Fabienne S, Anne B, Sophie D et al. Effects of Itraconazole therapy in Allergic Bronchopulmonary Aspergillosis. ***Chest*** 1999; 116: 1665-1668.