Albendazole-induced Recurrent Hepatitis

A 5-year-old male child presented with repeated episodes of acute-hepatitis, each episode occurring after 2-3 days of administering albendazole. He presented to us during the fourth such episode with complaints of acute onset fever, anorexia and vomiting followed by yellowish discoloration of eyes and urine. Each episode lasted 2-3 weeks, the intervening periods remaining uneventful. Liver was palpable 3.5 cm below the right costal margin. It was mildly tender and soft. There were no signs of chronic liver disease. Serum bilirubin on admission was 11.5 mg/dL(Direct- 9.5 and indirect-2.0). Serum alanine transaminase, aspartate transaminase, alkaline phosphatase and gamma glutamyl transpeptidase (GGT) were 2720 IU/L, 4100 IU/L, 1247 IU/L and 26 IU/L, respectively. Albumin and globulin levels were 3.3 g/dL and 3.0 g/dL, respectively. Prothrombin time was 22 seconds (INR-1.6, control 12.6 secs) and aPTT was 31.0 secs (N-25-35 sec). Ceruloplasmin level was 35.64 mg/dL (N >20 mg/dL). HBsAg, anti HCV Ab, IgM HAV and IgM HEV, antinuclear antibodies, anti LKM antibody and anti smooth muscle antibody were negative. His condition improved within 2 weeks with subsidence of jaundice and hepatomegaly. On follow up, at 2 months, he was asymptomatic without hepatomegaly and with normal levels of bilirubin.

Albendazole (methyl 5-propylthio-2-benzimidazole-carbamate) is a widely used broad spectrum antihelminthic drug. Mild adverse effects like nausea, vomiting and pruritus have been occasionally reported [1]. However, reports of albendazole induced significant liver toxicity are rare. Moreover, most of the previous incidences have been reported following prolonged administration [1]. Recurrent hepatitis following single dose administration of albendazole is rare [2].

As all the common etiological markers of chronic and recurrent hepatitis were negative and due to temporal relation of albendazole ingestion with onset of self-limiting clinical jaundice four times in two years, a possibility of albendazole induced idiosyncratic hepatotoxicity was considered. He scored 5 on Naranjo Scale [3], categorizing as probable ADR. On Roussel Uclaf Causality Assessment Method of the Council for International Organizations of Medical Sciences scale [4,5], this child scored 9 points categorizing as 'highly probable' association of albendazole with DILI (drug induced liver injury).

We, as clinicians, need to be aware of this rare but significant adverse effect of this commonly and often empirically used drug.

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Is It Safe to Use Inhaled Iloprost in Infants With Pulmonary Hypertension ?

Pulmonary arterial hypertension (PAH) is a rare disorder characterized by increased pulmonary arterial pressure and vascular resistance due to the impaired endothelial wall and smooth muscle functions of the pulmonary vessels [1,2]. The PAH in children is either idopathic

(IPAH) or associated with congenital heart diseases (CHD), especially with left to right shunts [3]. In the treatment, nitric oxide, prostanoids, magnesium sulphate, endothelin receptor antagonists and phosphodiesterase-5 inhibitors are used. Prostacyclins vasodilate the pulmonary vessels and prevent the endothelial cell damage to control PAH [4]. The most common side effects of prostacyclins is headache, systemic hypotension, allergic reactions, chest pain, dyspnea, nausea and vomiting [2,4]. The optimum dosage with the minimum side effects is 0.3 ng/kg/min for the inhalation and 0.6 ng/kg/min. for the intravenous administration of iloprost (synthetic analog of prostacyclin) [4].

To evaluate the safety of inhaled iloprost in infants with PAH, we analyzed its side effects retrospectively in our pediatric cardiology and cardiovascular surgery clinic. We evaluated 52 infants (27 females) with PAH-CHD hospitalized for the surgical correction of their cardiac anomalies in the last year. Their mean age was 13.5±4.7 months (3-24 months) and the mean pulmonary arterial pressure (PAP) was 39±11.6 mmHg. (25-70 mmHg). They received iloprost inhalation (Ilomedin, Schering AG) 6 times/day at a dosage of 0.3 ng/kg/min for 7-15 days (mean 10.6 ± 2.8 days) preoperatively. Their mean PAP was 28 ± 12.3 mmHg after the iloprost treatment. The difference in the mean PAP values was statistically significant (P<0.05). The infants were monitorized during the inhalation. They did not develop systemic hypotension (mean arterial pressure was 72±8.7 mmHg) and their vital signs were stable.

Among the side effects encountered in the 29 infants (55.7%) during the inhalation, 22 (75.8%) had rash on the cheeks and around the mouth, 4 (13.7%) had agitation, 2 (6.8%) had nausea and vomiting just after the inhalation and 1(3.4%) had bronchospasm. We had to stop the iloprost treatment only in one infant with bronchospasm attacks. Symptomatic relief was provided for other symptoms such as rash, nausea, vomiting and agitation, so these infants continued the iloprost inhalation. There was no pathologic change in the blood cell counts, liver and renal function tests of the infants after the inhaled iloprost administration.

Inhaled iloprost seems to be a safe and efficient therapy for the infants with PAH if it is used in a controlled manner.

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How to Treat Inadequately Treated First Episode of Nephrotic Syndrome

A 2-year-old female child diagnosed as Nephrotic syndrome 1st episode was put on daily steroid therapy as per IAP guidelines for the steroid sensitive nephrotic syndrome [1]. She went into remission during the first half of 2nd week of daily steroid therapy. Parents complied with the treatment till continuation of daily steroid therapy *i.e.* 6 weeks. Despite medical advice parents did not put the child on alternate day steroid therapy for the erroneous impression of complete cure of the disease. Within ten days of discontinuing steroids child had recurrence of the disease. On restarting the daily steroids child went into remission during initial 3 days only. As per consensus guidelines shall we treat this child as first relapse of nephrotic syndrome or as the continuation of first episode of nephrotic syndrome? Since the child did not receive alternate day steroids at all, she does not fulfill the criteria of relapse exactly as per IAP consensus guidelines. Type and duration of steroid therapy will vary according to this distinction.

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