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The role of ursodeoxycholic acid and Curcuma in children with hepatitis A: case reports and literature review

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ABSTRACT

Introduction:

Hepatitis A is a liver disease caused by the hepatitis A virus (HAV), a self-limiting disease, providing lifelong immunity. The transmission of HAV is fecal-oral. Liver cell damage occurs due to the T-lymphocytes-associated immune system.

Case presentation:

A 9-year-old girl came to the hospital with complaints three days earlier complaining of fever, fluctuation, not chills. The body feels weak, nauseous, have no appetite, eyes look yellow, urine is like tea, normal stool color. The patient has never received hepatitis A immunization. The patient's sclera is jaundice, right upper abdominal pain, no hepatomegaly. Complete blood count within normal limits, AST: 1523 U/L, ALT: 1254 U/L, total bilirubin: 4.33 mg/dL, direct bilirubin: 1.18 mg/dL, indirect bilirubin: 2.15 mg/dL, Anti-HAV IgM reactive. Diagnosis is acute hepatitis A. Treatment is bed rest, low-fat diet, ursodeoxycholic acid therapy, and Curcuma. The patient went home after seven days of treatment in good condition.

Conclusion:

Ursodeoxycholic acid and Curcuma play a role in the patient's clinical and laboratory improvement. Counseling on personal and environmental hygiene must be frequently communicated to the public and emphasize prevention with active hepatitis A immunization.

Keywords: Hepatitis A, ursodeoxycholic acid, Curcuma, HAV immunization.

1. INTRODUCTION

HAV is an RNA virus that belongs to the Heparnavirus genus of the Picornaviridae. The virus is stable at low pH and moderate temperature, but it is inactivated by high temperature, chlorine, and formalin. HAV is transmitted via the fecal-oral route. Generally, patients have hepatitis due to contact with infected patients during an outbreak in schools due to contaminated water or food. The incubation period for HAV is 15 to 50 days. HAV RNA can be detected in stools at least one week before the onset of histologic and biochemical evidence of hepatitis[1], and it can be detected for at least 33 days after the onset of disease[2].

Currently, hepatitis A incidence was much lower than before the global hepatitis A immunization in 1999. Israel's Hepatitis A incidence in 1993-1998 was 50.4 cases per 100,000 population, and after the global hepatitis A immunization program, the incidence was reduced to 2.2- 2.5 cases per 100,000 population in 2002-2004[3].

Several studies have used ursodeoxycholic acid (UDCA) and Curcuma to reduce aminotransferase enzymes in various liver diseases, including hepatitis.

2. CASE PRESENTATION

A 9-year-old girl came to the hospital with complaints three days earlier complaining of fever, fluctuation, not chills. The body feels weak, nauseous, have no appetite, eyes look yellow, urine is like tea,

normal stool color. The patient has never received hepatitis A immunization. On physical examination, the patient appears conscious, and vital signs are within normal limits. ENT, mouth, Heart & Lungs, no abnormalities. The patient's sclera is jaundice, right upper abdominal pain, no hepatomegaly.

On laboratory examination, Hb 12.2 g/dL, leukocytes 3,980/uL, platelets 197,000/uL, hematocrit 35.7%, Diff Count: basophils 0%, eosinophils 2%, stems 1%, segments 30%, lymphocytes 50%, monocytes 17%. ESR 1 hour 32 mm, 2hour 51mm. Blood glucose 91 mg/dL, Ureum 18 mg/dL, creatinine 0.42 mg/dL. AST: 1523 U/L, ALT: 1254 U/L, total bilirubin: 4.33 mg/dL, direct bilirubin: 1.18 mg/dL, indirect bilirubin: 2.15 mg/dL, Anti-HAV IgM reactive. Diagnosis is acute hepatitis A. Treatment is bed rest, low-fat diet, UDCA and Curcuma. The patient went home after seven days of treatment in good condition.

3. DISCUSSION

Hepatitis A diagnosis was made based on fever, weakness, nausea, no appetite, yellow eyes and skin, sclera jaundice, epigastric abdominal pain, AST 1523 U/L, ALT 1254 U/L, total bilirubin 4,33 mg/dl, direct bilirubin 1.18 mg/dl, indirect bilirubin 2.15 mg/dl, and anti-HAV IgM reactive. The possibility of hemolytic anemia can be excluded because the complete blood count is within normal limits. The possibility of malaria can also be excluded because the patient is not pale, the fever is atypical, and there are no chills. Hepatitis A outbreak already occurred when the patient is sick, and her schoolmates suffer from hepatitis A.

Increased AST ALT value >10x requires the patient to take bed rest. To date, there is no specific treatment for hepatitis A. Therapy is only symptomatic so that the patient's body condition remains stable, active while maintaining liver function is not burdened with activity. Patients receive a low-fat diet to reduce the burden on liver metabolism.

UDCA and Curcuma can be hepatoprotectors and can improve the patient's clinical condition. UDCA has been widely researched and has various benefits for the liver so that the liver is protected from various toxins and free radicals. The various mechanisms of action of UDCA include anti-inflammatory action, immunomodulation, cytoprotection, and anti-apoptotic action, choleretic action, coordinate mithochondrial integrity, alteration of cell signalling[4,5].

Shahramian et al. researched children who had recurrent seizures. One hundred children who received valproate acid + UDCA compared to control 100 children who only received valproate acid, it was proven that after one month and three months of treatment, AST levels were lower in the group of children who received valproate acid + UDCA ($p < 0.001$)[6]. Researchers Simental - Mendía et al found UDCA had a hepatoprotective effect by significantly reducing liver function markers, namely, ALT ($p = 0.0002$), AST ($p < 0.0001$), GGT ($p < 0.0001$), alkaline phosphatase ($p < 0.0001$), bilirubin ($p = 0.04$). The results of this present meta-analysis suggest a hepatoprotective effect of UDCA by reducing serum liver function tests[7]. Oh et al. studied 168 patients with impaired liver function and fatty liver. It turns out that in the group given UDCA for eight weeks compared to controls showed significant clinical and laboratory improvements ($p < 0.05$)[8]. Sato et al. proved that UDCA could reduce SGOT SGPT and GGT levels in hepatitis C patients[9].

Reizis et al. studied 145 children suffering from Hepatitis A, B, and C. Group 1 received UDCA at a dose of 10-15 mg/kg BW/day, and the second group received no medication. Research reveals a significant inverse relationship between apoptosis of peripheral blood lymphocytes (PBL) and leukopenia. The apoptotic PBL significantly correlated with disease severity, including increased bilirubin, ALT, and viral replication. The course of disease and apoptosis PBL was improved by UDCA treatment. The apoptosis level in hepatitis A and B viruses who received UDCA was lower than those who did not receive UDCA ($p < 0.05$). Likewise, in chronic disease hepatitis B and C, apoptosis was lower in the UDCA group than in the non-UDCA group ($p < 0.001$); this means that PBL apoptosis is closely related to the progression and severity of hepatitis A, B, and C in children. Furthermore, the improved course and outcomes of the disease following UDCA treatment are associated with reducing PBL apoptosis[10].

Tabrizian et al. studied 152 children suffering from hepatitis A. Group 1 received UDCA for six months, and group two received no medication. The ALT value in the group that received UDCA had lower levels than the control group after one month and two months of treatment. The AST value in the group receiving UDCA had significantly lower levels than the control group after receiving treatment for one month ($p=0.02$), two months ($p<0.001$), three months ($p=0.04$). After six months of treatment, both the ALT and AST values were close to normal. Conclusively, UDCA accelerated achieving a biochemical response in children with acute hepatitis A[11]. Conclusively, UDCA accelerated reducing aminotransferase enzymes in children with acute hepatitis A.

Curcumin exhibits pleiotropic effects such as anti-inflammatory, antioxidant, anticancer, antiviral, and neurotrophic activity[12], and thus it possesses hepatoprotective properties[13]. Farzaei et al. showed that curcumin exerts remarkable protective and therapeutic effects of oxidative associated liver diseases

through various cellular and molecular mechanisms. Those mechanisms include suppressing the proinflammatory cytokines, lipid peroxidation products, PI3K/Akt and hepatic stellate cells activation, and ameliorating cellular responses to oxidative stress. Curcumin itself acts as a free radical scavenger over different kinds of ROS activity via its phenolic, β-diketone, and methoxy group[14].

Kim et al. showed that curcumin extract suppressed HBV replication by increasing p53 protein levels so that curcumin could be used as an antiviral drug[15]. Gheibia et al. in animal studies found that combination therapy UDCA + curcumin was adequate for treating non-alcoholic fatty liver disease (NAFLD)[16].

During treatment, the patient received 15 mg/kg BW/day of UDCA and 2 x 2 tablespoons of curcumin syrup. After seven days of treatment, the patient's complaints were much reduced, was able to eat as before, the eye's sclera light yellowish, clear yellowish urine so that the patient could go home and seek outpatient treatment. After four weeks of the treatment since the diagnosis of hepatitis was made, the patient's condition was good, and AST ALT was almost normal.

Since HAV transmitted predominantly by the fecal-oral route, prevention can be aided by improved sanitary conditions, adherence to sanitary practices (e.g., handwashing), heating foods appropriately, and water and foods avoidance from endemic areas. Handwashing is highly effective in preventing the transmission of the virus since HAV may survive for up to four hours on the fingertips. Chlorination and individual disinfecting solutions are sufficient to inactivate the virus.

When the patient is being treated, a hepatitis A outbreak occurs. It is recommended that all the patient's family be immunized against hepatitis A. Currently, hepatitis A immunization is only done independently. Hepatitis A immunization should be mandatory for inclusion in the national immunization program. Hepatitis A vaccine is administered in a two-dose schedule and is recommended for all children at one year of age (i.e., 12 to 23 months) and as a catch-up vaccine for all children and adolescents 2 to 18 years who have not previously received the vaccine.

4. CONCLUSION

Ursodeoxycholic acid and Curcuma play a role in the patient's clinical and laboratory improvement. Counseling on personal and environmental hygiene must be frequently communicated to the public and emphasize prevention with active hepatitis A immunization.

AUTHORS' CONTRIBUTIONS

Melani Sugiarti Wijaya Kangmartono wrote the case epidemiology and introductory section and Harapan Parlindungan Ringoringo wrote the whole review.

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