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CHILD HEALTH CARE

TEACHING FILES (GRAND ROUNDS)

TENOFOVIR AND HEPATITIS B - HOW TO MANAGE?

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Clinical Problem:
Case- A 16 years old girl was referred to us for positive serum HbsAg test. She has acute lymphoblastic leukemia diagnosed at age of nine years for which she received multiple blood transfusions. Her chemotherapy lasted for two and a half years. At age of 15 years she was detected to be HbsAg positive on screening. Her HIV ELISA and hepatitis C antibody test were negative. Her hepatitis E antibody was also positive and hepatitis B (HBV) viral load was >105 copies/ml. She underwent a liver biopsy which showed ground glass appearance of hepatocytes without fibrosis or inflammation. She received 15 doses of interferon Alpha along with Lamivudine for 1 year. She was subsequently referred for further management. On physical examination, her weight was 51 kgs (10th percentile), There was no icterus and no hepatosplenomegaly. Her liver function test showed bilirubin 0.6 mg/dl, SGOT- 84 IU/L, SGPT- 118 IU/L, total proteins of 7.6 gm/dl, albumin of 4 gm/dl, prothrombin time of 10 sec (control= 25 sec), partial thromboplastin time of 21.3 sec (control= 25). Ultrasound abdomen and doppler of portal system was normal. Her HBeAg antigen was positive (1194.9 units) and HBV viral load was 10,80,00,000 copies/ml. She was started on Adefovir. However, she continued to remain e antigen positive and HBV viral load was still elevated (1,092,078 copies/ml) at end of 2 years of treatment though her LFT had normalized. Her mutation analysis showed sensitivity to Lamivudine. She was continued on Adefovir and Lamivudine was reintroduced. However, even after 2 years, her HBV viral load was 40,97,589 copies/ml and e antigen was still positive. Thus, her therapy was stopped and she was advised follow up. In the next 3 months, her liver enzymes started rising again. She was later started on Tenofovir Disoproxil Fumarate.

How should this child be monitored on Tenofovir Disoproxil Fumarate?

Discussion:
Tenofovir Disoproxil Fumarate (TDF) is a nucleotide analog with excellent viral suppression and a good safety profile. TDF comes as a tablet or in powdered form which can be administered orally. It can be used either as primary therapy or as secondary therapy for patients having lamivudine resistance.[1] In a randomized controlled trial, to test the efficacy of TDF as compared to placebo, conducted on adolescents aged 12-18 years, it was found that TDF decreased HBV DNA in 89 percent of patients.[2] However TDF is found to be nephrotoxic causing renal tubular dysfunction and causes decrease in bone density.[3,4] Hence, renal function tests must be monitored before starting the therapy as well as during the therapy and caution must be taken while administering TDF along with other potential nephrotoxic drug eg NSAIDS.[5] Tenofovir should be avoided in children as it causes decrease in bone density, more in children.

Before initiation of therapy with tenofovir, the parameters to be checked include - HIV status, renal function tests, urine glucose, urine protein, serum phosphorus, bone density (in patients with a history of bone fracture or have risk factors for bone loss); liver function tests (to be done every 3 months during therapy and for several months after discontinuation of tenofovir), signs/symptoms of HBV relapse or exacerbation following discontinuation of therapy.[7] Children in whom antiviral therapy has been stopped, should be monitored every three months for at least one year to look for reactivation, flares or signs and symptoms of liver failure. For most patients, treatment with TDF should result in low viremia (HBV DNA <2000 IU/mL). In a few patients who do enter HBeAg-negative state during treatment with TDF (the inactive chronic HBV phase), the optimal duration of therapy is not clear. Practice in adults is to continue treatment for at least one year after seroconversion and sometimes indefinitely.[7,8]

Compliance with ethical standards
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Conflict of Interest: None

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