Asian Pacific Journal of Tropical Disease

journal homepage: http://www.apjtcm.com

Original article https://doi.org/10.12980/apjtd.7.2017D6-402

Hospitalized pediatric antituberculosis drug induced hepatotoxicity: Experience of an Indonesian referral hospital

Heda Melinda Nataprawira*, Ranti Astria Hannah, Hani Hilda Kartika

Departement of Child Health, Faculty of Medicine, Universitas Padjadjaran, Dr. Hasan Sadikin General Hospital, Bandung, Jl. Pasteur no. 38 Bandung, Indonesia 40163. 62-22-2034953/55

ARTICLE INFO

Article history:
Received 4 Nov 2016
Received in revised form 23 Nov 2016
Accepted 15 Apr 2017
Available online 12 May 2017

Keywords:
Antituberculosis drug induced hepatotoxicity
Tuberculosis treatment
Children
Risk factors

ABSTRACT

Objective: To determine the characteristics and risk factors of pediatric antituberculosis drug induced hepatotoxicity (ADIH) in Dr. Hasan Sadikin Hospital, a referral hospital in West Java, Indonesia.

Methods: Medical records of hospitalized pediatric ADIH from October 2010 to October 2015 were reviewed retrospectively through computer-based search. Descriptive data were presented as percentage. Analytical case-control study on characteristics of ADIH was conducted using *Chi*-square and Mann Whitney test.

Results: Fifty (3.5%) out of 1424 pediatric TB patients developed ADIH; 20 (40%) were boys and 30 (60%) girls. More than half were under 5 years old and 33 (66%) were malnourished. ADIH occured in 29 (58%) cases treated for pulmonary TB, 15 (30%) for extrapulmonary TB and 6 (12%) for both; 34 cases (68%) occured during the intensive phase. We identified hepatic comorbidities including CMV infection [1 (2%)] and typhoid [1 (2%)], and other diseases treated by hepatotoxic drugs such as chemotherapeutic drugs, antiepileptics, and antiretroviral drugs [9 (18%)]. Case-control analysis of 50 ADIH cases and 100 TB controls without ADIH showed that the correlation between gender, age, type of TB, nutritional status and comorbidities to occurence of ADIH was statistically insignificant (P = 0.26, 0.765, 0.495, 0.5349 and 0.336, respectively). Pediatric ADIH was treated using modified British Thoracic Society guidelines.

Conclusions: Pediatric ADIH in our hospital is quite frequent, thus identifying risk factors and development of pediatric guideline is mandatory. Further study is needed to identify other risk factors such as genetic acetylator status.

1. Introduction

Childhood TB along with the adverse effect of its treatment is a major health burden. Approximately one million children were diagnosed with TB worldwide in 2014, with Indonesia ranking second after India amongst countries with the highest burden of TB in the world[1]. Antituberculosis drugs are proved effective to eradicate TB, although they can cause some serious adverse events, namely, gastrointestinal disturbances, hepatotoxicity, rash, and fever[2,3]. Recently, the new increased dosage recommendations of the essential antituberculosis drugs (isoniazid, rifampicin and pyrazinamide) by the World Health Organization in 2010, although effective and well-tolerated by children, have also raised concerns regarding antituberculosis drug induced hepatotoxicity (ADIH)[4]. Adverse effects of antituberculosis drug such as hepatotoxicity may potentially cause significant morbidity and mortality as well as affect treatment compliance and outcome of TB treatment[3,5]. Isoniazid, rifampicin and pyrazinamide could all potentially cause varying severity of hepatotoxicity[1,3]. Hepatotoxicity, a serious and often fatal side effect of TB treatment, is otherwise known as ADIH/ATDIH[2,6], drug-induced hepatic injury[7], antituberculosis drug induced liver injury (DILI)[8,9], and antituberculosis drug induced hepatitis[10]. Clinical manifestation of ADIH could range from asymptomatic increase of serum transaminases and bilirubin, to acute liver failure[2,8,9].

The diagnosis of ADIH was made by the presence of clinical jaundice and/or raised serum total bilirubin level (> 1.5 mg/dL) and/or 3–5 fold rise of serum alanine aminotransferase (ALT) above normal levels in patients receiving antituberculosis therapy, in exclusion of known viral hepatitis (HBV, HCV), chronic liver disease, and liver dysfunction due to any other hepatotoxic

*Corresponding author: Heda Melinda Nataprawira, MD, Professor of Pediatrics in Universitas Padjadjaran, Pediatric Pulmonology Consultant in Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.
E-mail: heda_1155@yahoo.com
Tel: +62 811229294
The journal implements double-blind peer review practiced by specially invited international editorial board members.