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MAJOR PHARMACOLOGY

KEY WORD:

ANTITUBERCULOUS AGENTS / HEPATOTOXICITY / ALANINE TRANSAMINASE ENZYME (ALT) / TUBERCULOUS SHORT COURSE THERAPY

PAKAMARD TIANWAN : ALANINE TRANSAMINASE AND ANTITUBERCULOUS AGENTS-INDUCED HEPATOTOXICITY DUE TO SHORT COURSE THERAPY IN TUBERCULOUS PATIENT. THESIS ADVISOR : ASSO. PROF. VILAILAG IM-UDOM, DOCTORAT EN PHARM. THESIS CO-ADVISOR : LT. COL. SURAJIT SUNTORNTAM, MD. 110 pp. ISBN 974-332-831-9.

This prospective study is to determine the relationship of enzyme alanine transaminase level, parameter to indicate hepatotoxicity, in new, 15-45 years old, tuberculous patient in short course therapy of standard recommended antituberculous agents (isoniazid, rifampicin, pyrazinamide and/or ethambutol ) doses. The study is in a 60-bed hospital, Satuk Hoapital in Buriram, during March 1998 to July 1999. The patients have been followed up for 4 - 6 months after antituberculous therapy. Enzyme alanine transaminase (ALT) level is the parameter . The enzyme level were measured prior to drug treatment and after 2 weeks, 1, 2, 3, 4, 5 and 6 month treatment.

23 consecutive new tuberculous out-patient (age 32.18 years; 16 male, 7 female) has been conducted. 13% (3/23) of the patient have HBs antigen test positive value. Normal blood or urine sugar and normal blood pressure. The mean level ALT ( $\pm$ SEM) prior to drug treatment and after 2 weeks, 1, 2, 3, 4, 5 and 6 month treatment were 32.85 ( $\pm$ 4.31), 33.96 ( $\pm$ 3.65), 35.28 ( $\pm$ 5.43), 33.69 ( $\pm$ 4.86), 33.98 ( $\pm$ 3.39), 49.27 ( $\pm$ 16.09), 29.41 ( $\pm$ 2.94) and 28.77 ( $\pm$ 2.17) respectively. No sign such as jaundice etc. detected in this study.

Nonparametric statistics, Kruskal-Wallis test, is used. After the doses of antituberculous agents were given, ALT levels are not significantly different. In patient with abnormal baseline ALT, in patient with positive HBsAg test , in patient with pyrazinamide dose more than 30mg/kg/day, or in patient's age more than 35 years old. There are no significant different of ALT change and time after treatment.

The elevation of ALT more than 2 upper limit of normal (ULN) rate is not associate with gender, age, body mass index and dose of antitubercular agents. There are some evident that asymptomatic ALT elevation to 3 upper limit of normal ( $>100$ U.) but ALT level is reversible to normal level ( $<35$ U.) without monitoring intervention.

At present in Thailand, there is no liver function test in the medical practice of tuberculous short course therapy. In this study support the practice that no order for liver function test before and during usage of antituberculous agents short course therapy in the middle-age tuberculous patient is appropriate. If there is an evidence that abnormal liver function elevation , to keep patient follow more frequently without interrupt antituberculous agents at once is recommended. It might be useful for physician determine in drug monitoring.

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