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公益財団法人結核予防会
Japan Anti-Tuberculosis Association

Simultaneous quantification of first line anti-tuberculosis drugs in human plasma

Background

World Health Organization recommended a standard 6 month courses of 4 anti-tuberculosis drugs to treat for the new tuberculosis case. Of these, isoniazid, rifampicin, pyrazinamide and ethambutol are the most widely used as first-line treatments.

Although the majority of tuberculosis patients respond well to standardized short course regimen it has been shown that around 5 to 10 percentage of patients exhibited poor response to standard therapy, low plasma drug concentrations may contribute to clinical failure or relapse.

Method for measuring standard anti-tuberculosis drug concentrations is necessary to facilitate early screening of therapeutic failure

We aim to develop and validate a sensitive, specific and reproducible LC-MS/MS method of first line anti-tuberculosis drug in human plasma.

Experiment

Plasma sample containing isoniazid, pyrazinamide, rifampicin and ethambutol.

Samples with the spiked drug standards were extracted using protein precipitation.

- Liquid chromatography and amide column separated all drugs in acid condition and detected with mass spectrometry within 3 minute/sample.
- Quantification was achieved by multiple reaction monitoring (MRM) in positive ion mode.

Integration of peak area and data analysis was performed using QuanLynx V4.1 software.

Output

The established simple, rapid and sensitive method for simultaneous determination of rifampicin, isoniazid, pyrazinamide and ethambutol concentrations in human plasma will facilitate therapeutic drug monitor (TDM) for anti-tuberculosis drugs in Thailand.

Outcome

TDM has already been recommended in difficult TB patients such as those with HIV infection, Diabetes, Malnutrition and those who poor response to standard therapy. The developed method will be useful for individualized approach for optimization dosage adjustment of anti-tuberculosis drugs to achieve best therapeutic effect and to avoid adverse drug reactions.

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