Enriching medication review with a pharmacogenetic profile: a case of tamoxifen adverse drug reactions

C. Jeiziner¹, C. K. Stäuble², Markus L. Lampert¹, Kurt E. Hersberger¹, H. E. Meyer zu Schwabedissen²

¹ Pharmaceutical Care Research Group, Department of Pharmaceutical Sciences, University of Basel, 4001 Basel, Switzerland
² Biopharmacy, Department of Pharmaceutical Sciences, University of Basel, 4056 Basel, Switzerland

Introduction

Pharmacogenotyping is applied to determine the hereditable component of a patient’s susceptibility to experience therapy failure and/or adverse drug reactions (ADRs). We present the case of a female patient diagnosed with breast cancer and treated with tamoxifen as recurrence therapy who experienced various ADRs.

Methods

After an initial medication review by a pharmacist, pharmacogenetic panel testing was conducted applying the commercial test Stratipharm® by humatrix AG (Pfungstadt, Germany). The Stratipharm® tool provides not only the results of genetic testing, but also drug-specific interpretation of the corresponding phenotype (pharmacogenetic profile) according to available evidence, see Figure 2 for warning levels.

Results

We gathered the patient’s medication (see Table 1), analyzed the pharmacogenetic profile revealing variants in three cytochrome P450 (CYP) enzymes (see Table 2), and gave recommendations (see Figure 3).

![Figure 1: The major metabolite of tamoxifen is formed by demethylation catalyzed by CYP3A4 among other CYPs. The metabolite N-desmethyl-tamoxifen is then oxidized by CYP2D6 to endoxifen, which is up to 100 fold more active than tamoxifen. (adapted after Klein et al. PharmGKB, 2013)]

![Figure 2: Warning levels by Stratipharm®: normal; indication; suspicion; danger](Image)

![Figure 3: Drug boxes with PGx result (result of pharmacogenotyping); Note: There are no pharmacogenetic data for mistletoe preparation, metamizole and lorazepam.](Image)

![Table 1: Patient’s medication at the time of the medication review](Table)

![Table 2: Pharmacogenetic profile of the patient](Table)

![Tamoxifen: CYP2D6 Intermediate Metabolizer](Note)

![Ibuprofen: CYP2C9 Intermediate Metabolizer](Note)

![Pantoprazole: CYP2C19 Ultrarapid Metabolizer](Note)

Conclusion

As a result of this pharmacist-led medication review supplemented with pharmacogenetic panel testing, concrete genotype-driven recommendations for the treating gynecologist were compiled. Contrary to our expectations (due to the patients’ experienced ADRs), the pharmacogenetic profile revealed that tamoxifen was probably not sufficiently activated in the patient, thereby resulting in ineffectiveness. This case revealed the added value of a large pharmacogenetic panel test and the complexity of integrating a pharmacogenetic profile into a recommendation.

Author

Chiara Jeiziner
chiara.jeiziner@unibas.ch
Pharmaceutical Care Research Group, University of Basel
Postfach 2148; 4001 Basel, Switzerland
www.pharmacare.unibas.ch

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