Practical implications of pharmacogenetics in antidepressant treatment

The case of amitriptyline

Metabolism, a key player in the dose-exposure-response chain, is a focus of promising genetically-oriented investigations underpinning the usefulness of genetic testing in the pharmacokinetic field. Several pharmaceutical companies are today integrating pharmacogenetic aspects in product labels and actionable genotype-guided dosing recommendations are available. Conversely, many questions related to the implementation of personalised psychiatric therapy remain unanswered.

Is genotyping apt to determine the metaboliser status of patients receiving treatment for depression and translate biomarkers into personalised medicine?

Can pharmacogenetics support the re-evaluation of tricyclic antidepressants with respect to effectiveness and safety, compared to newer, more expensive drugs?

Should there be harmonisation at International, European and National level, in terms of what pharmacogenomic information is listed in drug labels?

OBJECTIVES

Investigate the incidence and impact of genetic polymorphisms in patients receiving treatment for depression in Malta

Determine allele frequencies of both CYP2D6 and CYP2C19 and examine potential additive effects which would support combined dosing recommendations

Evaluate genotype-phenotype association in relation to metaboliser status, measured blood drug/metabolite concentrations and clinical outcome

Assess feasibility and clinician perception of pharmacogenomic-guided individualisation of treatment for depression, compared to the current standard of psychiatric care

Analyze effect of regulatory initiatives in supporting the implementation of pharmacogenomics in drug surveillance and clinical practice

Pharmacoeconomic analysis of routine genotyping and worth of engineering point-of-care tests

STUDY DESIGN


Results interpreted in line with gene/drug clinical practice guidelines

Potential recommendations, if any, for treatment plan revision

Clinical outcomes observed on patient follow-up

Retrospective Analysis

Past hospitalisations related to depression or adverse events from its treatment and the antidepressant switching strategies adopted.

Standard of Care

Drugs with pharmacogenomic recommendations being prescribed at one time and the dose differences with respect to metaboliser status.

Are non-extensive metabolizers being prescribed regular doses or are physicians empirically identifying patients with aberrant metabolism?

Prospective Correlations

The total range of variables encountered is included in the statistical analysis, combining both genetics and environmental factors such as age and age of onset, lifestyle, comorbidities, and concomitances with special focus on concomitant CYP inhibitors, in attempt of explaining an appreciable percentage of variation.

Further Observations

Comparison of genotyping techniques, clinician disposition in implementing pharmacogenetic-guided dosing recommendations, and the implications of the evolving regulatory context, particularly referral procedures assessed by the European Medicines Agency and review of pharmacogenomic data in national authorisations.

References