Biomarker assay to enable safe corticosteroid withdrawal

Using hypothesis-free metabolomics screening, a list of seven biomarkers has been identified that, when combined, are highly sensitive in predicting corticosteroid dose and, thus, the risk of adrenal insufficiency on corticosteroid withdrawal. Quantitative assays for these metabolites will create a ‘kit assay’, which can be commercially developed for clinical use.

Predicts risk of adrenal insufficiency as a side effect of corticosteroid treatment

Test consists of measuring a small panel of biomarkers

Relies on use of liquid chromatography-mass spectrometry (LC-MS) for analysis

Tests pharmacodynamic rather than pharmacokinetic parameters

A simple alternative to the relatively insensitive and time-consuming assays currently in use, e.g. SynACTHen test

Can be developed into a ‘kit assay’ for clinical use

Ability to carry out testing at most clinical labs due to the common use of LC-MS

Measures corticosteroid overtreatment more effectively than current steroid day curve measurements

The Challenge

Corticosteroids are the 2nd most commonly prescribed class of drugs, behind NSAIDs, and are used for a wide range of inflammatory conditions. However, they have numerous side-effects, including adrenal insufficiency (AI), even for low dose corticosteroids. Diagnosing AI is difficult and expensive, and relies on the SynACTHen test, which is not routinely performed, leading to substantial under-diagnosis of AI. Pharmacokinetic monitoring of corticosteroids is unreliable, and no pharmacodynamic test exists to detect corticosteroid side effects. A pharmacodynamic test would also be useful for dose adjustment in patients receiving corticosteroid replacement therapy and for screening in patients with suspected Cushing’s syndrome.

Technology

Seven key biomarkers have been identified from metabolomics screening of patient samples. These biomarkers are measured using standard LC-MS techniques and can provide pharmacodynamic information of corticosteroid over-treatment from patient samples. This allows optimization of the corticosteroid dose regime for each patient, prediction of adverse effects of overtreatment, including adrenal insufficiency, and improvement of the diagnosis of Cushing’s syndrome.

Exemplification Data

Using LC-MS metabolomic screening on plasma samples from 117 individuals with congenital adrenal hyperplasia (taking known doses of corticosteroids), the analysis demonstrated a clear cut-off in dose-response relationships, such that the metabolome distinguished doses above or below the equivalent of 5 mg of prednisolone each day (the physiological replacement dose).

Applications

- Medical devices
- Diagnostic/assay kit

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