Case report: Non-response to fluoxetine in a homozygous 5-HTTLPR S-allele carrier of the serotonin transporter gene.

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We report the case of a 50-year-old male with major depressive disorder (MDD) to illustrate the challenge of finding effective antidepressant pharmacotherapy and the role that the patient's genetic makeup may play. Recent treatment attempts before clinic admission included venlafaxine and fluoxetine. Venlafaxine was discontinued due to lack of response, and subsequently switched to fluoxetine based on pharmacogenotyping of the P-glycoprotein transporter (P-gp, encoded by; ABCB1;) by the outpatient psychiatrist. Despite steady state serum levels within the therapeutic range, the patient did not benefit from fluoxetine either, necessitating admission to our clinic. Here a clinical pharmacist-led medication review including additional pharmacogenetic (PGx) analysis resulted in the change of the antidepressant therapy to bupropion. Under the new regimen, established in the in-patient-setting, the patient remitted. However, based on the assessed pharmacokinetics-related gene variants, including; CYP; s and; ABCB1; , non-response to fluoxetine could not be conclusively explained. Therefore, we retrospectively selected the serotonin transporter (SERT1, encoded by; SLC6A4;) for further genetic analysis of pharmacodynamic variability. The patient presented to be a homozygous carrier of the short allele variant in the 5-HTTLPR (S/S) located within the; SLC6A4; promoter region, which has been associated with a reduced expression of the SERT1. This case points out the potential relevance of panel PGx testing considering polymorphisms in genes of pharmacokinetic as well as pharmacodynamic relevance.

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