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Polygenetic Risk Scores and Metabolic Side Effects in Clozapine Treatment of Schizophrenia

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Background: A substantial proportion of patients with schizophrenia do not respond to atypical or typical antipsychotics. A trial of clozapine should be considered for these patients although its use is associated with a low risk of serious adverse side-effects like agranulocytosis, ileus, weight-gain and diabetes. Clozapine is the only available drug of choice for treatment-refractory patients on usual antipsychotic treatment. We compared polygenetic risk scores associated with schizophrenia with regard to treatment-resistance and clozapine response.

Method: We identified 1191 patients with psychotic disorders. Of these 709 patients had a confirmed diagnosis (SADS-L) of schizophrenia (SZ) or schizoaffective disorder (SZA).

Results: We could confirm that 197 patients with a SZ or SZA diagnosis (28%) had been on clozapine. For most of these polygenetic risk scores could be calculated. Among these, 146 patients remained alive and still on clozapine (74%). Numerically polygenetic risk scores were lower for those ever on clozapine (n=193) compared with 431 SZ & SZA patients never on clozapine, but nonsignificantly so. Numerically those still on clozapine (mean time 14.1 years) had a lower polygenic score than those no longer on clozapine (mean time 2.5 years) but the difference was non-significant. Risk of diabetes type 2 had a standardized morbidity ratio of 3,9 for women and 1,9 for men in the sample. Polygenetic scores associated with body mass index (BMI) in this cohort are currently being prepared for analysis.

Conclusion: Polygenetic risk scores associated with SZ did not differ with regard to treatment resistance and response to clozapine treatment.

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