Clinical and biochemical study of d-serine metabolism among schizophrenia patients

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Abstract:

Schizophrenia is a typical N-methyl-d-aspartate receptor (NMDA-R) hypofunction disorder. Decreased d-serine (d-Ser) levels in the periphery occur in schizophrenia and may reflect decreased availability of d-Ser to activate NMDA-R in the brain. Objective: The objective of this study was to investigate the role of d-Ser metabolism in the pathogenesis of schizophrenia via biochemical assays and correlates, the serum level of d-Ser, d-serine racemase (SR) (responsible for its formation from l-serine [l-Ser]) and d-amino acid oxidase (DAAO) (responsible for its catabolism), among different clinical types of schizophrenia patients. Patients and methods: This cross-sectional case/control study was carried out on 100 patients and 50 controls. They were recruited from the outpatient psychiatric unit of the Neuropsychiatric Department of Assiut University Hospital, Upper Egypt. The type of schizophrenia was determined according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), while the severity of schizophrenia was determined according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Serum d-Ser levels were estimated using high-performance liquid chromatography (HPLC), while serum SR and DAAO were measured using commercially available enzyme-linked immunosorbent assay kits. Results: There were significantly lower mean serum levels of d-Ser and SR and significantly higher mean serum levels of DAAO (P-value <0.01 for each) among schizophrenia patients when compared with the control group. Paranoid schizophrenia had the highest frequency, with a significantly lower serum levels of d-Ser and SR in the residual type and significantly higher serum levels of DAAO in undifferentiated and catatonic types. Combined receiver operating characteristic curve for serum d-Ser, SR and DAAO indicated that the best serum level cutoff points at which schizophrenia manifestations started to appear were ≥61.4 mg/L for d-Ser, ≥15.5 pg/mL for SR and ≥35.6 pg/mL for DAAO. Conclusion: The present study confirms that disturbed d-Ser metabolism could be implicated in the pathogenesis of schizophrenia.

Keywords:

d-serine, serine racemase, d-amino acid oxidase, schizophrenia, HPLC

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