RED BLOOD CELL MEMBRANE FATTY ACID ANALYSIS IN NEVER-MEDICATED FIRST-EpISODE AND CHRONIC MEDICATED-SCHIZOPHRENIC PATIENTS

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INTRODUCTION

Reduced n-3 and n-6 polysaturated fatty acids (PUFAs) content in red blood cell (RBC) membranes and abnormal membrane phospholipid metabolism were repeatedly implicated in the etiology of schizophrenia. Reduced levels of PUFAs in RBC membranes were found both in drug-naïve first-episode schizophrenic patients and chronically ill, medicated ones. Reduced PUFa level, namely docosahexaenoic (DHA, 22:6n-3) and arachidonic (AA, 20:4n-6) acids, in the brain and RBCs of schizophrenic patients was accompanied with increased activity of phospholipase A2 (PLA2) enzymes in the temporal cortex and serum. The object of the study was to compare the phospholipid fatty acid (PLFAs) profile of RBC membranes between groups of schizophrenic patients and non-psychiatric controls. Based on given FAs profiles, we aimed to assess the status of lipid homoeostasis in the RBC membrane PLs and the direction of the desaturase enzyme activities in our subjects.

PATIENTS AND METHODS

Gas-chromatography analysis of fatty acids content in RBC was performed in the group of non-psychiatric controls (Group 1; N=16), never-medicated first-episode schizophrenic patients (Group 2; N=6), and chronic medicated patients (Group 3; N=23). Differences between groups of subjects were investigated using nonparametric Kruskal-Wallis ANOVA and Median test, and the analysis of covariance (ANCOVA). Group, gender and smoking status were used as categorical predictors, while body mass index (BMI) and age were used as covariates in the ANCOVA analysis. The level of statistical significance was set to 0.01. All statistical analyses were conducted using the Statistica software package for Windows, StatSoft, Inc., (2008), Version 7.1.

RESULTS

RBC membranes of schizophrenic patients (both first-episode and chronically ill) significantly differed from non-psychiatric controls in fatty acid (FA) content and values of calculated indexes. Kruskal-Wallis ANOVA test additionally showed significantly reduced level of EPA (20:5n-3) in the membrane phospholipids of chronic medicated-schizophrenic patients compared to controls, decreased DHA/AA (22:6n-3/20:4n-6) ratio in the first-episode patient and increased delta-6-desaturase (DDO) index and D6D/DDO ratio in chronic medicated patients. Using ANCOVA analysis, first-episode and chronic medicated groups of patients (Groups 2 and 3) could be significantly distinguished only for 22:5n-3 fatty acid content. First-episode schizophrenic patients were found significantly differed in stearoyl-CoA desaturase index (18:1n-9) and oleic acid (18:1n-9), while in the majority of cases it was possible to significantly distinguish healthy controls from schizophrenic patients regardless of illness duration or medication treatment (group 1 from pooled groups 2 and 3) for essential linoleic acid (LA, 18:2n-6), DHA (22:6n-3), n-3 FAs and n-6 FAs content, saturated (SFA) and polysaturated fatty acids (PUFA) content, values of several indexes such as stearoyl-CoA desaturase index (D9C18), double bond index (DBI), peroxidizability index (PI), and DBI/ACL (average chain length) ratio. ANCOVA further revealed a significant association between monounsaturated fatty acid (MUFa) content, PUFa/MUFa ratio and ACL, and BMI. Gender, age and nicotine usage did not significantly affect the fatty acid content of the RBC membranes in our sample.

CONCLUSIONS

1. The results confirmed a disturbance of lipid homoeostasis in RBC membranes as an intrinsic feature of schizophrenia (found both in first-episode and chronic medicated schizophrenic patients) and PUFA deficit (of both n-3 and n-6 series). Probable causes might be:

   a) deprivation of PUFAs from diet - which was shown to alter expression of AA and DHA signaling cascades in rat frontal cortex increasing PLA2, and COX-2 activities;
   b) the conversion rate of essential fatty acids to long-chain forms - which largely depended on the activity of the rate-limiting enzyme delta-6-desaturase - D6D;
   c) lower activity of stearoyl-CoA desaturase - D9C18 - that is indicative of increased energy expenditure and reduced lipogenesis in the liver;
   d) the presence of oxidative stress - revealed as decreased DBI, PI, and PUFa/SFA ratio.

2. Reduced LA, EPA, DHA, n-3, n-6 FAs, and PUFA content, increased SFA content, decreased DHA/AA and PUFa/SFA ratios, and decreased PI and DBI and D9C18 indexes were found regardless of illness duration and antipsychotic treatment.

3. Drugs affecting fatty acid metabolism and providing the recovery of lipid homoeostasis in the cellular membranes, along with specific medical nutrition therapies, might have beneficial effects in schizophrenia.

References


Acknowledgements

This work was supported by the Croatian Ministry of Science, Projects No. 062-00000002-021 and 062-0982522-0369.