SUMMARY

The life span in schizophrenia is shorter by 20% as compared to the rest of the population. Patients with schizophrenia suffer from somatic morbidity and mortality more than the general population. Patiens with schizophrenia die of cardiovascular diseases twice more often than non-schizophrenic subjects. Cardiovascular mortality in schizophrenia recently increases as against the general community. The reason is the life style characterized with a lack of movement, wrong dietary habits, smoking, and insufficient somatic care of schizophrenic patients. Adverse effects of neuroleptic drugs also play a role in this process. Even if modern medicaments – second generation antipsychotics - are recently available, cardiovascular morbidity and mortality in schizophrenia escalates.

In the assessment of the treatment results in mentally ill people, the total effectiveness of therapy, quality of life of the patients, and their subjective satisfaction with the treatment are emphasized nowadays. Recently the adverse effects of psychiatric medication are studied comprehensively. We also take into account these adverse effects, which have been neglected so far. Venous thromboembolism and other cardiovascular complications due to neuroleptic treatment belong to them.

Venous thromboembolism (VTE) in patients treated with antipsychotic medication has been documented from its beginning in the 1950s. An increased attention has been paid to this topic in the last decade. Recent scientific evidence is mostly based on observational studies and case report series. An increased risk for VTE is associated with therapy with clozapine or low potency first generation antipsychotics. In addition to this, reports on VTE induced by other second generation antipsychotics (olanzapine, risperidon) become more frequent in the literature. The most imporatnt risk of a pathological blood clotting occurs in the first three months after the antipsychotic drug is prescribed.

Sedation, obesity, antiphospholipid antibodies, increased activation and aggregation of thrombocytes, hyperhomocysteinemia and hyperporlactinemia belong to possible etiopathogenetic factors in venous thromboembolism. The diagnosis of schizophrenia or bipolar affective disorder itself, hospitalization or stress with activation of the sympathetic nerve and increase in catecholamine blood level also act as prothrombogenic factors. Prospective studies are necessary to clarify biological mechanisms involved in the association of antipsychotics with venous thromboembolism.

The aim of the described ANTRE (ANtipsychotics, Thrombosis, Embolism) project is to study the problem of venous thromboembolism in patients treated with antipsychotics. In the epidemiological analysis *(part I)*, we ascertained an increased exposition to antipsychotic treatment in VTE patients in comparison with subjects with arterial hypertension (odds ratio 2.76; 95% CI = 1.01-7.55). In a series of VTE vignettes induced by olanzapine, we focused on finding relevant risk factors. We suggested possible mechanisms of VTE etiopathogenesis in patients treated with olanzapine as well as other antipsychotics *(part II)*. We compiled the so far missing guidelines for VTE prevention in hospitalized psychiatric patients *(part III)*, verified and adjusted them in a routine clinical practice (part *IV)*. The prospective study *(part V)* will make evaluation of etiopathogenetic mechanisms of pathological blood clotting in patients with schizophrenia possible. We compare hemostatic, coagulation, immunological, and biochemical variables before and three months after the start of antipsychotic pharmacotherapy in psychotic patients, and in a group of healthy volunteers without antipsychotic treatment. The results of the pilot study support the paradigm of the presence of a pro-coagulatory state in an acute psychosis, and the possible influence of antipsychotics on thrombogenesis.