Should psychosis be treated with tPA like a stroke? Evidence for pathological coagulopathy in psychosis

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Background

Schizophrenia and related psychosis spectrum disorders are heterogeneous illnesses with many proposed underlying genetic and environmental etiologies. Many published studies report that antipsychotic therapy is associated with a state of hypercoagulability. However, fewer studies have examined whether increased coagulability exists in unmedicated schizophrenia (SZ) or other psychoses. Some studies have reported a full remission of psychotic symptoms with warfarin, a well-known anticoagulant, raising the possibility that psychosis may be associated with coagulopathy.

Objective

The present review describes the available literature on biomarkers of coagulopathy in patients with SZ and other psychoses, raising the possibility that anticoagulant therapy may represent a novel therapeutic strategy in schizophrenia.

Methods

A PubMed search using the keywords “psychosis” OR “schizophrenia” AND (“coagulation” OR “tissue plasminogen activator” OR “thrombomodulins”) for studies published between 2012 and 2023 yielded 290 results. Studies were included for final analysis if they were (1) controlled studies; (2) reported on individuals with a clinical diagnosis of schizophrenia or psychoses related to psychiatric illness; (3) in the English language. Studies were excluded from review if they (1) were review articles; (2) case reports; (3) animal studies; (4) focused on antipsychotics as a factor in coagulopathy.

Results

Seven studies met study criteria and were included for qualitative synthesis. Five included patients with SZ and related psychoses, while two also included patients with major depression and bipolar disorders. Numerous plasma proteins involved in regulating coagulation were identified as being low in patients with SZ, including thrombolytic agents such as tissue plasminogen activator (tPA), plasmin, protein S, and plasminogen, although one study found that tPA was reduced in chronic SZ but elevated in first-episode SZ (FES). Contributing to hypercoagulability, FES patients had elevated levels of plasminogen activator inhibitor-1 (PAI-1) and soluble P-selectin (sP-sel), as well as a higher PAI-1/tPA ratio. The risk of deep vein thrombosis and pulmonary embolism was found to be increased not only in SZ but depressive and bipolar disorders. SZ patients had a high prevalence of markers of low tPA/plasmin, including hyperinsulinemia, hypertriglyceridemia, hyperhomocysteinemia, and antiphospholipid antibodies, all of which decrease or increase tPA or PAI-1 activity, respectively. Patients with psychosis spectrum disorders presenting with acute psychosis had increased markers of thrombogenesis, including plasma levels of D-dimers, factor VIII, and sP-sel, which remained elevated one year after medication initiation.

Limitations

Most studies included some patients that were not antipsychotic naïve; most did not control for potential confounding factors (BMI, mobility, smoking status, etc.).

Discussion

Taken altogether, these findings suggest that the association between hypercoagulability and psychosis spectrum disorders may not be purely iatrogenic in nature but a persistent feature of the disease. Further studies are warranted to confirm this hypothesis.

References