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• Forum •

Treatment of prodromal schizophrenia

To cure sometimes, to relieve often, to comfort always

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Schizophrenia is a severe mental disorder that affects approximately 1% of the population worldwide. It is associated with major clinical and psychosocial morbidity and places significant burden on the affected individuals, their families and society.[1] Research in the past two decades has convincingly demonstrated that tertiary prevention in schizophrenia is possible and that decreasing the delay in the initiation of treatment can improve clinical and functional outcomes.[2] This finding has led to increased interest in testing the feasibility of secondary prevention focussed on individuals who are at high-risk of developing schizophrenia. In an attempt to capture the clinical profiles of such individuals, different operationalized definitions have been proposed such as At Risk Mental States (ARMS), Attenuated Psychotic Symptoms (APS), Brief Limited Intermittent Psychotic Symptoms (BLIPS), Ultra High Risk Individuals (UHR),[3,4,5] Early Initial Prodromal States (EIPS) and Late Initial Prodromal States (LIPS).[6] The common theme across these definitions is the presence of functional impairment and subthreshold psychotic symptoms. The forum piece by Zhao and colleagues[7] mentions one of these on-going efforts: the psychosis task force of the American Psychiatric Association (APA) had considered the inclusion of 'Attenuated Psychosis Syndrome'(APS) as a new diagnostic entity in DSM-5 (www.dsm5.org).

Many studies have been conducted to validate these concepts.[4,5] The emerging consensus is that the predictive validity of the high-risk status is poor since, regardless of the definition used, less than 40% of individuals considered high-risk will convert to syndromal schizophrenia or a schizophrenia spectrum disorder.[5,7,8] Moreover, the reported conversion rates are lower in the more recent publications.[7] A considerable percentage of non-converters (15-54%) remit fully;[8] the remainder are likely to be diagnosed later with non-psychotic disorders, particularly anxiety disorders and substance use disorders.[9] In addition, the reliability of the APS in the DSM-5 field trial[10] was poor; screening of unselected psychiatric patients using the APS criteria did not result in the identification of a unique clinical population.[11] Finally, epidemiological studies have suggested that psychotic-like experiences,when present in young individuals, are usually transitory and may be considered a variation in normal developmental trajectories.[12] A fundamental argument for adopting any formal clinical diagnosis is that there is a 'sufficient amount of etiological and prognostic homogeneity among patients belonging to a given diagnostic group so that the assignment of a patient to this group has probability implications which it is clinically unsound to ignore'.[13] It could be argued that none of the definitions for subsyndromal psychotic states used to date satisfies this fundamental principal and, therefore,that the clinical utility of APS and related syndromes remains questionable.

There are eight studies that have focused on the effect of pharmacological, psychological, or combination treatments on the clinical and functional outcomes of individuals considered at high risk for schizophrenia.[5,14,15] Taken together, these studies suggest that focused treatment is modestly effective in reducing the rates of conversion to psychosis compared to no treatment or treatment as usual (Relative Risk=0.36; 95%CI: 0.22-0.59).[14] However, this advantage appears to dissipate 2-3 years following treatment cessation.[5,14] Unfortunately, the heterogeneity of the interventions used in these studies makes it impossible to arrive at any evidence-based recommendation for a specific type of treatment. Nevertheless, all of the interventions led to some degree of symptomatic improvement.[5,14]

In summary, it could be argued that efforts to identify 'prodromal schizophrenia' have largely failed. Focused interventions in people currently identified as high-risk for schizophrenia, be they pharmacological or psychological, have failed to produce the disease-modifying results hoped for. Thus, early intervention for secondary prevention for schizophrenia remains beyond our reach.

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In a climate of limited (and in many cases reducing) treatment resources for chronic mental health disorders such as schizophrenia, having separate services for high-risk individuals may prove a public health experiment that we cannot afford to support. Nevertheless, help-seeking patients with psychotic features deserve our attention and care even when they do not fulfil any diagnostic criteria.

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