Relapse in Schizophrenia

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Introduction

Schizophrenia is characterised not only by its florid and extraordinary positive symptoms, but also negative and disorganisation symptoms; these symptoms affect almost all aspects of mental function in emotion, language, motor, as well as perception and reasoning. Clinical observations have suggested that there are a great variety of courses and outcome in schizophrenia. The premorbid and prodromal phase refers to the period prior to illness onset in which vulnerability traits or subclinical symptoms are expressed, respectively. First-episode psychosis refers to the period when a patient presents with a diagnosable psychotic disorder for the first time, usually characterised by frank psychotic symptoms of hallucinations, delusions and behavioural disturbances.\(^1\)

Outcome is often conceptualised in terms of remission, recovery and relapse. Remission is a state when these psychotic symptoms subside. Recovery is remission from psychotic symptoms, as well as attaining adequate social and occupational functioning where some patients can achieve. Relapse is usually defined as the re-emergence of psychotic symptoms. A 20-year follow-up of the Madras study showed that about 40% of patients relapsed with complete remission in between, 44% relapsed with partial remission in between; and only 8% had complete remission.\(^2\) Importantly, this long-term follow-up study indicated that the level of disability incurred is high and relapse is the typical pattern. This article will first introduce the concept of relapse and its associated costs, followed by investigating both naturalistic and controlled studies on the risk of relapse. It will end with a brief discussion on the important clinical decision concerning medication discontinuation and relapse.

Defining Relapse

Relapse can be defined more broadly or more narrowly. Narrow definition of relapse involves the definite re-emergence of psychotic symptoms associated with significant disturbance in functioning and social behaviour.\(^3\) According to Johnstone, relapse could also be defined as Type I, the reappearance of schizophrenic symptoms in a patient who has been free of them following the initial episode, and Type II, the exacerbation of persistent positive symptoms.\(^4\) Clinical instruments such as the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impressions (CGI) and the Brief Psychiatric Rating Scale (BPRS) are often used for operationally defining relapse.

In response to these diverse approaches in measuring symptoms, some researchers adopt a broader definition of relapse, such as ‘rehospitalisation’ being a proxy for relapse.\(^5\)\(^,\)\(^6\) However, rehospitalisation can result from a much wider range of other clinical scenarios such as suicidal attempt, violence, medication side effects, and thus relapse is only one of the many possible causes for rehospitalisation. In reality, rehospitalisation is usually the most expensive part in the mental health cost for psychotic patients, the measurement of rehospitalisation would be most relevant in health economics considerations.\(^7\)

Relapse Costs

Consequence of relapse can be enormous. Medical costs, non-medical costs and productivity losses associated with relapses are enormous from the economic perspective.\(^8\)\(^-\)\(^11\) Studies have found that patients have a poorer response to treatment in subsequent relapse episodes, as well as a longer time to remission with each subsequent episode.\(^12\)\(^-\)\(^14\) To the patients, a relapse with re-emergence of psychotic symptoms may imply the necessity of staying on medication for a considerably longer period of time or even on a long-term basis. This fact could be particularly devastating to a young patient who has been making an otherwise smooth recovery from his or her first-episode illness.\(^15\)

Relapse Rates: Naturalistic and Controlled Studies

Relapse rates in schizophrenia have been studied extensively in both naturalistic and controlled studies. Despite the fact that studies varied in relapse definitions and duration of follow-up, the risk of relapse is still high. Naturalistic studies have found that the cumulative relapse rate was 70%–82% up to 5 years following the first admission or episode.\(^16\)\(^-\)\(^17\) In Hong Kong, a naturalistic longitudinal follow-up study of 93 first-episode psychosis patients found that relapse rates were 21%, 33%, and 40% in the first, second and third year respectively.\(^18\) Conclusions drawn from naturalistic studies, however, failed to exclude the fact that the high relapse rate is a result of medication discontinuation where it is not uncommon in patients with psychotic disorders.\(^19\)\(^-\)\(^20\)

In contrast, double-blind randomised placebo-controlled trials where discontinuation was controlled,
have shown that early discontinuation of antipsychotics therapy results in more relapses at 1 year: 63% vs 36%, 21
61% vs 27%, 22 41% vs 0%. 23 In Hong Kong, relapse was studied in a randomised controlled trial on remitted first-episode psychosis patients who have been on maintenance medication for at least 1 year. It was found that relapse rates for those discontinuing medication was 79% while continuing medication was 41%. 24 These findings all point to the importance of continuing medication in preventing relapse.

Consideration of Medication Discontinuation

Discontinuing medication is tempting and seems logical to many patients when their psychotic symptoms have subsided, and is consistent to our usual conceptualisation of recovery. Although antipsychotic maintenance treatment seems to be effective in preventing relapse, 25-26 controlled studies suggested that the subsequent rate of relapse could be substantial even on maintenance medication. 21-24 Long-term maintenance therapy is also increasingly recognised as a costly option, as it could lead to substantial long term metabolic or neurological side-effects, as well as psychological and economic consequences. 25 The clinical decision on whether to continue the medication is hence complex. To patients and their families, the uncertainty and psychological burdens surrounding potentially lifelong continuation of medication may also be substantial. In brief, medication discontinuation should be a joint and planned decision involving the patients, the carers and the clinicians. The clinicians should discuss openly with the patients all the possible options and consequences, and also look beyond the short-term risk and focus on the long-term health risks and benefits for the patient. After all, there is a small proportion of patients who could potentially remain relapse free even without maintenance medication.

References