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Predictors of favourable outcome in young people with a first episode psychosis without antipsychotic medication

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ABSTRACT

Introduction: Data from the literature suggests that some first episode psychosis (FEP) patients may recover without antipsychotic medication. There is however no reliable way to identify them. In a previous paper we found, in a cohort of 584 FEP patients, that those consistently refusing medication had poorer pre-morbid functioning, less insight, higher rate of substance use and poorer outcome. However, some medication refusers, had a favourable outcome. The study aim was to identify predictors of good short term outcome despite non-exposure to medication.
Methods: The Early Psychosis Prevention and Intervention Centre (EPPIC) admitted 786 FEP patients between 1998 and 2000. Data were collected from patients' files using a standardized questionnaire. Data on medication adherence was available in 584 patients. Among the 17.9% of patients who consistently refused medication over the entire treatment phase we compared patients who had a favourable symptomatic and functional outcome with those who did not.
Results: Among patients who consistently refused medication, 41% achieved symptomatic remission and 33% reached functional recovery. Predictors of symptomatic remission were a better premorbid functioning level, higher education and employment status at baseline. Predictors of functional recovery were a shorter duration of the prodrome phase, less severe psychopathology at baseline and lower cannabis use.
Conclusions: Despite limitations mainly linked to the fact that non-exposure to antipsychotic medication was based on patient's treatment refusal, this study identified some characteristics which may contribute to the identification of a sub-group of FEP patients who may have good short term outcome without antipsychotic treatment.

1. Introduction

Risk and benefit ratio should always guide treatment choice in medicine. The staging approach recently proposed for early intervention in psychiatry defines discrete stages of illness development where treatment needs may be different (McGorry, 2007; McGorry et al., 2006, 2008). In regards to antipsychotic medication, the idea of minimizing side-effects while reaching symptom remission at low doses was emphasised during the development of early intervention centres, and is reflected in the current guidelines for the treatment of early psychosis (International Early Psychosis Association Writing Group, 2005; Lambert et al., 2003; NICE, 2014). However, the widespread implementation of early detection strategies has led, over the years, to the reduction in duration of untreated psychosis (DUP) (Chan et al., 2016; Marshall et al., 2014). This reduction in the DUP has led to a change in the clinical profile, with young people presenting with less severe psychotic symptoms and a lower level of deterioration in functioning (Chen et al., 2011). It is possible that this earlier clinical presentation may warrant a different treatment approach.

Abbreviations: CGI, Clinical Global Impressions; DUP, duration of untreated psychosis; EPPIC, Early Psychosis Prevention and Intervention Centre; FEP, first episode of psychosis; FEPOS, First Episode Psychosis Outcome Study; GAF, Global Assessment of Functioning; MLCI, Modified Location Code Index; MVSI, Modified Vocational Status Index; NA, Never received adequate dose of antipsychotic medication; OR, Odds ratio; SCID, Structured Clinical Interview for DSM; SOFAS, Social and Occupational Functioning Assessment Scale; SUD, substance use disorder.

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The earlier stage of a mental health disorder is an ideal opportunity to provide safer, more acceptable, affordable and effective interventions (McGorry et al., 2007). For example, psychological and psychosocial interventions have been demonstrated to reduce the severity of psychotic symptoms and reduce relapse rates, when provided alongside antipsychotic medication (Lloyd-Evans et al., 2011). One randomised controlled trial, in individuals with a diagnosis of schizophrenia who elected not to take antipsychotic medication, demonstrated that cognitive behavioural therapy was effective in reducing the severity of psychotic symptoms (Morrison et al., 2014). While there is no doubt that antipsychotic medications are effective in reducing positive psychotic symptoms (Leucht et al., 2013), they are associated with serious cardiometabolic side effects, amongst other side effects, that are associated with a reduced life-expectancy (Correll et al., 2009; Curtis et al., 2012).

Yet at present, all clinical guidelines, recommend the use of antipsychotic medication in individuals with a full-threshold first episode of psychosis (Buchanan et al., 2010; International Early Psychosis Association Writing Group, 2005; NICE, 2014). Therefore, with the progression of early intervention for psychosis services and the advent of other effective interventions, it is now a valid to ask the question: 'Can young people with a first episode of psychosis recover without the use of antipsychotic medication?' There is an absence of clinical trial data to address this important question, therefore the exploration of the outcomes within a large, naturalistic, epidemiological cohort of young people with an 18 month follow-up who received treatment at an early intervention for psychosis service and which included a subgroup who declined antipsychotic medication, could provide valuable insights. In fact, such a study design may even offer some advantages over a clinical trial, as often trial participants are not fully representative of the total population affected by the disorder of interest, due to exclusion criteria often relating to risk to self or substance abuse.

In such a context, it seems relevant to explore the factors that may characterise FEP patients who could do well without antipsychotic medication (Bola and Mosher, 2002, 2003). As long ago as 1939, Langfeldt et al. had suggested that some individuals could recover from psychosis without treatment (Langfeldt, 1939). Characteristics of good prognosis without antipsychotics were symptoms of psychotic depression, family history of depression, absence of schizoid personality traits, acute onset and presence of a precipitating cause. It has been suggested that estimates of drug-free responders in acute psychosis may range between 10 and 40% (Bola and Mosher, 2002). Further, it was postulated that amongst people with early phase schizophrenia, those who had fewer diagnostic symptoms of schizophrenia, older age and higher level of functioning were more likely to respond to strategies of delayed introduction of antipsychotic medication in the context of intensive psychological and milieu intervention.

In a previous paper based on an epidemiological FEP cohort study of a large sample composed of all young people with a first episode of psychosis treated at EPPIC between 1998 and 2000, factors predicting various degrees of adherence to treatment with antipsychotic medication were explored (full adherence = 34%; partial adherence = 47%; non-adherence = 19%) over the treatment period (Lambert et al., 2010). It was found that the group who had been not received an adequate dose of antipsychotic medication (NA), defined as taking less than three weeks of antipsychotic over the entire treatment period, had poorer outcomes than both other groups (Lambert et al., 2010). However, considering potential heterogeneity in the sub-group of those who were non-adherent and the possible favourable outcome of a subgroup of them, the current study was designed with the aims to: (i) compare NA-group with the other young people with a FEP in regards to their premorbid, baseline and outcome characteristics; (ii) calculate the proportion of the NA-group with favourable outcome and (iii) identify the pre-morbid and baseline characteristics that may predict good short term outcomes in the NA-group.

2. Methods

2.1. Material and methods

The First Episode Psychosis Outcome Study (FEPOS) involved a file audit of an epidemiologically based cohort of 786 young people with a first-episode of psychosis who were attending the Early Psychosis Prevention and Intervention Centre (EPPIC) between 1998 and 2000. A brief description of the context, sample, and study design is provided here and additional details can be found in previous publications (Cotton et al., 2009; Schimmelmann et al., 2008).

2.2. Context and sample

EPPIC provides a specialized, comprehensive early intervention program for young people experiencing their first episode of psychosis (FEP) with a usual episode of care of 18 months (McGorry et al., 1996). EPPIC's catchment area (Melbourne's north-west and western suburbs) had a population of approximately 880,000 residents at the time of the study and EPPIC had the mandate to treat all FEP patients aged 15–29. Between 1 January 1998 and 31 December 2000, 786 patients were treated at the EPPIC clinic, which aimed to provide treatment according to the Australian Clinical Guidelines for Early Psychosis (International Early Psychosis Association Writing Group, 2005).

2.3. Assessments and measures

For each young person treated at EPPIC, information on pre-treatment, baseline (admission to EPPIC), and outcome characteristics was systematically documented in a structured file audit. Assessments were based on the Royal Park Multi-diagnostic Instrument for Psychosis (McGorry et al., 1990a,b). Each file contains information compiled during the 18 month treatment period from various sources using high quality assessments carried out by trained clinicians. The clinical notes were originally entered by either the case-manager, treating doctor (registrar) or the responsible consultant psychiatrist. In the first three months of treatment, clients were typically seen weekly and then this is extended to fortnightly, or more frequently if clinically indicated. Two experienced psychiatrists assessed all files using a standardized questionnaire (Conus et al., 2007). This questionnaire includes a large section on demographic and illness-related variables as well as questions derived from the following assessment tools and scales: the Drug and Alcohol Assessment Schedule (McGorry et al., 1990a,b), the duration of untreated psychosis scale (McGorry et al., 1990a,b), the Clinical Global Impressions-severity of illness scale (CGI) (Busner and Targum, 2007), the Global Assessment of Functioning Scale (GAF) (First et al., 1995), the Modified Vocational Status Index (MVSI) and the Modified Location Code Index (MLCI) (Tohen et al., 2000).

2.4. Diagnostic assessment, validity, and inter-rater reliability

Clinical diagnoses at EPPIC are the consensus result of an intensive diagnostic and treatment process within the first 6 weeks of entry to service (baseline diagnosis) by well-trained clinicians working in a specialized assessment and crisis intervention team. This diagnosis was then reviewed according to occurring clinical events. Diagnoses of psychosis and comorbidities were given according to criteria of the DSM-IV classification of mental disorders, first on the basis of available data within 6 weeks after admission (baseline diagnoses) and second on the basis of all information gathered in the file (final diagnosis). In case of disagreement with clinical diagnoses reported in the file, a consensus rating between both research psychiatrists and the patient's case manager was performed. The validity was established using the following procedure: Between 1998 and 2000, 230 of the 786 patients treated at EPPIC have been included in prospective trials. Their main and

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