



The effect of lifetime adversities on resistance to antipsychotic treatment in schizophrenia patients



Ahmed N. Hassan^{a,b,c}, Vincenzo De Luca^{a,b,*}

^a Department of Psychiatry, Centre for Addiction and Mental Health, 250 College Street, M5T 1R8 Toronto, Ontario, Canada

^b Department of Psychiatry, University of Toronto, Canada

^c Department of Psychiatry, King Abdulaziz University, Abdullah Sulayman, Jeddah 22254, Saudi Arabia

ARTICLE INFO

Article history:

Received 23 August 2014

Received in revised form 29 October 2014

Accepted 31 October 2014

Available online 22 November 2014

Keywords:

Treatment-resistance

Antipsychotics

Schizophrenia

CTQ

SLESQ

ABSTRACT

Aim: The aim of this study is to examine whether there is an association between cumulative life adversities and treatment-resistant schizophrenia.

Methods: We recruited 186 participants diagnosed with schizophrenia spectrum disorders. Adverse life-events were assessed using the Stressful Life Events Screening Questionnaire (SLESQ) and the Childhood Trauma Questionnaire (CTQ). Treatment resistant status was identified using the criteria of the American Psychiatric Association for refractory schizophrenia. We performed a multiple logistic regression model, including life adversities, to predict the treatment resistant status controlling for confounding variables.

Results: Forty two percent of the patients were found to be treatment resistant ($n = 78$) and 58% were non-treatment resistant ($n = 108$). The treatment resistant group had higher score on both SLESQ and CTQ (4.5 ± 3.3 and 54.7 ± 19.7) than the non-treatment resistant group (2.5 ± 2.3 and 47.7 ± 17.5) and the difference between the two groups was significant for both SLESQ ($p < 0.001$) and CTQ ($p = 0.011$). After adjustment for demographic variables and previously reported risk factors of treatment resistance, the association remained significant for SLESQ (OR = 1.20, 95% CI 1.05–1.38; $p = 0.009$) but not for CTQ ($p = 0.13$).

Discussion: The results suggest that cumulative lifetime adversities could have an independent effect on the resistance to treatment in schizophrenia spectrum disorders. Routine assessment of trauma exposures and an individualized bio-psycho-social formulation is necessary for a personalized treatment.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Antipsychotic treatment has the ability to ameliorate schizophrenia symptoms. However, approximately 20 to 30% of schizophrenia patients fail to respond to pharmacotherapy despite their adherence (Kane et al., 1988).

The prevalence of treatment resistant schizophrenia has ranged in several studies from 5% up to 60% (Elkis, 2007; Dammak, 2013). This wide range was due to the different criteria used to define treatment resistance. Treatment resistant patients have more severe symptoms, greater disabilities, higher suicidal risk and lower quality of life than non-treatment resistant patients (Kane et al., 1988; Mamo, 2007). In addition, the burden of treatment resistant patients is between 60 to 80% of the total cost of schizophrenia (Kennedy et al., 2014).

Several demographic and clinical factors have been identified for their ability to predict poor response to treatment in schizophrenia such as early age of onset at psychosis which has been consistent across

different studies (Hollis, 2000; Reichert et al., 2008) and duration of untreated psychosis (Owens et al., 2010).

Other risk factors for treatment resistance includes family history of psychosis, family environment of highly expressed emotions (Butzlaff and Hooley, 1998; Murray and Van Os, 1998; Malaspina et al., 2000), substance abuse history (Gupta et al., 1996), and male gender (Murray and Van Os, 1998). In addition, negative symptoms, such as flat affect were able to predict poor response to treatment (Cuesta et al., 1994).

Despite the previous search for prognostic factors, to date, the effect of the cumulative lifetime adversities on ongoing treatment has not been investigated.

Cumulative lifetime adversity is the exposure to potential traumatic events that threaten the life or the physical or the mental integrity of the subject or of those around him (Shrira et al., 2011).

Cumulative childhood adversities increased the risk of onset of several psychiatric disorders and their continuity increases the risk of relapse (Turner and Lloyd, 1995). Trauma and specifically childhood trauma has a close tight with psychosis onset. A meta-analysis of 41 studies revealed that all types of childhood adversities increased the risk of psychosis (Varese et al., 2012). Furthermore, childhood abuse predicted psychotic symptoms in a dose–response relationship which

* Corresponding author at: Dept of Psychiatry, Centre for Addiction and Mental Health, 250 College Street, M5T 1R8 Toronto, Ontario, Canada. Tel.: +1 416 535 8501.

E-mail address: vincenzo.deluca@camh.ca (V. De Luca).

remained significant after controlling for family history of psychosis (Janssen et al., 2004).

Childhood trauma has been also found to be a risk factor for symptoms that are commonly found in treatment resistant schizophrenia such as persistent positive symptoms, suicidal behavior and substance abuse (Scheller-Gilkey et al., 2002; Roy, 2005; Üçok and Bıkmaz, 2007).

Overall, the relationship between lifetime adversities and treatment resistant in schizophrenia is not clear. In this study we aimed to compare the prevalence of adverse lifetime events in treatment resistant and non-treatment resistant schizophrenia.

2. Materials and methods

2.1. Sample

A total of 186 participants were recruited from the Center for Addiction and Mental Health (CAMH), a Canadian teaching hospital located in Toronto. After consenting to the study, subjects were assessed using a structured interview. Participants were included if they were older than 18, diagnosed with schizophrenia or schizoaffective disorder and fluent in English. We excluded patients with a total duration of illness of three years or less. The main reason of their exclusion is because in the first three years of the illness, most of the psychiatric services classify them with a “provisional” diagnosis of psychosis rather than a confirmed diagnosis of schizophrenia.

Most of the participants were stable or in maintenance phase. Patients in the acute phase of the illness were excluded.

The clinical diagnosis of schizophrenia or schizoaffective disorder was confirmed by means of the SCID-I/P. Age at onset of psychotic symptoms and age when the antipsychotic treatment was initiated were collected during the SCID and the duration of untreated psychosis was estimated.

In addition, medical charts were reviewed for documentation about their functioning, treatment prognosis, past/current medications and details about their interventions trials (dose, duration and reasons for switching) to determine the treatment status (history of failure of two or more antipsychotic trials of adequate duration and adequate dose) using the criteria of the American Psychiatric Association for treatment resistant schizophrenia (Lehman et al., 2004).

2.2. Trauma screening measures

Two screening measures were used to evaluate the presence of trauma in each participant: the Stressful Life Events Screening Questionnaire (SLESQ) and the Childhood Trauma Questionnaire (CTQ).

The SLESQ is a 13 item screening questionnaire that reliably covers general stressful and traumatic events in the individual's lifetime. It includes different lifetime aspects such as life-threatening illnesses or accidents, sexual, emotional and physical abuse, robbery or weapon threats, sudden death of family members or close friends, and any other horrifying experiences in both the adulthood and the childhood. Its purpose is to identify all traumatic experiences from childhood to adulthood as quickly and efficiently as possible while avoiding sub-threshold events that is not considered traumatic to the patient (Goodman et al., 1998).

The CTQ is a 28-item self-report inventory that provides a brief, reliable, and valid screening for history of abuse and neglect during childhood (Bernstein and Fink, 1998). The questionnaire covers five different aspects: physical abuse, emotional abuse, emotional neglect, sexual abuse, and physical neglect. This measure will paint a picture of the nature, severity, duration, and frequency of abuse during childhood.

2.3. Statistical analysis

The analysis was performed using the statistical package STATA 11.2. All tests were two-tailed. The level of significance was set at $p \leq 0.05$.

The differences between the two groups (treatment resistant and non-treatment resistant) were explored using Pearson's chi square test or two-sample *t*-test. A 95% confidence interval (CI) was calculated for each mean score of SLESQ and CTQ in both groups. Also, a 95% CI was calculated for the difference in the mean score of both SLESQ and CTQ between the two groups and a two-sample *t*-test was used to determine if there was a significant difference between the two groups.

Exposures to adverse life events, measured by SLESQ, were grouped into high exposure (≥ 4 traumatic events) and low exposure (< 4 traumatic events), based on the evidence that four traumatic events or more confers higher risk for major mental illness (Caspi et al., 2003).

A binary logistic regression analysis was conducted with treatment status (resistant or non-resistant) set to be the dependent variable with adjustment of the confounders. Variables were entered if they were differently distributed between the two groups or they were previously identified as potential predictors for poor treatment outcome in schizophrenia such as: age of onset (Hollis, 2000; Reichert et al., 2008), male gender (Murray and Van Os, 1998), family history of psychosis (Murray and Van Os, 1998; Malaspina et al., 2000), history of drug or alcohol abuse/dependence (Gupta et al., 1996) and duration of untreated psychosis (Owens et al., 2010). All analyses were corrected for the age at the time of the assessment.

3. Results

In our sample, there were 78 (41.9%) treatment resistant participants and 108 (58.1%) non-treatment resistant participants. Seventy percent of our sample consisted of male patients. General data including clinical-demographic variables are presented in Table 1. Psychosis-related variables for the two groups are presented in Table 2.

Overall, 92.3% of treatment resistant participants and 82.4% of non-treatment resistant had at least one lifetime exposure to an adverse event. The most frequently reported life adversities by SLESQ in both groups were emotional abuse (42.5%), childhood physical abuse/assault (35.5%), traumatic bereavement (33.9%), adult physical abuse/assault (31.2%), sexual molestation (24.2%) and sexual assault (18.8%).

On SLESQ, treatment resistant participants reported an average of 4.5 lifetime traumatic events with a standard deviation of 3.3 (95% CI 3.8–5.2), on the other hand non-treatment resistant participants reported an average of 2.5 lifetime traumatic events with a standard deviation of 2.3 (95% CI 2.1–2.9). On CTQ, treatment resistant patients reported a total score of 54.7 with a standard deviation of 19.7 (95% CI 50.3–59.1) while non-treatment resistant patients had a total score of 47.7 with a standard deviation of 17.5 (95% CI 44.3–51). The scores in the treatment resistant group were significantly higher for both SLESQ ($p < 0.001$) and CTQ ($p = 0.011$) than those in the non-treatment resistant group.

When considering specific types of abuse during childhood (Fig. 1), treatment resistant participants reported higher scores than those of non-treatment resistant participants for sexual abuse ($p = 0.0019$), emotional abuse ($p = 0.0046$) and emotional neglect ($p = 0.0412$). Both physical abuse and physical neglect scores were not significantly different between the two groups ($p = 0.877$ and $p = 0.0503$ respectively).

Within the treatment resistant patients, 55.1% had four or more lifetime adverse events, while only 23% of non-treatment resistant patients had four or more lifetime adverse events; this difference was significant ($p < 0.001$) and the odds ratio was 4.1 (95% CI 2.2–7.8).

In terms of other variables and previously known predictors of resistance, there were significant associations ($P < 0.05$) between treatment resistant status and history of alcohol/recreational drug abuse, total duration of illness, family history of psychosis, previous suicidal attempt, duration of untreated psychosis and early age at onset. The average age at onset of psychosis was 21 ± 6 for the treatment resistant group and 25 ± 7 for the non-treatment resistant subjects.

متن کامل مقاله

دریافت فوری ←

ISIArticles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات