Early Response in Adolescents with Schizophrenia is not Associated with Remission at Six Months

Sadot Arceo MD¹; Rosa Elena Ulloa MD¹

Abstract

Objective: The objectives of present study were to determine the frequency of early response (ER), defined as a 20% decrease in total baseline PANSS score at three weeks and to compare the rate of symptomatic and functional remission between schizophrenic adolescents with and without ER. Methods: The sample included 61 patients (65% males) with a mean age of 15 (+ 1.54) y.o., 88.5% on their first episode of psychosis who were evaluated with PANSS and PSP scales. They were evaluated with PANSS at week three and with PANSS and PSP at month six. Results: Twenty-three patients (37.7%) showed ER. There were no significant differences in the rate of symptomatic or functional remission at month six between responders and non-responders. Conclusions: Early response to antipsychotic treatment can be observed in adolescent patients, however, it is not associated with remission at six months.

Key Words: early response, antipsychotic, schizophrenia, remission, adolescents

Introduction

According to the results of double-blind controlled clinical trials, the clinical response to antipsychotic treatment in adolescents with schizophrenia can be observed after six weeks of treatment (NICE, 2013). However, studies in adult patients reported a decrease in the severity of symptoms such as conceptual disorganization, hallucinatory behavior, and unusual thought content within the first 24 hours (Kapur et al., 2005) or weeks of treatment (Agid, Kapur, Arenovich, & Zipursky, 2003); these findings led to define early response (ER) as a 20% reduction in the total score of the PANSS (Levine & Leucht, 2012). A recent study reported that female gender, a higher educational level, a higher PANSS-excitement factor score and a shorter duration of untreated psychosis predicted ER at week three in patients on their first psychotic episode and that ER predicted response at week eight (Chung et al., 2016). In addition, a study in first-episode patients reported that response at week four was associated with responder status at week

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16 (Gallego et al., 2011). In a post hoc analysis of data from an aripiprazole trial in adolescents, the authors reported that 48% of patients showed ER at week three, although there were no differences in clinical and demographic characteristics between early responders and non-early responders, ER predicted response at week six (Correll et al., 2013). Studies on ER have used different methodologies, patient populations and diverse follow-up periods. Thus, despite early response as a predictor of remission could show therapeutic value, it is not known whether it is associated with other demographic and clinical characteristics or with a higher frequency of remission in adolescents. The present study aimed to determine the frequency of ER in Mexican adolescents with schizophrenia. In addition, we wanted to compare the demographic and clinical characteristics as well as the rate of symptomatic and functional response after six months of pharmacological treatment between patients with and without ER.

### Methods
The sample included 61 adolescents aged 12 to 17 who were consecutively recruited from the inpatient (78.6%) and outpatient (21.4%) services at the Child Psychiatric Hospital in Mexico City, a public tertiary level mental health facility. The guidelines marked in the declaration of Helsinki were followed, written subject assent and parental informed consent were obtained from all of the participants. They were evaluated with the validated Spanish version of the MINI International Neuropsychiatric Interview (Sheehan et al., 2010), the Positive and Negative Syndrome Scale (PANSS; Fresan et al., 2005) and the Personal and Social Performance (PSP) (Ulloa et al., 2015) scale for schizophrenia. The raters were psychiatrists, child psychiatrists and psychologists who showed 80% of agreement on the scales scores.

Patients were mainly males (65%) with a mean age of 15 (+1.54) y.o., 88.5% were on their first episode of psychosis with a mean duration of illness of 13.9 (+16.88) months. Patients received antipsychotic treatment with risperidone (N=52, 85.2%), olanzapine (N=4,6.6%), quetiapine (N=3, 4.9%), haloperidol and perphenazine (N=1, 1.6% each). They were reevaluated at week three with PANSS and at month six with PANSS and PSP. Patients were described as early responders if they had a 20% reduction in baseline total PANSS score at week three. Symptomatic remission was described following Andreasen criteria (Andreasen, 2006), as scores of <3 on the following PANSS items: Delusions (P1), unusual thought content (G9), conceptual disorganization (P2), hallucinatory behavior (P3), mannerism/posturing (G5), blunted affect (N1), social withdrawal (N4) and lack of spontaneity (N6) at month six. Functional remission was defined as a total PSP global score of 70-100 at month six. Data were analyzed with descriptive statistics, chi square and Student t tests.

### Results
Twenty-three patients (37.7%) were considered as early responders, these patients had a higher severity of psychotic symptoms and a higher frequency of comorbid major depressive disorder. There were no significant differences in the rate of symptomatic or functional remission at month six between patients with and without ER (Table 1).

### Discussion
Present results showed that more than a third of patients had an early response, particularly those with more severe symptoms and those with a comorbid major depressive disorder (MDD). The frequency of ER was higher than that reported in an adult sample (Levine et al., 2012), but lower than that reported in studies with adolescent samples which did not show differences in the clinical characteristics of patients with and without ER (Correll et al., 2013; Stentebjerg-Olsen et al., 2015). These contrasts could be explained in part by the different criteria to determine ER and in the clinical characteristics of the samples, such as the

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**Table 1. Demographic and clinical characteristics of patients with and without early response**

<table>
<thead>
<tr>
<th></th>
<th>Early response (N=23)</th>
<th>Non early-response (N=38)</th>
<th>Statistics, (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>16 (69.6%)</td>
<td>24 (63.2%)</td>
<td>X² = 0.26</td>
<td>0.61</td>
</tr>
<tr>
<td>First-episode psychosis</td>
<td>20 (87%)</td>
<td>34 (89.5%)</td>
<td>X² = 0.8</td>
<td>0.76</td>
</tr>
<tr>
<td>Duration of illness (m) mean</td>
<td>17.21 ± 22.73</td>
<td>11.96 ± 12.00</td>
<td>t = 1.18 (-14.1-3.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>PANSS total mean</td>
<td>106.52 ± 22.51</td>
<td>91.21 ± 19.99</td>
<td>t = -2.68 (-26.8 - -3.79)</td>
<td>0.01</td>
</tr>
<tr>
<td>MDD</td>
<td>4 (17.4%)</td>
<td>1 (2.6%)</td>
<td>X² = 4.14</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean antipsychotic chlorpromazine equivalents doses</td>
<td>205.78 ± 61.68</td>
<td>229.78 ± 63.66</td>
<td>t = 1.45 (-9.1-57.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Symptomatic remission</td>
<td>4 (17.4%)</td>
<td>8 (21.1%)</td>
<td>X² = 0.12</td>
<td>0.72</td>
</tr>
<tr>
<td>Functional remission</td>
<td>7 (30.4%)</td>
<td>14 (36.8%)</td>
<td>X² = 0.26</td>
<td>0.61</td>
</tr>
</tbody>
</table>

No mathematical correction was made for multiple comparisons.
percentage of subjects on their first episode and the baseline PANSS score.

Patients with ER did not show a higher frequency of functional or symptomatic remission, which did not allow to include ER as an outcome predictor in this sample. These results contrast with those of Levine’s study with adult patients on their first psychotic episode which showed that subjects with ER in the initial four weeks of treatment maintained a significant improvement for the next 44 weeks. However, it is important to note that differences with the non-ER group were not significant after that point (Levine et al., 2012).

Present results should be taken with caution given the sample size and the fact that the severity of patients’ illness was at least moderate. However, they point to the need for longitudinal studies in order to determine whether ER is a predictor of long-term remission in adolescents.

Acknowledgements / Conflicts of Interest
The authors have no financial relationships to disclose.

References


