Efficacy of Long Acting Injectable Antipsychotics in Early Onset Schizophrenia

Linda Pietras RN-BC
Mercyhurst University

Author Note
This integrative review table was prepared for Nurse 301 Research & Evidence-Based Practices, Spring 2016, taught by Dr. Karen Morahan.
### Purpose of Study
To examine how Risperidone long acting injectable (LAI) effects patient adherence to medication and long term stabilization of schizophrenia.

### Independent Variables
- **Risperidone LAI**

### Dependent Variables
- Patients were assessed at baseline and at 6 month intervals up to 18 months for adherence, efficacy, Risperidone LAI dosage, number and duration of hospitalization, social functionality and reintegration to work, studies and independent living.

### Theory
- Physiological

### Sample
- A total of 25 participants diagnosed with schizophrenia with a comorbid disorder.

### Study Design
- Naturalistic prospective study

### Instruments of Measure
- **Clinical Global Impression (CGI) scale**
- **Global Assessment of Functioning (GAF)**

### Results
- Treating with Risperidone LAI can reduce relapse number and duration of readmission. Improved cognitive symptoms, the quality of life and prognosis.

### Limitations
- No randomization or comparative group.
- Small number of patients.

**Strengths**
- Results compared with whole cohort (120 patients)

---

Source:
| history of malignant syndrome, pregnant or breast feeding female, history of clozapine treatment, known allergies, hypersensitivity or intolerance to risperidone, and patients who had not given informed consent. |   |   |   |
Source:
Ng, Ka Ying Bonnie & Taylor, Mark (2012). Should long-acting (depot) antipsychotics be used in early schizophrenia? A systematic review. *Australian & New Zealand Journal of Psychiatry*. Retrieved February 6, 2016 from [www.anp.sagepub.com](http://www.anp.sagepub.com)

<table>
<thead>
<tr>
<th>Purpose of Study</th>
<th>Independent Variables</th>
<th>Dependent Variables</th>
<th>Theory</th>
<th>Sample</th>
<th>Study Design</th>
<th>Instruments of Measure</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>To determine if LAI antipsychotics should be used for early treatment of schizophrenia to decrease non-adherence and improve stabilization.</td>
<td>LAI antipsychotics</td>
<td>Improved symptom reduction, remission, medication adherence and decreased hospitalization</td>
<td>Physiological</td>
<td>10 Research studies collected from electronic databases.</td>
<td>Peer reviewed articles, case controlled, cohort, RCT’s, open label or follow up studies</td>
<td>Positive and Negative Syndrome scale (PANSS) Global Assessment of Functioning (GAF) Adverse Event (AE) Extrapyramidal symptom rating scale (ESRS) Clinical global impressions severity (CGI-S) Social and functional</td>
<td>Improved symptom reduction in 40% of patients. Over two thirds of patients sustained remission and readmission rates decreased. Patient discontinuation of medication decreased using LAI. ESRS scores decreased related to less side-effects.</td>
<td>Open-label nature of some studies. No control group for comparison in some studies. Small sample sizes of studies. <strong>Strengths</strong> RCT’S showed patients more adherent to Risperidone LAI compared to oral antipsychotics. Comprehensive review of the Literature.</td>
</tr>
</tbody>
</table>
in early stages of their disease. Treatment with LAI form of antipsychotics.

**Exclusion Criteria:**
Did not meet inclusion criteria.

| assessment scale (SOFAS) | Public Health guidelines promote early prevention of morbidity and mortality. Use of LAI’s promote effective delivery and improved patient outcomes to achieve remission. |
Source:

<table>
<thead>
<tr>
<th>Purpose of Study</th>
<th>Independent Variables</th>
<th>Dependent Variables</th>
<th>Theory</th>
<th>Sample</th>
<th>Study Design</th>
<th>Instruments of Measure</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>To evaluate the effect of treatment with oral and long-acting injectable (LAI) antipsychotics on long-term outcomes in patients with first episode psychosis (FEP) or schizophrenia.</td>
<td>LAI antipsychotic compared to Oral antipsychotics</td>
<td>Improved symptoms, remission and cognition</td>
<td>Physiological</td>
<td>A total of 785 articles were reviewed.</td>
<td>Systemic review of randomized and nonrandomized prospective clinical trials</td>
<td>Positive and Negative Syndrome Scale (PANSS)</td>
<td>Remission rates increased during the first year after initiation of antipsychotic treatment for patients with FEP.</td>
<td>Small sample meeting criteria.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased relapse</td>
<td></td>
<td>19 articles met inclusion criteria.</td>
<td>Brief Psychiatric Rating Scale (BPRS)</td>
<td>Untreated FEP decreased the chance of patients later achieving remission.</td>
<td>Lack of uniformity in terminology.</td>
<td></td>
</tr>
</tbody>
</table>

**Inclusion Criteria:**
Studies that reported randomized and nonrandomized prospective clinical trials on the long term effects of oral or long-acting injectable antipsychotics on measures of relapse,

**Strengths:**
Systematic review of the literature.
remission, or cognition in patients with first episode psychosis or early schizophrenia. Studies reporting the effects of antipsychotics in patients with longer disease history were reviewed for comparison.

**Exclusion Criteria:**
Studies that focused on study design, health economics and outcome research; studies containing cross-sectional, retrospective or secondary analysis;

**executive functioning, working memory, speed of processing and attention.**

Cognition improved for up to 2 years with antipsychotic treatment for patients with FEP.

Antipsychotic treatment reduced risk of relapse for patients with longer disease history.

LAI more effective than oral treatment in preventing relapse.

Treatment with atypical antipsychotics result in faster recovery and sustained remission as compared to first generation antipsychotics.
| studies with less than 50 patients, duration of study less than 12 weeks, publication dates prior to 2000, antipsychotic no longer in use, augmentation therapy, elderly patients, comorbid substance abuse and depression. |  |  |  |  |

<table>
<thead>
<tr>
<th>Purpose of Study</th>
<th>Independent Variables</th>
<th>Dependent Variables</th>
<th>Theory</th>
<th>Sample</th>
<th>Study Design</th>
<th>Instruments of Measure</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of the efficacy of paliperidone palmitrate (PP) versus oral antipsychotics (OAP) for relapse prevention.</td>
<td>Paliperidone palmitrate LAI versus oral antipsychotics</td>
<td>Relapse symptoms, functioning, quality of life, treatment satisfaction and tolerability.</td>
<td>Physiological</td>
<td>769 Patients recently diagnosed with schizophrenia (within 1-5 years)</td>
<td>An international, 24 month randomized, prospective, active-controlled, open label, rater-blinded, study</td>
<td>Time to relapse</td>
<td>Time to relapse: 469 days for patients receiving paliperidone palmitrate (PP) versus 249 days for oral antipsychotics (OAP).</td>
<td>Potential bias among clinicians favoring oral medication over LAI.</td>
</tr>
<tr>
<td>Inclusion Criteria</td>
<td>Aged 18-65 years</td>
<td>Patients with an acute episode of schizophrenia with a PANSS total score of 70-120 at screening.</td>
<td>Diagnosis of schizophrenia according to DMS IV criteria made</td>
<td>PANSS total and subscale scores</td>
<td>Marder factor scores</td>
<td>Clinical Global Impression (CGI) Scale and CGI-Change</td>
<td>Symptom improvement (PANSS): greater improvement in symptom control day 8 and endpoint for patients receiving PP versus OAP.</td>
<td>Lack of control over other non-pharmacological treatment variables.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Strengths</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Large sample</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pragmatic open-label study adds clinically relevant information of treatment effectiveness complementing</td>
</tr>
</tbody>
</table>
Efficacy, Long Acting Injectable Antipsychotics and Schizophrenia

- 1-5 years previously and a history of greater than 2 relapses requiring psychiatric hospitalization in the preceding 24 months (current acute episode included).

**Exclusion criteria**
Patients antipsychotic- naïve, treatment resistant or unsuitable for treatment with an atypical oral antipsychotic or oral haloperidol monotherapy, or had received clozapine

- European Quality of Life-5 Dimensions (EQ-5D)
- Subjective Well Being under Neuroleptics Scale (SWN-S)
- Treatment Satisfaction Questionnaire for Medication (TSQM)
- Physician’s Treatment Satisfaction (7-point categorical scale).

Functional health and wellbeing (CGI, PSP, SF-36, SWN-S): both PP and OAP had comparable improvement results.

Quality of life (EQ-5D): OAP scores at 12 month showed higher scores on EQ-5D, however, both PP and OAP had comparable improvement results at endpoint.

Patient Treatment satisfaction (TSQM): PP showed significant evidence of RCT’s
<table>
<thead>
<tr>
<th>Within the previous 3 months.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of long acting treatment within three injection cycles before screening.</td>
</tr>
<tr>
<td>Starting a psychotherapy program within 2 months preceding baseline.</td>
</tr>
<tr>
<td>History or current symptoms of tardive dyskinesia</td>
</tr>
<tr>
<td>History of neuroleptic malignant syndrome.</td>
</tr>
<tr>
<td>Involuntary Hospitalization</td>
</tr>
</tbody>
</table>

**Improvement to OAP.**

Physician’s treatment satisfaction:
Greater improvements were observed for PP versus OAP in scores for safety, mode of administration and overall satisfaction.
Purpose of Study | Independent Variables | Dependent Variables | Theory | Sample | Study Design | Instruments of Measure | Results | Limitations |
--- | --- | --- | --- | --- | --- | --- | --- | --- |
To investigate attitudinal themes to antipsychotic long acting injections (LAIs) in patients in an early intervention team (EIT) | Prescribed either a LAI or an oral antipsychotic | Attitudinal themes to antipsychotic LAIs | Physiological | A total of 11 patients aged range 18 – 40 years actively participating in the early intervention team (EIT) from 0-3 years. Participants were ‘purposively’ sampled to represent the following groups: Prescribed either a LAI or an oral antipsychotic, either 1st generation or second generation | Interviews were conducted and analyzed according to grounded theory. Recruitment stopped when saturation of themes was reached | Qualitative Study | Audio recorded interviews or written notes | Lack of knowledge and misperception about LAIs that were identified indicate that patients need to be provided with balanced and accurate information about LAIs | Small sample |

**Strengths**

Evidence of study shows patient willingness to try LAIs when shared decision making is present.

**Limitations**

Further study using qualitative methodology is needed.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>second generation;</th>
<th>Clinicians need to stop reinforcing negative perceptions of LAIs as used for last resort for “revolving door patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals who chose not to take antipsychotic medication and with varying levels of insight.</td>
<td>Male or female patients; patients from either white or other ethnic minority groups.</td>
<td>A shared decision-making process is necessary.</td>
<td></td>
</tr>
</tbody>
</table>

**Exclusion criteria:**
Patients lacking capacity to consent to be interviewed, too unwell to participate in the interview.
process and patients not proficient in the English language were excluded.

**Inclusion criteria:** Participants were outpatients under the care of an EIT.
# Efficacy, Long Acting Injectable Antipsychotics and Schizophrenia


<table>
<thead>
<tr>
<th>Purpose of Study</th>
<th>Independent Variables</th>
<th>Dependent Variables</th>
<th>Theory</th>
<th>Sample</th>
<th>Study Design</th>
<th>Instruments of Measure</th>
<th>Results</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>To examine the risk of re-hospitalization, drug discontinuation and mortality</td>
<td>Oral and depot antipsychotics</td>
<td>Decreased re-hospitalization</td>
<td>Physiological</td>
<td>2,588 Patients hospitalized for the first time with diagnosis of schizophrenia between 2000 and 2007 in Finland aged 16-65 years.</td>
<td>Nationwide cohort study of all people in Finland</td>
<td>Data collected from Finnish National Hospital Discharge Register base case linkage</td>
<td>Use of depot antipsychotics was associated with a significantly lower risk of re-hospitalization than use of oral formulations of the same compounds. The oral antipsychotics clozapine and olanzapine were associated with significantly lower re-hospitalization risk.</td>
<td>None Identified.</td>
</tr>
<tr>
<td><strong>Inclusion Criteria</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients who had received any antipsychotic medication within the first 30 days after discharge. Patients diagnosed with</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Strengths**
Large study design
Patients who had not purchased any antipsychotics prescription (code N05A) within 6 months before admission.

**Exclusion Criteria**
Patients not reported to have diagnosis of schizophrenia ICD – 10 code F20

54% of patients either did not purchase antipsychotic prescription within 30 days of hospital discharge or used their initial antipsychotic medication for less than 30 days.

Use of any antipsychotics was associated with lower mortality