Trattamenti farmacologici con LAIs tra evidenze e pratica clinica

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BRAINSTORMS—Clinical Neuroscience Update

Long-acting injectable antipsychotics: shall the last be first?

Stephen M. Stahl

A paradigm shift is afoot in which the “last shall be first,” namely, use of long-acting injectable (LAI) antipsychotics, rather than being reserved for use only at the last stages of schizophrenia, may be shifting to first-line treatment of early episodes of this illness.

Take-Home Points

- Long-acting injectable (LAI) formulations of antipsychotics have traditionally been used for those patients with schizophrenia with the most severe symptoms, poorest compliance, most hospitalizations, and poorest outcomes, namely at the latter stages of their illness.

- However, early episode patients at the beginning of their illness may have the most to gain from LAI antipsychotics, at a time when schizophrenia is most treatable and when avoidance of recurrences and rehospitalizations may lead to the biggest gains in outcome.

- Administration of LAI formulations of antipsychotics to schizophrenia patients after first hospitalization is associated with better outcomes.

Technologies that can prolong the action of a single dose of an antipsychotic for several weeks have been available since the 1960s, and are known collectively as long-acting injectable antipsychotics (LAIs). Originally introduced for the classical (conventional, first generation) antipsychotics, and more recently for some of the atypical (second generation) antipsychotics, LAIs have only ever attained a low percentage of total prescriptions for antipsychotics. This low level of use has occurred despite the fact that up to half of patients with schizophrenia are noncompliant. LAIs have instead become “niched” for patients who are at the later stages of schizophrenia (Figure 3), and LAI treatment has been stigmatized as well, since patients receiving LAIs are more likely to be minorities, less likely to be veterans, have more psychiatric hospitalizations, are more likely to have been arrested, are more likely to use alcohol and illicit substances, and...
Figure 1. A Paradigm Shift for LAIs: The Last Shall Be First?

- **proposed use of LAIs**
  - first episode treatment
  - early episode treatment

- **current use of LAIs**
  - last episode treatment

**AGE**
- onset of full schizophrenia syndrome
- asymptomatic but at risk
- prodrome: onset of negative symptoms, asocial features, subsyndromal

- **II**
- **I**
- **III**
- **IV**
Guidelines sur les antipsychotiques atypiques d’action prolongée (APAPs) dans les premiers épisodes psychotiques

Guidelines on long-acting injectable atypical antipsychotics for first-episode schizophrenia

J.-M. Azorin

<table>
<thead>
<tr>
<th>Tableau 1. Arguments pour et contre l’utilisation des APAPs dans le traitement des premiers épisodes psychotiques, d’après [16].</th>
</tr>
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<tbody>
<tr>
<td><strong>Pour</strong></td>
</tr>
<tr>
<td>Limitation des rechutes liées à un défaut d’adhésion au traitement</td>
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<tr>
<td>Certains individus ayant un degré élevé de fonctionnement peuvent préférer les formes à action prolongée.</td>
</tr>
<tr>
<td>La bonne tolérance liée à une faible variation des taux plasmatiques est susceptible d’avoir un effet favorable sur l’adhésion au traitement.</td>
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<tr>
<td>La période la plus favorable pour prescrire un APAP est celle qui précède la sortie de l’hôpital.</td>
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</table>
TEXAS MEDICATION ALGORITHM PROJECT
PROCEDURAL MANUAL

SCHIZOPHRENIA TREATMENT ALGORITHMS
Tami R. Argo, PharmD, MS, BCPP
M. Lynn Crismon, PharmD
Alexander L. Miller, MD
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Brandon Suehs, PharmD

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MODEL OF MANAGEMENT (MO.MA) FOR THE PATIENT WITH SCHIZOPHRENIA: CRISIS CONTROL, MAINTENANCE, RELAPSE PREVENTION, AND RECOVERY WITH LONG-ACTING INJECTABLE ANTIPSYCHOTICS (LAIs)

“Consider offering depot /long-acting injectable antipsychotic medication to people with psychosis or schizophrenia: who would prefer such treatment after an acute episode where avoiding covert non-adherence (either intentional or unintentional) to antipsychotic medication is a clinical priority within the treatment plan. [2009] 1.5.6 Using depot/long-acting injectable antipsychotic medication 1.5.6.1 When initiating depot/long-acting injectable antipsychotic medication: take into account the service user’s preferences and attitudes towards the mode of administration (regular intramuscular injections) and organisational procedures (for example, home visits and location of clinics) take into account the same criteria recommended for the use of oral antipsychotic medication (see sections 1.3.5 and 1.3.6), particularly in relation to the risks and benefits of the drug regimen initially use a small test dose as set out in the BNF or SPC. [2009]”
Review

Long-acting injectable antipsychotics in early psychosis: a literature review

Robin Emsley,1 Bonginkosi Chiliza,1 Laila Asmal,1 Mpogisheng Mashile1 and Paolo Fusar-Poli2

Abstract

Aim: There are sound reasons for considering the use of long-acting injectable antipsychotics early in the course of schizophrenia. We reviewed available literature on the subject.

Method: We conducted an electronic database search and critically reviewed all studies in which a long-acting injectable antipsychotic was evaluated in early psychosis patients.

Results: There is a need for well-designed studies as most of those reported were open-label and non-comparative, and samples were frequently small.

Conclusions: The available evidence does suggest that long-acting injectable antipsychotics can be used safely and effectively in early stages of the illness, and that they may be associated with better outcomes than with oral medications. However, this is largely supported by evidence from naturalistic cohort studies and a small number of controlled trials of risperidone long-acting injection. Evidence for olanzapine and paliperidone long-acting injectables in particular is limited.

Key words: depot, early psychosis, long-acting antipsychotic, schizophrenia.
ORIGINAL RESEARCH

Efficacy and Effectiveness of Depot Versus Oral Antipsychotics in Schizophrenia: Synthesizing Results Across Different Research Designs

Noam Y. Kirson, PhD; Peter J. Weiden, MD; Sander Yermakov, MS; Wayne Huang, MPP; Thomas Samuelson, BA; Steve J. Offord, PhD; Paul E. Greenberg, MS, MA; and Bruce J. O. Wong, MD

ABSTRACT

Objective: Nonadherence is a major challenge in schizophrenia treatment. While long-acting (depot) antipsychotic medications are often recommended to address adherence problems, evidence on the comparative effectiveness of depot versus oral antipsychotics is inconsistent. We hypothesize that this inconsistency could be due to systematic differences in study design. This review evaluates the effect of study design on the comparative effectiveness of antipsychotic formulations. The optimal use of different antipsychotic formulations in a general clinical setting depends on better understanding of the underlying reasons for differences in effectiveness across research designs.

Data Sources: A PubMed literature review targeted English-language studies (2000–2011) with information on relapse, hospitalization, or all-cause discontinuation for depot and oral antipsychotic treatment arms in schizophrenia. The time frame was chosen to reflect research focused on the newer generation of antipsychotic agents. The search required at least 1 term from each of the following categories: (1) schizophrenia; (2) inject, injection, injectable, injectibles, injected, depot, long-acting; and (3) iloperidone, fluphenazine, haloperidol, paliperidone, risperidone, olanzapine, asenapine, flupentixol, flupenthixol, lurasidone, clozapenthixol, fluspirilene, zuclopenthixol, zuclopenthixol.

Study Selection: Thirteen relevant studies were identified by 2 independent reviewers; these studies included information on 19 depot-oral comparisons.

The cornerstone of long-term maintenance therapy of schizophrenia patients is relapse prevention. Relapse prevention is necessary—albeit not sufficient—for eventual successful rehabilitation.1 In practice, the effectiveness of maintenance antipsychotic treatment is often undermined by poor adherence to therapy. Not only is nonadherence the single greatest modifiable risk factor for relapse,2,3 it is also often undetected, resulting in lost opportunities to employ psychosocial interventions for adherence, as well as uncertainty as to the relative contribution of lack of efficacy versus adherence problems to poor outcomes.

While no single adherence intervention is universally effective, long-acting injectable (depot) formulations are considered one of the most important pharmacologic interventions available to address adherence problems in schizophrenia.4 Relative to oral formulations, long-acting depot delivery systems are thought to help maintain adherence (or delay nonadherence) in many individuals who would otherwise discontinue their oral therapy. Therefore, long-acting depot formulations are often recommended for individuals who are known to have patterns of nonadherence to oral antipsychotic
Figure 2. Meta-Analysis of Adjusted Risk Ratios, by Study Design

Effectiveness of Depot vs Oral Antipsychotics

Study | Favors Depot | Favors Oral | RR | 95% CI | Weight
--- | --- | --- | --- | --- | ---
RCTs
Gaebel et al, 2010 |  | □ | 0.58 | 0.39-0.86 | 15.13
Gaebel et al, 2010 | □ |  | 0.50 | 0.38-0.67 | 17.14
Kane et al, 2010 | □ |  | 2.03 | 1.31-3.16 | 14.38
Keks et al, 2007 | □ |  | 0.92 | 0.72-1.19 | 17.27
Macfadden et al, 2010 | □ |  | 1.07 | 0.84-1.37 | 17.76
Rosenheck et al, 2017 | □ |  | 0.89 | 0.70-1.13 | 17.82
Pooled RCTs | □ |  | 0.88 | 0.64-1.22 |

Prospective studies
Ciudad et al, 2008 | □ |  | 0.80 | 0.60-1.06 | 24.18
Kim et al, 2008 | □ |  | 0.30 | 0.14-0.67 | 6.15
Olivares et al, 2009 | □ |  | 0.52 | 0.43-0.64 | 28.07
Olivares et al, 2009 | □ |  | 0.86 | 0.57-1.39 | 17.07
Zhu et al, 2008 | □ |  | 0.59 | 0.43-0.81 | 22.53
Pooled prospective studies | □ |  | 0.62 | 0.48-0.81 |

Retrospective studies
Emsley et al, 2008 | □ |  | 0.25 | 0.09-0.70 | 5.02
Emsley et al, 2008 | □ |  | 0.38 | 0.22-0.64 | 15.06
Tavcar et al, 2000 | □ |  | 0.71 | 0.49-1.01 | 26.45
Tihonen et al, 2006 | □ |  | 0.61 | 0.38-0.99 | 17.91
Tihonen et al, 2011 | □ |  | 0.16 | 0.02-1.05 | 1.53
Tihonen et al, 2011 | □ |  | 0.69 | 0.35-1.35 | 10.48
Tihonen et al, 2011 | □ |  | 0.46 | 0.16-1.34 | 4.66
Tihonen et al, 2011 | □ |  | 0.64 | 0.41-1.02 | 18.89
Pooled retrospective studies | □ |  | 0.56 | 0.44-0.71 |

Adjusted Relative Risk (log scale)

□ Hospitalization
□ Relapse
□ All-cause discontinuation

Abbreviations: RCT = randomized controlled trial, RR = risk ratio.
Terapia antipsicotica continua vs intermittente: tassi di ricadute (12 mesi)

Depot Clinic  Safety and tolerability of long acting injectable antipsychotics versus oral antipsychotics: A metanalysis of randomized controlled studies comparing the same antipsychotics

(English) By: Misawa F; Kishimoto T; Hagi K; Kane JM; Correll CU, Schizophrenia Research [Schizophr Res], ISSN: 1573-2509, 2016 Oct; Vol. 176 (2-3), pp. 220-30; Publisher: Elsevier Science Publisher B. V.; PMID: 27499361;

Objective: We aimed to assess whether long-acting injectable antipsychotics (LAIs), which are initiated in a loading strategy or overlapping with oral antipsychotics (OAPs) and which cannot be stopped immediately, are associated with greater safety/tolerability issues than OAPs.

Method: Systematic review and meta-analysis of randomized controlled trials (RCTs) comparing LAIs and OAPs, including only LAI-OAP pairs of the same OAP (allowing oral risperidone and paliperidone as comparators for either risperidone or paliperidone LAI). Primary outcome was treatment discontinuation due to adverse events. Secondary outcomes included serious adverse events, death, ≥1 adverse event and individual adverse event rates.

Results: Across 16 RCTs (n=4902, mean age=36.4 years, males=65.8%, schizophrenia=99.1%) reporting on 119 adverse event outcomes, 55 (46.2%) adverse events were reported by ≥2 studies allowing a formal meta-analysis. Out of all 119 reported adverse events, LAIs and OAPs did not differ significantly regarding 115 (96.6%). LAIs were similar to OAPs regarding the frequency of treatment discontinuation due to adverse events, serious adverse events, all-cause death and death for reasons excluding accident or suicide. Compared to OAPs, LAIs were associated with significantly more akinesia, low-density lipoprotein cholesterol change and anxiety. Conversely, LAIs were associated with significantly lower prolactin change.

Conclusion: LAIs and OAPs did not differ on all serious and >90% of individual adverse events. However, more studies focusing on adverse event frequencies, severity and time course associated with LAI vs OAP formulations of the same antipsychotic are needed. Additionally, adverse events data for LAIs after stopping overlapping oral antipsychotic treatment are needed.
Depot Clinic

Treatment adherence in schizophrenia: A patient-level meta-analysis of combined CATIE and EUFEST studies

### Independent variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (OR) for worse non-adherence</th>
<th>95% Confidence interval</th>
<th>Chi-square</th>
<th>p-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol/drugs at 6 months</td>
<td>2.017</td>
<td>1.380-2.948</td>
<td>13.13</td>
<td>0.0003</td>
</tr>
<tr>
<td>Insight at 6 months</td>
<td>1.420</td>
<td>1.264-1.596</td>
<td>34.69</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hostility at 6 months</td>
<td>1.372</td>
<td>1.160-1.623</td>
<td>13.64</td>
<td>0.0002</td>
</tr>
<tr>
<td>Akathisia at 6 months</td>
<td>1.332</td>
<td>0.885-2.004</td>
<td>1.89</td>
<td>n.s.</td>
</tr>
<tr>
<td>Parkinsonism at 6 months</td>
<td>0.716</td>
<td>0.492-1.043</td>
<td>3.03</td>
<td>n.s.</td>
</tr>
<tr>
<td>Dyskinesia at 6 months</td>
<td>0.737</td>
<td>0.471-1.152</td>
<td>1.79</td>
<td>n.s.</td>
</tr>
<tr>
<td>Positive symptoms at 6 months</td>
<td>1.022</td>
<td>0.987-1.058</td>
<td>1.46</td>
<td>n.s.</td>
</tr>
<tr>
<td>Study (CATIE vs. EUFEST)</td>
<td>4.770</td>
<td>3.267-6.963</td>
<td>65.51</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>0.992</td>
<td>0.978-1.006</td>
<td>1.33</td>
<td>n.s.</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.271</td>
<td>0.951-1.698</td>
<td>2.62</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

*Note: All analyses were performed using logistic regression of adherence to medication treatment at six months.*

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*Images and graphs are not transcribed.*
Many patients with schizophrenia have problems adhering to their medication regimen. Numerous factors affect patients’ adherence, such as patient and illness characteristics; medication efficacy, tolerability and formulations; provider and system characteristics; and patients’ support networks. To compound this problem, accurately measuring adherence is challenging. Data suggest that clinicians should use multiple methods to assess patients’ adherence, including supplementing their own clinical judgment and patient reports with more objective measures. Patients with poor social support, substance abuse disorders, or a history of florid psychosis and those in the earlier phases of their illness may be at risk for nonadherence. Assessing patients for nonadherence is a key step in determining their optimal form of treatment and avoiding frequent switching or deterioration. Doing so, clinicians can identify patients who would potentially benefit from a long-acting injectable (LAI) antipsychotic, which can be a valuable treatment option. Because lack of adherence increases the risk of hospitalization and does not help prevent suicide attempts, clinicians should address barriers to adherence, provide psychoeducation about medication-taking behaviors, and offer a wide range of antipsychotic treatment options, including LAIs, to improve patient outcomes.
Drivers of non-adherence

- Poor insight/cognition
- Complicated/inconvenient regimens
- Substance abuse
- Positive symptoms
- Poor social support
- Intolerable side effects/AEs
- Patient attitudes to treatment

Non-adherence

CONCLUSIONS:

This analysis of the available literature strongly suggests that further observational studies on patients with schizophrenia treated with LAIs are needed to systematically assess their demographic and clinical characteristics and the relationships between them and patient outcome. Besides the good efficacy and safety profile of LAIs, health care staff must also take into account the importance of establishing a therapeutic alliance with the patient and his/her relatives when selecting the most appropriate treatment. LAIs seem to be a good choice not only because of their good safety and efficacy profile, but also because they improve compliance, a key factor to improving adherence and to establishing a therapeutic alliance between patients with schizophrenia, their relatives, and their health care providers.
Depot Clinic

GOOD COMPLIANCE

- Late
- Long
- Yes
- Mild
- Low
- Oral
- No

Evaluate patient’s interest in taking Depot treatment considering:
- Insight of illness severity
- Educational level
- Therapeutic alliance
- Possibility of sharing the therapeutic decision with the physician

POOR COMPLIANCE

- Age at Onset
- Length of Illness
- Insight
- Positive and Negative Symptoms
- Drug Abuse
- Percentage of Relapse
- Frequency of Hospitalizations
- Ongoing Therapy
- Previous Depot
- Young
- Short
- No
- Severe
- Yes
- High
- High
- Oral/Depot
- Yes

Evaluate patient’s interest in switching to atypical depot, considering:
- Severity of illness
- Dosages of ongoing therapy
- Efficacy profile of the depot
LAI versus oral: A case-control study on subjective experience of antipsychotic maintenance treatment

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d Therapeutic psychiatric community, Campo del Vescovo Union, La Spezia, Italy

ABSTRACT

Background: To present real-world evidence on the differences between long-acting injectable (LAI) and oral antipsychotic maintenance treatment (AMT) in terms of subjective well-being, attitudes towards drug and quality of life in a sample of remitted schizophrenic subjects.

Methods: Twenty outpatients with remitted schizophrenia treated with either olanzapine or paliperidone and switching from the oral to the LAI formulation of their maintenance treatment were recruited before the switch (LAI-AMT group). A group of 20 remitted schizophrenic subjects with oral AMT and matching main sociodemographic, clinical and treatment variables made up the control group (oral-AMT group). All participants were assessed in terms of objective (PANSS, YMRS, MADRS) and subjective (SWN-K, DAI-10, SF-36) treatment outcomes at baseline (T0) and after 6 months (T1).

Results: Between T0 and T1, general psychopathology of the PANSS, DAI-10, and all but one of the SWN-K dimensions (except for social integration), showed significantly higher percentages of improvement in the LAI-AMT group compared to the oral-AMT group. A generalized expansion of health-related quality of life, with better functioning in almost all areas of daily living, was reported by the LAI-AMT group after the 6-month period. In contrast, the oral-AMT group reported a significant worsening of health-related quality of life in the areas of emotional role and social functioning in the same period.

Conclusions: Our study indicates possible advantages of LAI over oral antipsychotic formulation in terms of subjective experience of maintenance treatment in remitted schizophrenic patients. Size and duration of this study need to be expanded in order to produce more solid and generalizable results.
Conclusions: In RCTs, which are less representative of real-world patients than naturalistic studies, pooled LAIs did not reduce relapse compared with OAPs in schizophrenia patients. The exceptions were FGA-LAIs, mostly consisting of fluphenazine-LAI studies, which were all conducted through 1991. Because this finding is vulnerable to a cohort bias, studies comparing FGA-LAI vs second-generation antipsychotics-LAI and LAI vs OAP RCTs in real-world patients are needed.
Poor adherence to oral antipsychotics is the most common cause of relapse. The discontinuation rate for oral antipsychotics in schizophrenia ranges from 26% to 44%, and as many as two-thirds of patients are at least partially nonadherent, resulting in increased risk of hospitalization. A very helpful approach to improve adherence in schizophrenia is the use of long-acting injectable (LAI) antipsychotics, although only a minority of patients receive these. Reasons for underutilization may include negative attitudes, perceptions, and beliefs of both patients and health care professionals. Research shows, however, significant improvements in adherence with LAIs compared with oral drugs, and this is accompanied by lower rates of discontinuation, relapse, and hospitalization. In addition, LAIs are associated with better functioning, quality of life, and patient satisfaction. A need exists to encourage broader LAI use, especially among patients with a history of nonadherence with oral antipsychotics. This paper reviews the impact of nonadherence with antipsychotic drug therapy overall, as well as specific outcomes of the schizophrenia patient, and highlights the potential benefits of LAIs.
RESEARCH REPORT

The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia

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*The members of the Italian Network for Research on Psychoses are listed in the Appendix.
Figure 1. Initial structural equation model. Neurocognition, social cognition, resilience and SLOF are latent variables (with arrows pointing to their respective indicators). PANSs POS, PANSs DISORG, BNSS avolition, BNSS-EE, depression, neurocognition and incentives are independent predictors. Social cognition, functional capacity, internalized stigma, resilience and service engagement are mediators, and SLOF is the dependent variable. PANSs – Positive and Negative Syndrome Scale, POS – positive, DISORG – disorganization, BNSS – Brief Negative Symptom Scale, EE – poor emotional expression, AVOL – avolition, PROC SPEED – processing speed, ATTN – attention, WORK MEM – working memory, VERB MEM – verbal memory, VIS MEM – visuospatial memory, PROBL SOLV – problem solving, TASIT – The Awareness of Social Inference Test, MSCEIT – Mayer-Salovey-Caruso Emotional Intelligence Test, PERC. SELF – perception of self, PERC. FUTURE – perception of the future, SOCIAL COMPET. – social competence, SLOF – Specific Level of Functioning, PERS – skills in self-care, ACTIV – community activities, ACC – social acceptability, INTER – interpersonal relationships. WORK – working abilities.
Depot Clinic

Fig. 2. Impact of treatment services on proximal and distal outcomes in schizophrenia.
Targets, attitudes, and goals of psychiatrists treating patients with schizophrenia: key outcome drivers, role of quality of life, and place of long-acting antipsychotics

Purpose: This survey of Italian psychiatrists was conducted to better define drivers of schizophrenia treatment choice in real-life practice, particularly for use of long-acting injectable (LAI) antipsychotics.

Methods: Between October 15 and December 15, 2014, 1,000 surveys were sent to psychiatrists who treat schizophrenic patients; 709 completed questionnaires were analyzed (71% response rate).

Results: The two most important factors determining therapy success were efficacy (75% of responses) and tolerability (45%) followed by global functioning (24%) and quality of life (17%). LAI antipsychotics were most often used to facilitate regular treatment monitoring (49%), and 41% of psychiatrists thought that patients with low adherence who had failed oral therapy were well-suited for LAI antipsychotics. Only 4% of respondents saw LAI antipsychotics as appropriate for patients without other therapeutic options.

Conclusion: Although efficacy and tolerability were the most common factors used to evaluate treatment success in schizophrenia, psychiatrists also consider QoL and global functioning to be important.

Keywords: quality of life, long-acting injectable antipsychotics, schizophrenia, survey
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Psychiatrists (%)

- Efficacy: 75%
- Tolerability/safety: 45%
- Adherence to treatment: 26%
- Global functioning: 24%
- Quality of life: 17%
- Cost: 1%
- Other: 1%
- No response: 10%
### Vantaggi
- Migliore aderenza al trattamento
- Evitamento del metabolismo di primo passaggio
- Aumento della biodisponibilità
- Concentrazioni plasmatiche più prevedibili e stabili
- Diminuito rischio di intossicazione accidentale o volontaria
- Basso rischio di sintomi “rebound” ed improvvisi ricadute
- Più frequente contatto tra paziente ed operatori

### Svantaggi
- Lento raggiungimento della concentrazione ottimale
- Gestione problematica degli effetti indesiderati per l’impossibilità ad interrompere il rilascio del farmaco
- Occasionale reazione locale nel sito di iniezione
- Sensazione di “essere controllato”
- Percezione dello “stigma”
- Elevati costi di acquisizione
Depot Clinic

Antipsicotici a rilascio prolungato nel trattamento della schizofrenia: una revisione della letteratura

Long acting injectable antipsychotics in the treatment of schizophrenia: a review of literature

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RIASSUNTO. Introduzione. I farmaci antipsicotici sono fondamentali nel trattamento della schizofrenia e l’assunzione di una costante e continua farmacoterapia è importante per il controllo dei sintomi e per la prevenzione delle ricadute. Tuttavia i tassi di non-aderenza in questo disturbo variano tra il 40% e il 90%. L’introduzione degli antipsicotici a rilascio prolungato (LAI) aveva come primo obiettivo il superamento della scarsa aderenza. Scopo. La presente revisione si focalizza sul ruolo dei LAI nel trattamento della schizofrenia, in particolare sugli antipsicotici di nuova generazione. É stata indagata la letteratura esistente, con particolare attenzione alle evidenze cliniche e sono stati esaminati sia i vantaggi sia gli svantaggi di questo tipo di trattamento. Risultati. Evidenze cliniche suggeriscono che il trattamento con LAI si associa a migliore aderenza, migliore outcome e ridotto numero di riospedalizzazioni. I LAI garantiscono una maggiore biodisponibilità, una correlazione più prevedibile tra dose del farmaco e concentrazioni plasmatiche, un maggiore profilo farmacocinetico permettendo la prescrizione di dosaggi minori con conseguente minore rischio di effetti collaterali. Gli antipsicotici di prima generazione LAI (FGA-LAI) condividono con i rispettivi composti orali un’aumentata suscettibilità a indurre sintomi extrapiramidali e discinesia tardiva, con minime differenze tra i composti. Gli antipsicotici di seconda generazione LAI (SGA-LAI), come le rispettive formulazioni orali, hanno rispetto a FGA-LAI il vantaggio di non causare disturbi del movimento, ma il loro uso è complicato dal rilascio ritardato (risperidone) e dal rischio della sindrome post-iniezione (olanzapina). Discussione e conclusioni. Nonostante i vantaggi individuati, i LAI non sono ancora utilizzati come ci si aspetterebbe. Una possibile spiegazione è imputabile ai clinici, influenzati da erronee convinzioni (per es., che il paziente non accetti questo tipo di trattamento) e informazioni (per es., aumentato rischio di effetti collaterali). Le attuali linee-guida sul trattamento della schizofrenia consentano l’utilizzo dei LAI nei pazienti che hanno dimostrato non-aderenza o ricorrenti ricadute legate alla scarsa o assente aderenza alla terapia e sottolineano l’importanza della preferenza del paziente. È sensibile che la prescrizione di LAI aumenterà nei prossimi anni sia per una maggiore disponibilità di SGA-LAI sia per il crescente utilizzo di trattamenti obbligatori anche extra-ospedalieri.
Treatment of early episode in patients with schizophrenia: the role of long acting antipsychotics.

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The use of long-acting injectable antipsychotics (LAIs) in schizophrenia is usually restricted to patients in long-term treatment, who prefer them to oral antipsychotics, and to patients with multiple relapses who have a history of non-adherence. However, preliminary evidence from patients in the early phases of the disease suggest that second generation LAIs may be superior to second generation oral medications with regard to the control of negative symptoms and psychosocial functioning. Moreover, several studies have found that psychiatrists are generally reluctant to prescribe LAI antipsychotics and under-estimate their acceptability by patients. Key elements to take into account when offering a LAI in the early course of schizophrenia should include their potential superiority in allowing early detection of non-adherence and in reducing the number of rehospitalisations and relapses.
CONCLUSIONS:
This claims-based analysis of posthospitalization adherence and rehospitalization outcomes in Medicaid patients with schizophrenia adds to the growing real-world evidence base of the benefits of LAI antipsychotic medications in routine clinical practice, particularly with regard to second-generation LAIs. As new SGA formulations become available for long-acting use, real-world studies with larger sample sizes will be needed to further delineate their potential advantages in terms of clinical outcomes and costs.
Article

Routine quality care assessment of schizophrenic disorders using information systems

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Abstract

Objective: To assess the quality of mental healthcare provided to patients with schizophrenic disorders in the Italian region of Lombardy.

Design: Forty-one clinical indicators were applied to Lombardy’s healthcare databases containing data on mental health treatments, hospital admissions, somatic health treatments and pharmaceutical prescriptions.

Setting: All public departments of mental health and private residential facilities in Lombardy.

Participants: All 28,227 patients with schizophrenic disorders that were under the care of Lombardy mental health services in 2009.

Interventions: N/A.

Main outcome measures: N/A.

Results: The care that was delivered to patients and family members was more frequent for first-episode cases than for prevalent ones. Seven out of ten patients made use of continuing care and, after hospitalization, more than half of the discharged patients received a follow-up visit by community mental health centre staff within 2 weeks of their discharge. Psychotherapeutic and psychoeducative treatments, such as employment and independent living support, were not widespread among these discharged patients. Antipsychotic drug dosage was usually within the recommended range. The adherence of first-episode patients to antipsychotic treatment was lower than that of prevalent patients, and the monitoring of metabolic side effects was not always consistent. Inappropriateness of hospital care, in terms of longer admission, readmission, compulsory admission and restraint, was limited. Mortality during the period was significant.

Conclusions: Clinical indicators demonstrate the strengths and weaknesses of the mental health system in Lombardy and they can be useful tools in the routine assessment of mental healthcare quality.
A: First-episode patients
1. Patient age at first contact with mental health services (years) 27.8
2. Patients with a waiting time >7 days for the first CMHC outpatient visit 18%
3. Mean number of patients' contacts with CMHCs per month 2.6
4. Mean number of carers' contacts with CMHCs per month 1.3
5. Patients with continuity of care in the first year of treatment (at least one contact out of every 90 days in the 365 days after their first contact during the year) 60%
6. Patients delivered multi-professional activities in CMHC 77%
7. Patients treated with psychoeducation (at least 4 sessions) 9%
8. Patients treated with psychotherapy (at least 3 sessions) 23%
9. Patients delivered home care in the first year of treatment (at least 3 home visits) 5%
10. Patients adherent to antipsychotic treatment at 180 days during the first episode 11%
11. Patients prescribed SGAs for the first time and monitored for hyperglycaemia and hyperlipidemia (at least 4 checks during the first 12 weeks after the beginning of the therapy) 47%

B: Acute episode and early post-acute period
12. Compulsory admissions 12%
13. Patients physically restrained at least once yearly during hospitalization 13%
14. Admissions with a length of stay higher than 30 days 12%
15. Unplanned readmissions within 4 weeks 21%
16. Patients with appropriate dosage of antipsychotic drugs at discharge (i.e. between 300 and 1000 mg CPZ-equivalent) 59%
17. Patients receiving a mental health outpatient visit within 14 days from discharge by GHPW 52%
18. Patients with home care following GHPW discharge (at least one home visit in the 2 weeks following discharge) 7%
19. Patients with continuity of clinical monitoring after hospitalization (at least one psychiatric visit per month in CMHC during the first 6 months after discharge) 27%

C: Recovery maintenance and promotion
20. Patients with continuity of care (at least one contact out of every 90 days in the 365 days after their first contact in the year) 67%
21. Patients with individualized care plan Data
22. Patients with case management Data
23. Patients delivered multi-professional care in CMHCs 72%
24. Patients with at least six CHMC contacts per year 67%
25. Carers with at least three CHMC contacts specifically addressed to family members per year 11%
26. Patients in the maintenance phase adherent to antipsychotic treatment after 180 days 49%
27. Patients who are prescribed only one type of antipsychotic drug 74%
28. Patients with appropriate frequency and dosage of depot/long-acting injectable antipsychotics 98%
29. Patients with appropriate clinical monitoring of depot/long-acting injectable antipsychotics (at least one psychiatric visit every 90 days) 89%
30. Patients not responding adequately to antipsychotic treatment with clozapine 14%
31. Patients with at least one psychiatric visit within 90 days after interrupting or stopping treatment with an antipsychotic 49%
32. Patients prescribed SGAs and monitored for hyperglycaemia and hyperlipidemia 47%
33. Patients treated with psychoeducation (at least 4 sessions) 12%
34. Patients treated with psychotherapy (at least 3 sessions) 1%
35. Patients involved in social, expressive, practice and physical activities in CMHCs and day-care facilities (activities delivered in residential care are excluded) 16%
36. Patients who received independent living support 1%
37. Patients who received employment support 5%

D: Common elements
38. Treatment gap in schizophrenia 40.1%
39. Dropout from mental healthcare 2.01
40. Mortality for persons with schizophrenia disorders (SMR) Data
41. Mortality due to suicide Data