Antipsychotic Treatment for Schizophrenia: Effects on Sexual Function


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ABSTRACT

Background: IC-SOHO (Intercontinental Schizophrenia Outpatients Health Outcomes) is a 3-year global, prospective, observational study examining health outcomes for outpatients with schizophrenia undergoing treatment with antipsychotics. In this presentation, we describe the effect of antipsychotic treatments on sexual functioning of patients with schizophrenia 6 months after enrolment.

Objective: To examine the side effects associated with sexual functioning in patients with schizophrenia following 6 months of antipsychotic therapy.

Method: Subjects > 18 years of age, undergoing treatment for schizophrenia in an outpatient setting and either changing or initiating antipsychotic treatment, were enrolled at the discretion of their psychiatrist. Two treatment groups were established for post hoc analysis: prolactin-elevating (consisting of typical antipsychotics, risperidone and amisulpride) and non-prolactin-elevating (all atypical antipsychotics except risperidone and amisulpride) antipsychotic treatments. Further analysis comparing sexual dysfunction in patients prescribed olanzapine, risperidone or haloperidol was conducted. Physicians recorded the presence of symptoms associated with sexual dysfunction, namely impotence, gynecomastia, galactorrhea, amenorrhea and loss of libido at baseline, 3- and 6 months after enrolment. Statistical significance for all analyses was determined, a priori, to be p<0.001.

Results: Problems associated with sexual dysfunction were commonly reported in this study. Fifty-one percent of patients reported sexual dysfunction at baseline (27% some problems, 24% unable to perform sexually) while 42% reported sexual dysfunction after 6 months of treatment (25% some problems, 17% unable to perform). Of the patients prescribed prolactin-elevating antipsychotics, 45% experienced loss of libido, 5% showed signs of gynecomastia, 33% experienced impotence/sexual dysfunction, 4% exhibited symptoms of galactorrhea, while amenorrhea was recorded in 30% of female patients after 6 months of treatment. Patients prescribed prolactin-neutral antipsychotic therapy however, had significantly lower incidence (p<0.0001) of loss of libido (29%), gynecomastia (2%), impotence/sexual dysfunction (20%), galactorrhea (1%) and amenorrhea (16% of females) compared with their counterparts on prolactin-elevating antipsychotics. Furthermore, patients prescribed olanzapine had a significantly (p<0.0001) lower incidence of impotence/sexual dysfunction, loss of libido, galactorrhea and amenorrhea compared with risperidone or haloperidol-treated patients. There was a significant difference (p<0.0001) in the frequency of patient-reported sexual dysfunction compared with psychiatrist-reported adverse events related to sexual function, with the reporting of sexual dysfunction by psychiatrists being lower than the self-reporting of sexual dysfunction by patients.

Conclusion: Problems related to sexual functioning are common in patients receiving antipsychotics. However, such sexual dysfunction is more prevalent in patients taking antipsychotics known to elevate serum prolactin levels, than in patients prescribed antipsychotics with a neutral effect on serum prolactin. Patients suffer from sexual dysfunction more frequently than is diagnosed by psychiatrists. Olanzapine is superior to risperidone and haloperidol in terms of sexual function side effects and may offer an alternative therapy for patients receiving antipsychotic treatment who present with these symptoms.

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The Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study was designed to investigate the pharmacological treatment patterns for schizophrenia in outpatient settings, and to examine how these treatment patterns are associated with health outcomes.

**BACKGROUND**

To report the frequency of side effects associated with sexual functioning in outpatients participating in the IC-SOHO study during the first 6 months of antipsychotic treatment.

**OBJECTIVE**

STUDY DESIGN

IC-SOHO

A 3-year, global, prospective, non-interventional, open-label, observational study of the health outcomes associated with antipsychotic medication therapy in outpatients treated for schizophrenia.

**DATA COLLECTION**

- Patients were included in the study alternating between the 2 groups based on the physician’s decision of treatment assignment.

**STATISTICAL ANALYSIS**

- Baseline, 3 and 6 months results are presented. Patients are grouped based on the antipsychotic medication initiated or changed to at baseline.
- Statistical significance was decided, a priori, to be \( p < .001 \).

*Any registered antipsychotic medication with schizophrenia as indication for use.

**PATIENT DEMOGRAPHICS**

**FREQUENCY OF PATIENT REPORTED ADVERSE EFFECTS RELATED TO SEXUAL FUNCTION BY REGION**

Patients treated in CEER reported the highest overall frequency of impotence/sexual dysfunction while patients treated in AR reported the lowest frequency and severity of sexual dysfunction.

**PATIENT ENROLLMENT BY REGION**

- **Total Intercontinental Sample Population** \( N = 7655 \)
  - Latin America Region (LAR), 35%
    - \( n = 2671 \)
    - 11 Countries
  - Asia Region (AR), 16%
    - \( n = 1256 \)
    - 3 Countries
  - Africa and Middle East Region (AMER), 19%
    - \( n = 1476 \)
    - 5 Countries
  - Central and Eastern Europe Region (CEER), 29%
    - \( n = 2252 \)
    - 8 Countries

**PATIENT REPORTED VERSUS PSYCHIATRIST PERCEPTION OF PATIENTS’ SEXUAL DYSFUNCTION AT 6 MONTHS**

- **Loss of Libido**
  - Not Present: 2684 (52%), Present: 296 (6%)
  - McNemar’s test: \( p < .0001 \)
- **Impotence/Sexual Dysfunction**
  - Not Present: 2610 (58%), Present: 67 (2%)
  - McNemar’s test: \( p < .0001 \)

* McNemar’s test

Patients reported problems with sexual functioning more frequently than psychiatrists.
At 3 and 6 months, significantly fewer olanzapine-treated patients had impotence/sexual dysfunction compared with risperidone and haloperidol-treated patients.

At 3 and 6 months, significantly fewer olanzapine-treated patients had loss of libido at 3 and 6 months.

**PRESENCE OF IMPOTENCE/SEXUAL DYSFUNCTION BY ANTIPSYCHOTIC**

- **Olanzapine**
- **Risperidone**
- **Haloperidol**

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Olanzapine</th>
<th>Risperidone</th>
<th>Haloperidol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of treatment (months)</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>% Patients with treatment emergent symptoms</td>
<td>5.9</td>
<td>6.9</td>
<td>4.3</td>
</tr>
<tr>
<td>% Patients with remission of symptoms</td>
<td>44.7</td>
<td>55.1</td>
<td>32.7</td>
</tr>
</tbody>
</table>

* p<0.001, Chi-squared test, olanzapine vs risperidone and olanzapine vs haloperidol.
† Not present at baseline, present after commencement of treatment.
‡ Present at baseline, no longer present at 3 and 6 months.

- Significantly fewer olanzapine-treated patients developed impotence/sexual dysfunction compared with risperidone and haloperidol-treated patients.
- More patients had remission of symptoms following 3 and 6 months of olanzapine treatment compared with patients taking risperidone and haloperidol.

**PRESENCE OF LOSS OF LIBIDO BY ANTIPSYCHOTIC**

- **Olanzapine**
- **Risperidone**
- **Haloperidol**

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</thead>
<tbody>
<tr>
<td>Duration of treatment (months)</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>% Patients with treatment emergent symptoms</td>
<td>10.9</td>
<td>10.8</td>
<td>17.8</td>
</tr>
<tr>
<td>% Patients with remission of symptoms</td>
<td>37.2</td>
<td>48.4</td>
<td>29.2</td>
</tr>
</tbody>
</table>

* p<0.001, Chi-squared test, olanzapine vs risperidone and olanzapine vs haloperidol.
† Not present at baseline, present after commencement of treatment.
‡ Present at baseline, no longer present at 3 and 6 months.

- At 3 and 6 months, significantly fewer olanzapine-treated patients developed loss of libido when compared with risperidone or haloperidol-treated patients.
- More patients had remission of symptoms following 3 and 6 months of olanzapine treatment compared to patients taking risperidone and haloperidol.

**GENDER DIFFERENCES REPORTING ADVERSE EFFECTS ASSOCIATED WITH SEXUAL DYSFUNCTION**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatrist perception</td>
<td>Baseline</td>
<td>3 Months</td>
</tr>
<tr>
<td>Loss of libido</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>Impotence/sexual dysfunction (%)</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td>Amenorrhea (%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Galactorrhea (%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Gynecomastia (%)</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

* p<0.001, Chi-square test, olanzapine vs risperidone and olanzapine vs haloperidol.
† Present at baseline, no longer present at 3 and 6 months.
‡ Not present at baseline, present after commencement of treatment.

- The psychiatrist reported impotence/sexual dysfunction significantly more often in male patients compared to female patients. No significant differences were observed in patient perception of sexual dysfunction between males and females.

**ADVERSE EFFECTS ASSOCIATED WITH SEXUAL FUNCTION BY PROLACTIN-ELEVATING AND PROLACTIN SPARING ANTIPSYCHOTICS**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Prolactin elevating1</th>
<th>Prolactin sparing2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of treatment (months)</td>
<td>Baseline</td>
<td>3</td>
</tr>
<tr>
<td>Loss of libido (%)</td>
<td>46</td>
<td>45</td>
</tr>
<tr>
<td>Impotence/sexual dysfunction (%)</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>Amenorrhea/other menstrual disturbances (%)</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>Galactorrhea (%)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Gynecomastia (%)</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

* p<0.001, prolactin elevating vs prolactin sparing, Chi-squared test.
† Prolactinelevating (typical antipsychotics and amisulpride, risperidone)
‡ Prolactin sparing (other atypicals: clozapine, olanzapine, quetiapine, ziprasidone, zotepine)

- More adverse effects were associated with prolactin elevating antipsychotics.

**ADVERSE EVENTS ASSOCIATED WITH PROLACTIN ELEVATION BY ANTIPSYCHOTIC**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galactorrhea</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Amenorrhea/other menstrual disturbances</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

* p<0.001, Chi-square test, olanzapine vs risperidone and olanzapine vs haloperidol.
† Female patients only.

- After 3 and 6 months, the proportion of patients experiencing side effects associated with prolactin elevation decreased with olanzapine therapy.
- Also, after 3 and 6 months, significantly fewer olanzapine-treated patients suffer from menstrual disturbances and galactorrhea, compared to risperidone and haloperidol-treated patients.
CONCLUSIONS

- When considering ways of improving the quality of life of patients with schizophrenia, it is important to include sexual functioning as a measure of their quality of life.
- Patients treated with olanzapine reported significantly less treatment emergent and greater remission rates from side effects associated with sexual functioning compared with risperidone and haloperidol.
- Patients treated with antipsychotics known to be associated with prolactin elevation had significantly higher incidences of loss of libido, impotence/sexual dysfunction, galactorrhea, amenorrhea and gynecomastia.
- Olanzapine offers patients a treatment alternative that does not negatively impact their quality of life with respect to their sexual functioning.