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Background and aims: Agitation is a common symptom in schizophrenia and bipolar mania, causing marked distress and posing considerable risks for patients. Intramuscular formulations of psychotropic medication can provide a fast acting treatment of severe agitation in patients with acute episodes of schizophrenia or mania. As effective as these treatments are, particular antipsychotics can be associated with a heightened risk of dystonia and related Extrapyramidal Symptoms (EPS). Patients presenting to emergency care settings are also likely to have coexisting intoxications and medical conditions that may contribute to this risk.

Methods: The aim of this observational prospective study was to document the safety and effectiveness of all IM psychotropic drugs during the 24 hours following an initial injection in acutely agitated patients suffering from schizophrenia or bipolar disorder under naturalistic conditions.

Results: Two-hundred-thirty-two (232) participating investigator sites (12 European countries) observed 1940 patients (mean age: 39 y, 42% female, 66% schizophrenia diagnosis). The primary endpoint was the occurrence of extrapyramidal symptoms (EPS), further endpoints were clinical severity measured by PANSS-EC and CGI-S. A total of 1311 (68%) patients received a monotherapy injection at baseline. Within 24 hours after the first injection, 190 (10%) of all 1940 patients experienced EPS. All intramuscular psychotropic drugs were shown to be effective in reducing measures of acute agitation.

Conclusion: This study provides favourable results on EPS related adverse events and effectiveness of intramuscular psychotropic medication for the management of acute agitation in patients within a naturalistic setting during the first 24 hours of treatment.

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Schizophrenia and substance use disorders: Effects of zyprasidone treatment

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Background and aims: The risk of abuse/dependence of alcohol or drugs in schizofrenia have been estimed about 4 times the prevalence in general population. This fact difficults the treatment results and efficcacy: more relapses, more treatments withdrawal and poorer prognosis. The aims of our study is to evaluate the effect of Zyprasidone, an atypical antipsychotic with 5HT propierties, in patients with schizofrenia and comorbid substance use disorder in a single, open, prospective-naturalistic design.

Method: 36 outpatients were selected with Schizofrenic disorder diagnosis (DSMIV) and abuse/dependence of at least 1 substance in which Zyprasidone was recommended (inneficacy, intolerance of prior treatments,..). They were evaluated clinically and data about actual consum and craving were collected at inicial visit and follow-up monthly (3 to 6 months). Results were analized with SPSS pack.

Results: The mean follow-up period was 3 month. 28 patients finished the evaluation showing a decrease in clinical measures (PANSS, ICG) with good tolerance (only 4 drop-outs associated to indesirable effects). The most frequent drug use disorder was tobacco followed by alcohol and cannabis.The results on number and frequency of drug use shows a slow tendency to reduce at the end of the evaluation as well the craving measures but no significant differences were found.

Conclusions: Our exploratory study with Zyprasidone, althougt metodological limitations, suggests that clinical schizofrenic symptoms can improve but also drug pattern use. Naturalistic studies of schizofrenia with comorbid substance use disorder can be useful to show the efficacy of antipsychotics in real clinical practice

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Changes in prolactin in olanzapine-treated adolescents with schizophrenia or bipolar mania: A pooled analysis of 4 studies

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Introduction: Prolactin (PRL) data from adolescents treated with olanzapine are presented.

Methods: Data from 454 adolescents (13-18, mean=15.9 yrs) with schizophrenia or bipolar mania were pooled from 4 olanzapine (2.5-20.0mg/day) studies (4-32 weeks; 2 double-blind, placebo-controlled studies [combined for acute phase endpoint PRL levels] with open-label extensions; 2 open-label studies). Age- and sex-specific Covance reference ranges defined normal PRL; categorical increases were based on multiples of the upper limit of normal (ULN). Baseline-to-endpoint PRL changes in adolescents were compared with data pooled from 84 olanzapine clinical trials in adults with schizophrenia or bipolar disorder.

Results: Olanzapine-treated adolescents had mean PRL increases at both the acute (11.4μg/L) and open-label endpoints (4.7μg/L). Of those patients with normal PRL levels at baseline (N=311), high PRL occurred in 54.7% at anytime; 32.2% at endpoint. The percentage of patients in which PRL levels shifted from normal-to-abnormal was smaller at endpoint than at anytime during treatment; 26.7% shifted to a higher category. Among patients with normal baseline PRL, 32.7% remained <=1X ULN; 32.3% increased to 1¬<=2X; 6.0%, >2-<=3X; and 1.2%, >3X at anytime; 4.6% had at >=1 potentially PRL-related adverse event. Adolescents had significantly higher mean changes at endpoint (p=.004), and a greater incidence of high PRL levels at anytime during olanzapine treatment (p<.001) versus adults.

Conclusion: Incidence of high PRL was significantly higher, and mean increases in PRL were significantly greater in adolescents versus adults. Mean increases and high PRL incidence were lower at the open-label compared with the acute phase endpoint.

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Changes in metabolic parameters in olanzapine-treated adolescents with schizophrenia or bipolar I disorder: A pooled analysis of 4 studies

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Introduction: The changes in metabolic parameters in olanzapine-treated adolescents were examined.

Methods: Data from 454 adolescents (13–18, mean=15.9 years) with schizophrenia or bipolar I disorder were pooled from 4 olanzapine (2.5–20.0mg/day) studies (4–32 weeks). Changes in metabolic parameters in adolescents were compared with those of olanzapine-treated adults (pooled from 84 clinical trials); changes in weight and BMI were compared with US age- and sex-adjusted standardized growth curves.

Results: Olanzapine-treated adolescents had significant increases from baseline-to-endpoint in fasting glucose (p=.021); total cholesterol, LDL, and triglycerides (p<.001); and significant decreases in HDL (p<.001). Significantly more adolescents gained >=7% of their baseline weight versus adults (65.1% vs. 35.6%, p<.001); mean change from baseline-to-endpoint in weight was significantly greater in adolescents (7.0 vs. 3.3kg, p<.001). Adolescents had significantly lower mean changes from baseline-to-endpoint in fasting glucose (0.3 vs. 0.1mmol/L, p=.002) and triglycerides (0.3 vs. 0.2mmol/L, p=.007) versus adults. Significantly more adults experienced treatment-emergent normal-to-high changes at anytime in fasting glucose (4.8% vs. 1.2%, p=.033), total cholesterol (6.9% vs. 1.1%, p=.001), LDL (5.8% vs. 1.5%, p=.014), and triglycerides (25.7% vs. 17.4%, p=.030). Compared with standardized growth curves, olanzapine-treated adolescents had greater increases from baseline-to-endpoint in weight (1.0 vs. 7.1kg, p<.001), height (0.5 vs. 0.7cm, p<.001), and BMI (0.2 vs. 2.2kg/m2, p<.001).

Conclusion: Olanzapine-treated adolescents may gain significantly more weight compared with adults, but may have smaller changes in other metabolic parameters. Clinicians may want to consider both efficacy and changes in metabolic parameters when selecting treatment options for individual adolescent patients.

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Olanzapine-induced metabolic abnormalities, switching from olanzapine to aripiprazole

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Background: Some atypical antipsychotics particularly clozapine and olanzapine have serious metabolic side effects like metabolic syndrome.

Objective: To determine whether olanzapine-induced metabolic abnormalities identified through monitoring can be changed by switching to aripiprazole in patients with schizophrenia.

Methods: Current research show that fifty stable outpatients suffering from metabolic side effects due to olanzapine medication were switched to an open-label, flexible-dose of aripiprazole (10-30 mg/day) in this 13-week naturalistic study. An extensive metabolic evaluation was conducted on all patients, at baseline, at 6 weeks, and at 13 weeks post switch. Metabolic abnormalities consist of new onset diabetes, impaired fasting glucose, impaired glucose tolerance, metabolic syndrome according to various definitions, and dyslipidemia. After 13 weeks of treatment with aripiprazole (mean dosage 16.8 mg / day), there was a significant decrease in body weight, body mass index, and waist circumference. The rates of in fasting glucose, fasting insulin, insulin resistance index, and serum lipids levels (cholesterol, triglycerides, low-density lipoprotein (LDL), LDL/HDL, Chol/HDL, and non-HDL cholesterol) were reduced. Also three subjects with recent onset diabetes were reversed at 3 months follow-up. The metabolic syndrome was reversed in 64% of patients at 3 months.

Conclusion: The change of psychotropic drug treatment from olanzapine to aripiprazole in stable outpatients with schizophrenia was generally well tolerated and was associated with significant improvements at 13 weeks. Results support the reversibility of olanzapine-induced metabolic abnormalities when detected early and followed by a switch to aripiprazole.

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Adherence to treatment and risperidone metabolism phenotypes

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Background and aims: CYP2D6 metabolizes risperidone into 9-hydroxi-risperidone, as well as other drugs. CYP2D6 shows genetic polymorphism, and 6-8% of Caucasians are ''slow metabolizers''. ''Fast metabolizers'' show lower plasma levels of risperidone and higher levels of 9-hydroxi-risperidone than ''slow metabolizers''. The aim of this study is to collect information about the hypothetical relationship between metabolism phenotype and parameters related to sanitary resources utilization in patients treated with risperidone.

Methods: Plasma levels of risperidone and 9-hydroxi-risperidone were determined in 52 patients treated at the Acute Unit setting, to establish their metabolism phenotype. Patients were grouped as fast (n=11), slow (n=13) or intermediate metabolizers (n=28), according to risperidone/9-hydroxi-risperidone ratio logarithm and using eighty and twenty percentiles as cut-points. Hospitalizations, emergency services utilization and visits to community mental health center during two years were recorded in the three groups.

Results: Fast metabolizers showed a higher mean number of visits to community mental health centers (35.7 vs 24.8, fast and slow metabolizers respectively, p=0.667), a higher mean number of hospitalizations (2.45 vs 1.3, fast and slow metabolizers respectively; p=0.091), a longer mean length of hospitalizations (57.3 vs 47.6 days, fast and slow metabolizers respectively; p=0.581) and a higher number of visits to emergency services (2.45 vs 1, fast and slow metabolizers respectively; p=0.01), although differences only reached statistical significance in this last parameter.

Conclusions: In spite of methodological limitations (mainly the small sample size), the present study shows some preliminary evidence about the influence of pharmacogenetic factors on the evolution of psychotic patients treated with risperidone.

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Effect of nice guidance on treatment of outpatients with schizophrenia in a uk depot clinic

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