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**PSYCHOPHARMACOLOGY - Free Communications**

**FC-32**

**Psychopharmacology V**

**FC-32-001**

**Pisa Syndrome induced by atypical antipsychotics**

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**Objectives:** Pisa syndrome, or tonic flexion of the trunk, long considered a side effect of prolonged exposure to conventional antipsychotics, has been reported as occurring with atypical antipsychotics. The authors report two cases of Pisa syndrome induced by atypical antipsychotics.

**Methods:** Literature review derived from the MEDLINE and PUBMED database.

**Results:** Case One - 38 years old male with type I Bipolar Disorder, presented with insidious onset tonic truncal flexion with axial rotation and difficulty in walking after exposure to olanzapine in doses up to 20 mg/day for 9 months. An objective causality assessment suggested that Pisa syndrome was probably related to olanzapine. There was improvement in his symptoms after 4 weeks switching olanzapine to zotepine in doses gradually titrated to 200 mg/day. Case Two – 26 years old male with moderate mental retardation, treated with long-acting risperidone 25 mg - 15/15 days for is aggressive and self-injurious behavior secondary to mood disorder, developed a acute onset of Pisa syndrome, when prescribed with 50 mg 15/15 dosage. The symptoms disappeared returning to 25 mg of long acting risperidone.

**Conclusions:** Pisa syndrome is a type of dystonia that has been associated with both typical and atypical antipsychotics. Both acute and insidious onset cases have been described in the literature, which have different course and treatment response. Once the patient presents Pisa syndrome, the treatment may include the reduction in dosage or discontinuation of the antipsychotic drug, associated to the introduction of an anticholinergic medication. In the follow-up drugs with low affinity for dopaminergic D2 receptors should be used.

**FC-32-002**

**Randomized placebo controlled trials of n-acetyl cysteine as adjunct therapy for schizophrenia and bipolar disorder**

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**Abstract:** Glutathione is the principal antioxidant of the brain. There is evidence of oxidative stress, lowered brain glutathione and genetic linkage involving glutathione metabolic genes in schizophrenia and bipolar disorder. N-acetyl cysteine (NAC) is a safe, orally bioavailable, precursor of glutathione. NAC has been shown to reverse animal models of oxidative stress, and raises brain glutathione levels. **Objectives:** To test the efficacy of NAC as an adjunct treatment for schizophrenia and for bipolar disorder. Methods: We performed double-blind, multicenter, randomised placebo-controlled trials, 140 people with schizophrenia and a separate RCT with 75 individuals with bipolar disorder. In both trials subjects received 2 g daily of NAC or placebo as add-on treatment to therapy as usual. Outcomes in the schizophrenia trial included the Clinical Global Impression (CGI) Severity and Improvement scales, the Positive and Negative Symptoms Scale (PANSS) and measures of general functioning and extrapyramidal side effects. Outcome measures in the bipolar study included measures of mania, depression, CGI, substance use, quality of life, functioning, and tolerability. The duration of both trials was 6 months. **Results:** Intent-to-treat analysis of the schizophrenia trial revealed that NAC significantly improved PANSS total (p = .009), PANSS negative (p = .018), and PANSS general (p = .035), CGI-Severity (p = .004), and CGI-Improvement (p = .025) scores. NAC treatment in the bipolar trial caused a significant improvement on the MADRS (p = .002) and most secondary scales at end point. Conclusions: These trials implicate glutathione deficits in the pathophysiology of these disorders, and supports NAC as a novel adjunctive treatment for both conditions. References: Berk et al. N-Acetyl Cysteine as a Glutathione Precursor for Schizophrenia: A Double-Blind, Randomized, Placebo-Controlled Trial. Biological Psychiatry 2008; 64, 361; Berk et al. N-Acetyl Cysteine for Depressive Symptoms in Bipolar Disorder: A Double-Blind, Randomized, Placebo-Controlled Trial. Biological Psychiatry 2008; 64, 468.

**FC-32-003**

**Prevalence of lower-than-expected plasma levels in medicated patients presenting for acute inpatient treatment**

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**Objectives:** Non-compliance or incomplete compliance with psychopharmacological medication by psychiatric patients is a frequent risk, prevalence rates ranging from 18 to 70% (numerical mean 44%). **Methods:** All patients who had to be admitted to the psychiatric inpatient wards of the University Clinics of Psychiatry and Psychotherapy I, Paracelsus Medical University, Christian Doppler Clinics from 01 June 2005 to 15 July 2005 were screened for pre-admission psychiatric medication. Plasma levels of antidepressants and antipsychotics were determined after solid-phase extraction by high performance liquid chromatography/mass spectrometry (LC/MS). **Results:** A total of 233 acute psychiatric admissions occurred, in the case of 58 admissions, patients did not have any pre-medication. The type of medication could not be determined in one patient, and the dose in 4 patients, nine patients had a pre-medication other than antidepressants or antipsychotics, remaining 161 admissions for the statistical analysis. 52% (83 of 161) of the admissions had actual plasma levels that were >2-fold below the plasma level that could be expected from their prescribed dosage, 21% (34 of 161) had actual plasma levels that were >2-fold above, including 23 (14.3%) patients had a plasma level of 0.0 mg/ml at admission. **Conclusions:** Our findings show, that under routine conditions, 52% of medicated patients had actual plasma levels that were more than 2-fold lower than the plasma levels that could be expected from the prescribed dosage. Our findings suggest that the risk for a patient of NOT having the intended level of medication in his/her blood is 3:1.

**FC-32-004**

**The anxiolytic etifoxine reduces the physical signs and anxiogenic effects of ethanol withdrawal in mice**

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**Objectives:** Change in the function of gamma-aminobutyric acidA (GABA) receptors attributable to alterations in receptor subunit composition, is one of main molecular mechanisms with those affecting the glutamatergic system which accompany prolonged ethanol intake. These changes explain in part the central nervous system hyperexcitability consequentely to ethanol administration cessation. In animal models as well as in humans, hyperexcitability associated with ethanol withdrawal expresses by physical signs such as convulsions and heightened anxiety. The present work investigated the effects of anxiolytic compound etifoxine on ethanol withdrawal paradigms in a mouse model. The benzodiazepine diazepam was chosen as reference compound. **Methods:** Ethanol was given to NMRI mice by a liquid diet at 3% for 8 days then at 4% for 7 days. Under these conditions, ethanol blood level ranged between 0.5 to 2g/l for a daily ethanol intake varying from 24 to 30g/kg. The convulsive behaviour on handling was scored on a rating scale (Watson et al., 1997) whereas anxiety-like behaviour was measured in the light/dark box test. Possible sedative and ataxic effects of etifoxine using the actimeter and rota rod tests were evaluated in normal animals. **Results:** Etifoxine (12.5-25mg/kg) and diazepam (1-4mg/kg) injected intraperitoneally 3h30min after ethanol removal, decreased the severity in handling-induced tremors and convulsions in the period of 4 to 6h after ethanol withdrawal. In addition, when administered 30min and 15min respectively before the light/dark box test, etifoxine (50 mg/kg) and diazepam (1mg/kg) inhibited enhanced aversive response 8 h after ethanol withdrawal. Contrary to diazepam, etifoxine had no effects on spontaneous locomotor activity and did not exhibit ataxic effects in normal animals.