AstraZeneca

Non-Interventional Study (NIS) Report

NIS Name/Code	MARIA
Edition Number	1.0
Date	11 November 2011

EpideMiological observAtional non-interventional study to Research the prevalence of bipolar criteria of hospital In-patients with schizophreniA and patients with recurrent depression (MARIA)

Study dates: Oct, 19 2009 – Nov, 29 2010

First Subject In: Nov, 30 2009

Last Subject Last Visit: Nov, 29 2010

Associated Document: T15 NIS Report (NISR), ed 1.0
Template Active Date: May 2010
8-P85-1-X Planning, Approval, Conduct and Reporting of Non-Interventional Studies (NISs)

NIS REPORT SYNOPSIS (IF APPLICABLE)

EpideMiological observAtional non-interventional study to Research the prevalence of bipolar criteria of hospital In-patients with schizophreniA and patients with recurrent depression (MARIA).

Rationale

The Bipolar Disorder (BD) is not recognized and under diagnosed condition worldwide. In 40% of patients BD is not detected at the first examination and in 2/3 of cases the proper diagnosis is made after about 10 years. In Hirschfeld et al.'s survey of support group participants diagnosed with bipolar disorder, 69% reported initial misdiagnosis by the first physician from whom they sought treatment, and misdiagnosed patients reported seeing a mean of 4 physicians before being diagnosed with bipolar disorder. BD is often misdiagnosed as recurrent depressive disorder, schizophrenia, anxiety or personality disorders.

Considering the difficulties in diagnosing bipolar disorder in clinical practice, and the necessity of sparing enough time to interview with patients' family to reach the correct diagnosis, and also considering the poor outcome if the disease is not detected or misdiagnosed as unipolar depressive disorder, which leads to mistreatment with antidepressants, screening instruments for bipolar disorder and quantitative instruments to assess the extent patients bipolarity in patients were developed. Hirschfeld et al. developed the Mood Disorder Questionnaire (MDQ) based on the DSM-IV symptoms to screen the lifetime history of a hypomania/mania syndrome. The original MDQ in English provided good sensitivity and excellent specificity according to the Structured Clinical Interview for DSM-IV (SCID) on an outpatient sample. The MDQ has been validated among a community-based sample against an abbreviated version of the SCID as low sensitivity and excellent specificity. Furthremore, Miller et al. reported that the MDQ had good sensitivity for bipolar I disorder (BD type I) but had lower sensitivity for bipolar type II or not otherwise specified (NOS) disorders. In 2004 the Bipolar Index was described by Dr. Gary Sachs. Unlike a DSM-based diagnostic system which emphasizes separate diagnostic categories and focuses on the hypomania symptoms, the Bipolarity Index emphasizes diagnostic features other than hypomania and places patients on a spectrum. In 2005 Angst et al. elaborated self-administered questionnaire, the hypomania checklist-32 (HCL-32). The primary goal of the HCL-32 is to identify hypomanic components in patients with MDD in order to help the clinician to diagnose BP-II and other BP spectrum disorders presenting in psychiatric and general medical practice. The instrument is designed to assess the personal and social role consequences of hypomanic symptoms. It also takes into account the subject's current overall affective status (low – as usual – high) as a potentially interfering variable in answering the questions. Several questions also have the potential to reveal the extent to which the patient has insight into his condition, which is important for treatment considerations.

Objectives

(a) Primary objective

The primary objective of this NIS is to provide estimation on patients' bipolarity using Bipolarity Index (BI) score in patients diagnosed with schizophrenia with episodic course/schizoaffective disorder and patients diagnosed with recurrent depression (according to ICD-10) and to analyze associations of BI with disease anamnesis and characteristics as well as with co-morbidity.

(b) Main secondary objectives

1. to describe hypomania signs using the Hypomania Checklist (HCL-32) in patients diagnosed with schizophrenia with episodic course/schizoaffective disorder and patients diagnosed with recurrent depression;

2. to identify the bipolarity profile of patients (positive or negative) based on the HCL-32 in study patient population and to evaluate the BI score, disease anamnesis and characteristics in patients screened positive and negative;

3. to analyse the association between BI score and level of patient's social functioning (including impact of employment status, family status, number of hospitalizations, patients' personal and social performance);

4. to estimate the proportion of patients who are diagnosed with Bipolar Disorder according to ICD-10 in the study patient population;

5. to assess patients bipolarity according to Angst criteria in study patients population;

6. to define the clinical features of the last depressive episode in patients diagnosed with recurrent depression.

Study design

This multicenter cross-sectional study designed to gather information on the presence of bipolar criteria ("bipolarity") in patients having current diagnosis of schizophrenia/ schizoaffective disorder or recurrent depression and never diagnosed with BD.

Psychiatrists enrolled patients meeting inclusion/exclusion criteria as they routinely attend the clinic or are examined in hospital in a consecutively manner.

The study was conducted in Russian Federation. 5 sites participated in the study and 750 patients were enrolled. The ratio between patients with schizophrenia/schizoaffective disorder and patients with recurrent depression in the study was 1:1.

Patient population selection criteria

Inclusion Criteria

- Male and female patients aged 18- 65 years old.
- Signed patient informed consent.
- In-patients with the diagnosis of schizophrenia with episodic course or schizoaffective disorder, OR in-patients and out-patients with the diagnosis of recurrent depression.
- The duration of the disease is 3 years and longer.
- Two or more episodes of the disease in the patients history.

Exclusion Criteria

- Subjects who are unwilling or unable to provide informed consent.
- Current diagnosis of Bipolar Disorder.
- Schizotypal Disorder.
- Schizophrenia with continuous course.
- Hebephrenic schizophrenia.
- Catatonic schizophrenia.
- Undifferentiated schizophrenia
- Schizophrenia, unspecified
- Organic affective disorder of intoxication induced affective disorder.
- Any other concomitant conditions which, in the judgment of investigator, will not allow the patient to complete the study procedures.
- Current participation in a clinical trial.

Study duration per patient

One routine visit to the psychiatrist.

Study variables

(a) Primary variable

Bipolarity Index, BI

(c) (b) Other variables

Hypomania Checklist, HCL-32

Angst criteria for bipolarity

Personal and Social Performance scale, PSP

Demographics and social characteristics: age, gender, recruitment setting, education level, employment status, and marital / family status.

Family history of psychiatric disorders.

Lifetime mental illness history: age of disease onset, age of the first symptoms onset, age of the first diagnosis of mental illness, age of the current diagnosis, first and further diagnoses, number of hospitalisations for the mental illness, lifetime history of the therapy with mood stabilisers and antidepressants, psychotropic therapy during the last year, number of the previous disease episodes, number of previous depressive episodes, history of suicide attempts, presence and characteristics of maniac/hypomaniac episode in patients lifetime history, number of manic/hypomanic episodes, the duration of the most prolonged episode.

Last disease episode characteristics: duration, for the depressive episode - assessment of retardation, anxiety, asthenia, affect liability, changes of appetite and taste preferences, weight loss / gain, hypersomnia / insomnia, increased , changes of sexual activity, panic attacks, memory disorders, increased interpersonal rejection sensitivity / conflict situations / frustration situations and diurnal variations of patient's state.

Current status: full psychiatric diagnosis according to medical records, according to ICD-10, smoking, alcohol and drug abuse, concomitant somatic diseases and conditions.

Study results

In this NIS modern bipolar disorders screening/assessment instruments (Bipolarity index and Hypomania checklist) were applied to the psychiatric patients (patients diagnosed with schizophrenia/schizoaffective disorder or recurrent depression) to explore the prevalence of bipolarity criteria in patients never diagnosed with BD. The personal and social dysfunction in study patient population were assessed using PSP scale. The results of this study could be useful for more accurate assessment of BD prevalence in psychiatric patient population, could help to improve the diagnostics of BD and management of bipolar patients.

Mania was found more prevalent in patients with schizophrenic disorders, while hypomania was more prevalent in patients with recurrent depression. At the same time, both mania and hypomania were also found in all groups of patients (with recurrent depression and patients with schizophrenic disorders respectively), although to less extent. Both hypomania and mania episodes had been observed in patients with recurrent depression in the past. Most of patients with episodic course schizophrenia experienced hypomania episodes in the past. Patients with schizoaffective disorders had hypomania episodes in the past in all cases, though a larger part of mania episodes in this group of patients were current. Suicidal risk in all groups of patients was also observed.

Remarkably, normothymics were prescribed in many cases despite the fact that bipolar disease was not formally diagnosed. Although in some cases the prescription of normothymics was due to reasons other than bipolar disease correction, it can be stated with high level of probability that prescription was based on reasonability of affective disorders treatment.

Thus, the conclusions of the study are as follows:

1. Bipolar disorder was underdiagnosed in sites participated in the study. This is due to low physicians' awareness in bipolar disorder diagnostics and ICD-10 insufficiency.

2. Current Russian statistics system is outdated with regards to registration of bipolar disorders and needs soonest modernization

3. It is necessary to set up working group and/or Advisory Board to discuss above mentioned problems and find a quick and competent solution of the listed tasks: a) to evaluate the prevalence of bipolar disorder in Russia; b) to work out the national concept on bipolar disorder, to prepare proposals for ICD-11; c) to work out adequate statistical methodology; d) to work out diagnostics and therapy standards for bipolar disorder.