Abstract

Objective: The aim of this post-hoc analysis was to evaluate the effect of depression severity on clinical response in patients with bipolar depression treated with lurasidone.

Methods: Patients with bipolar I depression in 2 registration trials were randomized to 6 weeks of once-daily, double-blind, placebo-controlled treatment with lurasidone monotherapy (20–60 mg/d or 80–120 mg/d; N=499); or with lurasidone adjunctive to lithium or valproate (20–120 mg/d; N=345). Two baseline depression severity groups were defined post-hoc: a moderate (Montgomery-Asberg Depression Rating Scale [MADRS] total score: 20–29) and a high (MADRS≥30) severity group. For each group, changes in MADRS total score were analyzed using a mixed model for repeated measures analysis.

Results: In the monotherapy study, 42.9% of patients were in the moderate severity group (mean MADRS total score: 26.0) and 57.1% were in the high severity group (MADRS: 33.9). In the adjunctive therapy study, 39.7% of patients were in the moderate severity group (mean MADRS: 25.7) and 60.3% were in the high severity group (MADRS: 34.0). In the monotherapy study, lurasidone vs. placebo effect sizes (Cohen’s d) for MADRS change at week 6 in the high severity vs. moderate severity groups were d=0.60 (P<0.001) vs. 0.40 (P=0.035) for the 20–60 mg/d dose range, and d=0.55 (P=0.002) vs. 0.50 (P=0.008) for the 80–120 mg/d dose range; and in the adjunctive therapy study, effect sizes for MADRS change in the high severity vs. moderate severity groups were d=0.25 (P=0.10) vs. d=0.41 (P=0.033). A treatment by baseline severity interaction test was non-significant for both the monotherapy and adjunctive therapy studies.

Conclusions: In this post-hoc analysis, the magnitude of endpoint improvement in depressive symptoms vs. placebo was comparable for patients with both moderate and high levels of baseline depression severity during for both monotherapy and adjunctive therapy with lurasidone.

Sponsored by Sunovion Pharmaceuticals Inc.

PS38

Psychotropic medication for bipolar patients in the psychiatric acute inpatient unit.

Hiroki Sasamori, Hiroki Yamada, Akira Yoshizawa, Kouchi Jinbo, Sachiko Yokoyama, Yuzuru Ishibe, Teppei Morita, Osamu Takashio, Akira Iwanami
Department of Psychiatry Showa University 6-11-11 Kitakarasuyama, Setagaya-ku, Tokyo, Japan

Abstract

Objective: In Japan, there are many regulation of national health insurance to the psychiatric acute inpatient unit. For example over 60% patients must be legal forced hospitalization on admission and have to discharge within 3 months. Therefore differences between medication in the psychiatric acute inpatient unit with guidelines clarify actual clinical medication.

Method: We researched medication of bipolar disorder in the pharmacotherapy of BP-I and BP-II.

Results: 1899 patients admitted to psychiatric acute inpatient units of Karasuyama Hospital. All patients admitted between 2010 and 2013 were retrospectively collected data: age, gender, prescribed mood stabilizers (MS), antipsychotics (AS) and/or antidepressants (AD) and their doses, and diagnosis.

Conclusion: It was more useful to use antipsychotics than mood stabilizer when the start of treatment in the actual clinical medication to bipolar disorder. While there are differences from guidelines the treatment of bipolar disorder had been largely successful on the rules of national health insurance in the psychiatric acute inpatient unit of Karasuyama Hospital. It is necessary to clarify the difference between the evidences and actual clinical medication.

PS39

Prescription Patterns for Bipolar Disorders in a Psychiatric Hospital in Japan

Masahiko Yamada1, Yasutaka Fujita1, Yuki Kait1, Yuko Kumamoto1, Kanzo Kurihara1, Akinori Masui1, Takahiro Miyazaki1, Goro Sato1, Hiromi Uji1, Masahiko Yamada1
1Kusatsu Hospital, Japan

Abstract

Objectives: We investigated the change in prescription patterns for bipolar disorders in our hospital during the latest five years. We also studied the difference in the prescription patterns between bipolar I (BD-I) and II (BD-II) disorders.

Methods: We used the prescription data of all the outpatients with bipolar disorders in the time period from 2010 to 2015 in our hospital.

Results: We identified 1971 patients (bipolarBD-I:53.1%, BD-II: 46.9%). During the surveyed period, the proportion of the patients for whom any MS(s) was prescribed decreased from 88.2% to 84.4%. Similarly, the proportion changed from 25.2% to 52.1 % for AS(s), and from 29.9% to 27.8% for AD(s).

Conclusion: We found a significant change in the prescription pattern for bipolar disorders in our hospital during the last five years.

PS40

Association of ANK3 Variants with Bipolar Disorder in the Korean Population: a case-control haplotype analysis

Chul-Hyun Cho†, Soojin Kim†, Dongho Geum†, Heon-Jeong Lee2, 2Department of Psychiatry, Korea University College of Medicine, Seoul, South Korea; 2Department of Biomedical Sciences, Korea University Medical School, Seoul, South Korea † These individuals contributed equally to this article as co-first authors. Corresponding author. Heon-Jeong Lee, MD, PhD, Department of Psychiatry, Korea University College of Medicine, 73 Inchon-ro, Seongbuk-gu, Seoul
Abstract
Bipolar disorder (BD) is a major psychiatric disorder characterized by an alternating mood episode such as major depressive episode, hypomanic episode, and manic episode. There have been various genetic studies on BD and previous studies reported several candidate genes considered to be associated with BD. ANK3 has been suggested as a possible susceptible gene of BD. In present study, we investigated the association of ANK3 variants with BD in the Korean population. We selected rs1938526 and rs10994336 of ANK3 for the study according to previous results of studies. After data qualification process including purifying DNA from blood samples, a total of 287 BD patients and 340 healthy controls were left. We performed case-control association analysis and case-control haplotype analysis on 2 of ANK3 single nucleotide polymorphisms (SNPs). We found no significant association between BD and control from case-control association analysis. However, we found that rs1938526/rs10994336 in ANK3 shows significant finding (overall P = 3.6 x 10^-7; permutation P = 0) from case-control haplotype analysis. The result of this study suggests that rs1938526 and rs10994336 of ANK3 could be as possible susceptible gene for BD in Korean population from haplotype analysis, although no significant genetic association. More research is needed to investigate and reconfirm ANK3 as a susceptible gene for BD as shown in previous and present studies.

Key Words: bipolar disorder, ANK3, polymorphism, haplotype analysis.

PS41
Hypermethylation of SLC6A4 promoter in psychiatric disorders suppresses its expression.
Tempei Ikegame1, Tatsuro Asai2, Miki Bundo3, Masahashi Ikeda4, Jun Ishigooka5, Kazuya Iwamoto1, Nakao Iwata3, Chihiro Kachiuchi4, Kiyoto Kasai5, Tadafumi Kato1, Yoshiha Kawaihara1, Shinsuke Koike1, Kenji Kondo1, Fumichika Nishimura1, Harumi Saida1, Tsukasa Sasaki1, Hiroko Sugawara1, Akane Yoshikawa1
1 The University of Tokyo, Japan, 2Fujita Health University, Japan, 3Tokyo Women’s Medical University, Japan, 4RIKEN Brain Science Institute, Japan, 5Shonan Kamakura General Hospital, Japan

Abstract
SLC6A4, encoding serotonin transporter (5-HTT), is a key molecule to elucidate the pathophysiology of psychiatric disorders because it regulates the concentration of serotonin, which is related to emotional behavior, in the brain. We have previously shown the promoter hypermethylation of SLC6A4 in the affected monozygotic twin discordant for bipolar disorder (BD). We also confirmed hypermethylation of specific two CpG sites (named CpG3 and CpG4) in lymphoblastoid cell lines (LCLs) and postmortem brains of patients with BD. However, the sample size in the previous study was relatively small, and LCLs have the possibility to be subjected to the artificial DNA methylation changes. In the present study, we tested DNA methylation levels of CpG3 and CpG4 in the SLC6A4 promoter using genomic DNA of peripheral blood cells (PBCs) of healthy controls (n = 454) and patients with BD (n = 447) from the Japanese population. We also examined DNA methylation levels of SLC6A4 promoter in schizophrenia (SZ, n = 411). In addition, we analyzed the relationship between DNA methylation level and genotype of 5-HTTLPR (5-HTT linked polymorphic region), which is a known functional DNA polymorphism of SLC6A4 promoter. As a result, we found a significant higher DNA methylation at CpG3 in patients with male BD and male SZ harboring particular L alleles compared to male controls. To examine the functional significance of DNA methylation at CpG3, we performed the luciferase reporter assay using in vitro methylated constructs and found that DNA methylation of CpG3 suppressed the transcriptional activity. Finally, using MRI images, we found a significant positive relationship between methylation level at CpG3 and the relative volume of right amygdala superficial region. These results suggest that hypermethylation at the CpG3 site has pathophysiological consequence such as downregulation of transcription and volume change of the amygdala.

PS42
A Genome-Wide Quantitative Trait Locus (QTL) Linkage Scan of NEO Personality Factors in Latino Families Segregating Bipolar Disorder
Byung Lee1, Michael Escamilla2
1 Pusan National University Hospital, Republic of Korea, 2 Texas Tech University Health Sciences Center, USA

Abstract
Objective: Personality traits have been suggested as potential endophenotypes for Bipolar Disorder (BP). We have previously reported on the heritability of factors in the Five Factor personality model (NEO) in a large sample of pedigrees segregating BP.1 A recent genome-wide linkage scan for bipolar disorder in these families reported BP susceptibility loci at 8q24 and 14q32.2 We subsequently performed a quantitative trait linkage analysis for the five NEO factors in this same set of families.

Methods: The present study utilized data from 3757 individuals from 686 extended pedigrees originally ascertained for having multiplex cases of BP. The majority of subjects also completed assessments using The NEO Personality Inventory, Revised (NEO PI-R). Raw scores for each of the five factors were analyzed for linkage analysis using SOLAR (Sequential Oligogenic Linkage Analysis Routines). All subjects were genotyped using the Illumina HumanLinkage-24 Bead Chip, with an average genetic coverage of 0.67 cM.

Summary of results: Suggestive evidence for linkage was found for neuroticism at 1p11.2 (LOD=2.52), 1p22 (2.26), 6q23.3 (2.32), 16p12 (2.73), 17q11.2 (2.24), extraversion at 4p15.3 (2.33), agreeableness at 4q31.1 (2.37), 5q34 (2.60), 7q31.1 (2.56), 16q22 (2.52), and conscientiousness at 4q31.1 (2.50). In addition, for the trait of openness, we found significant evidence of linkage to chromosome 3p24.3 (rs336610, LOD=4.75) and suggestive evidence at 1q43 (2.74), 2p26 (2.71), 5q35.1 (3.09), 11q14.3 (2.61), 11q21 (2.30), and 19q13.1 (2.52).

Conclusions: Our findings with regard to genetic loci for NEO personality traits support linkage findings of the openness trait to chromosome 19q13 and the agreeableness trait to 4q31 reported in other population based linkage studies. In terms of the genetics of BP in the Latino population we report a number of additional suggestive loci for personality traits (neuroticism, extraversion, agreeableness, and conscientiousness) not previously identified in linkage analyses for the BP phenotype itself.

PS43
Association ofCACNA1C Variants with Bipolar Disorder in the Korean Population
Soojin Kim1, Chul-Hyun Cho1, Dongho Geum1, Heon-Jeong Lee1,2
1 Department of Biomedical Sciences, Korea University Medical School, Seoul, South Korea, 2 Department of Psychiatry, Korea University College of Medicine, Seoul, South Korea. *Corresponding author.

Heon-Jeong Lee, MD, PhD, Department of Psychiatry, Korea University

136–705, Republic of Korea Tel: +82-2-920-6721, Fax: +82-2-929-7679, E-mail: leehjeong@korea.ac.kr