CURRICULUM VITAE - JORGE ROVNER

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Especialista en Psiquiatría y Psicología Médica

Médico Especialista Recertificado por la Asociación Médica Argentina

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Miembro del Colegio Argentino de Neuropsicofarmacología

Miembro del Comité ejecutivo de la Asociación Argentina de Psicofarmacología

Miembro de la Asociación Argentina de Psiquiatría Biológica

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Presidente y Fundador de la Asociación Argentina de Psicoterapia y Psiquiatría basada en el Budismo y el Zen

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Comité de Recertificación (CRAMA)

Por cuanto el Doctor: **Jorge Luis Rovner**

ha aprobado la evaluación efectuada por la Junta de Recertificación

de la Especialidad: **Psiquiatría**

por el término de 5 años, se le extiende el diploma que así lo acredita.

Buenos Aires, 19 de octubre de 2004.

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Facultad de Medicina

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Por cuanto Jorge Luis Rovner,
natural de la Pcia. de Tucumán, ha terminado el 6 de mayo de 1990 los estudios
correspondientes a la carrera de Medicina.
Por tanto: de acuerdo con lo dispuesto en las normas vigentes en esta Universidad le expedimos
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Buenos Aires, 24 de setiembre de 1990.

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certifican que **Jorge Luis Rovner**

por sus antecedentes curriculares y evaluación ante jurado cumple con lo dispuesto en las normas vigentes del Instituto Superior y con la disposición Nº 299 de fecha 11/2/88 de la Subsecretaría de Regulación y Control del Ministerio de Salud y Acción Social de la Nación. Por lo tanto, se le expide el presente Título de Médico Especialista en Psiquiatría.

Buenos Aires, 18 de Abril de 1997.

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V CONGRESO MUNDIAL DE ESTADOS DEPRESIVOS

V World Congress of Depressive Disorders

SIMPOSIO INTERNACIONAL DE DESORDENES COGNITIVOS

International Symposium of Cognitive Disorders

25 al 27 de setiembre de 2003 - Mendoza - Argentina

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Simposium

"Depresión mayor y dolor. Nuevas moléculas para nuevos desafíos"

Mendoza, 27 de setiembre de 2003

Lic. Silvia Sazlman
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HOSPITAL FRANCÉS
Servicio de Psiquiatría
Jefe: Dr. Miguel Márquez

Buenos Aires, 30 de Junio de 2004

Señor
Doctor Jorge ROVNER
PRESENTE

De mi mayor consideración:

Tengo el agrado de dirigirme a Ud. con el objeto de comunicarle que esta Dirección de la Carrera de Médicos Especialistas en Psiquiatría de la Unidad Académica "Francés" de la Facultad de Medicina de la Universidad Nacional de Buenos Aires, ha resuelto designarlo como Profesora de la materia "Filosofía".

Al agradecerle su colaboración, la que con seguridad jerarquizará el nivel docente de la Carrera, aprovecho la oportunidad para saludarlo con mi consideración más distinguida.

Dr. MIGUEL MARQUEZ

La Rioja 951 (1221ACI) Buenos Aires – Tel.: 4959-1500 Tel. 4957-0444 Fax 4957-6873
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Universidad de Buenos Aires
Facultad de Odontología
Hospital Odontológico Universitario

Buenos Aires, 24 de Junio de 1993.-

DR.JORGE LUIS ROVNER
CATEDRA DE FILOSOFICA
S/D.-

De nuestra mayor consideración:

Esta Comisión de Doctorado cumple en informarle, que ha sido aprobado el Plan de Cursos, que presentó oportunamente ante el mencionado Tribunal.-

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Con el Coauspicio de la Asociación de Psiquiatras Argentinos y Fundación para la Investigación Psicológica en la Comunicación

Buenos Aires, 20, 21, 22 y 23 de Octubre de 1999

Se extiende el siguiente diploma a:

Dr. J. L. Rovner; Dr. N. D. Flores

por cuanto ha participado en calidad de:

Autores del Poster

"Cambio de tratamiento de pacientes psicóticos de Haloperidol a Olanzapina: Estudio abierto de eficacia y seguridad."

Dr. Juan E. Mezzich
Secretario General WPA

Dr. Nestor F. Marchant
Presidente AAP

Dr. Juan José López Ibor
Presidente WPA

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Sustitución del haloperidol por olanzapina en pacientes psicóticos: un estudio multicéntrico abierto de seguridad y eficacia

Jorge Rovner, Héctor Battaglia, José Carrera, Adrián Corrales, Sergio Guerstein, Juan Liotta, Andrea López Mato, Jorge Marquet, Adriana Pavetti, Norberto Roisman, Omar Tallo, Julio Zarra, Daniel Flores y Grupo Argentino de Investigación en Neurociencias

Se supone que la esquizofrenia y las psicosis relacionadas son enfermedades del neurodesarrollo con varias etiologías involucradas. Durante décadas el tratamiento de la esquizofrenia estuvo basado en el uso de drogas neurolépticas (también llamadas antipsicóticos típicos). La aparición de una nueva clase de agentes terapéuticos, llamados antipsicóticos atípicos, dio nuevas oportunidades para el tratamiento y prevención de la evolución de la enfermedad. Contrastamos una nueva droga antipsicótica atípica -olanzapina*- con el antipsicótico típico de referencia, haloperidol, en un estudio abierto. La experiencia reproduce los procedimientos médicos de tratamiento de la enfermedad en la Argentina. Se demuestra que respecto del haloperidol, la olanzapina posee una superioridad estadística en términos de seguridad, eficacia y calidad de vida.

Palabras clave: Olanzapina - Haloperidol - Seguridad - Eficacia - Calidad de vida - Drogas neurolépticas - Antipsicóticos atípicos

Safety and efficacy: Comparing Olanzapine vs. Haloperidol in an open trial
Schizophrenia and related psycosis are likely to be neurodevelopmental diseases with several ethiologies involved. During decades the treatment of schizophrenia was based in the use of neuroleptic drugs (called typical antipsychotics). The appearing of a new class of therapeutic agents, called atypical antipsychotics, gave new opportunities for the treatment and prevention of the evolution of the disease. We compare a new atypical antipsychotic drug, Olanzapine against the gold standard of the typical antipsychotics, Haloperidol, in an open trial. The experience resembles the standards of care for Argentine psychiatrists in the treatment of the disorder. A statistical superiority of Olanzapine is demonstrated when compared to Haloperidol in safety, efficacy and quality of life.

Key words: Olanzapine - Haloperidol - Safety - Efficacy - Quality of life - Neuroleptic drugs - Atypical antipsychotics

Jorge Luis Rovner et al. Médicos Psiquiatras. Grupo Argentino de Investigación en Neurociencias.
Daniel Flores. Médico. Director Médico Laboratorio Elly Lilly (Argentina).

Grupo Argentino de Investigación en Neurociencias. Participaron también en la recolección de información los Dres. Arias Restrepo, Barani J., Belaga G., Bertoldi A, Boullosa O., Cafferata J., Calvo F., Capurro M., Castelli C., Catalán L., Curia J., Doria Medina R., Fahrer R., Fernández H., Garcia M., Gargoloff P., Giorrmano S., Grande A., Halberg M., Kijnan M., Lavaisse Maisson N, Masino R., Monforte J., Nuñez G., Padilla, Vacaflores G., Valeiras A., Vázquez G. y Wolos A.

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El tratamiento estadístico del presente estudio fue realizado por Armando Garsd, Ph.D.

* A los pacientes que participaron en en este estudio se les administró exclusivamente Zyprexa®.

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EFFECT OF HALOPERIDOL ON Ca^{2+} TRANSPORT IN ISOLATED SARCOPLASMIC RETICULUM VESICLES

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Key words: Ca^{2+}-ATPase. Ca^{2+} transport. Haloperidol. Neuroleptic malignant syndrome. Sarcoplasmic reticulum.

INTRODUCTION

The Neuroleptic Malignant Syndrome (NMS) is an idiosyncratic disorder associated with the administration of antipsychotic agents, which affects 1-3 % of the patients under neuroleptic medication, with up to 20 % mortality (1,17,27,30).

NMS is characterized by high fever (up to 42°C), diaphoresis, hypotension, tachycardia, muscular rigidity, metabolic and respiratory acidosis, rabdomyolisis, autonomic disfunction, altered level of consciousness, renal failure and death, high serum levels of creatine-phosphate-kinase, lactic dehidrogenase and some transaminases (1,11). The syndrome was reported to be induced by many neuroleptic agents: Zuclopenthixol (15), trifluperidol (28), fluphentixol

Acknowledgements: This work was supported by grants from the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) and from the Universidad de Buenos Aires, República Argentina. We are grateful to Jannsen Farmaceutica S. A. (Buenos Aires) for the supply of haloperidol, and some of the referenced bibliography.

13.1

Grosman, Claudio: Canales ionicos del protoescolex. Echinococcus granuloso reconstituido sobre bicapa lipidicous planos. | **Dir.:** Ignacio L. Reisin | Farmacia y Bioquímica

13.1

Simontacchi, Marcela: G oxidativos por ejes embrio Susana Puntarulo | Farma

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Rovner, Jorge Luis: Efecto de diferentes Cationes sobre la actividad de la Ca2+ATPasa y el transporte de Ca2+ en el reticulo sarcoplásmico. | **Dir.:** Dr. Guillermo Luis Alonso | Odontología

13.1

Caro, Andrés: Disponibi producción de radicales d semillas de Soja. | **Dir.:** D Farmacia y Bioquímica

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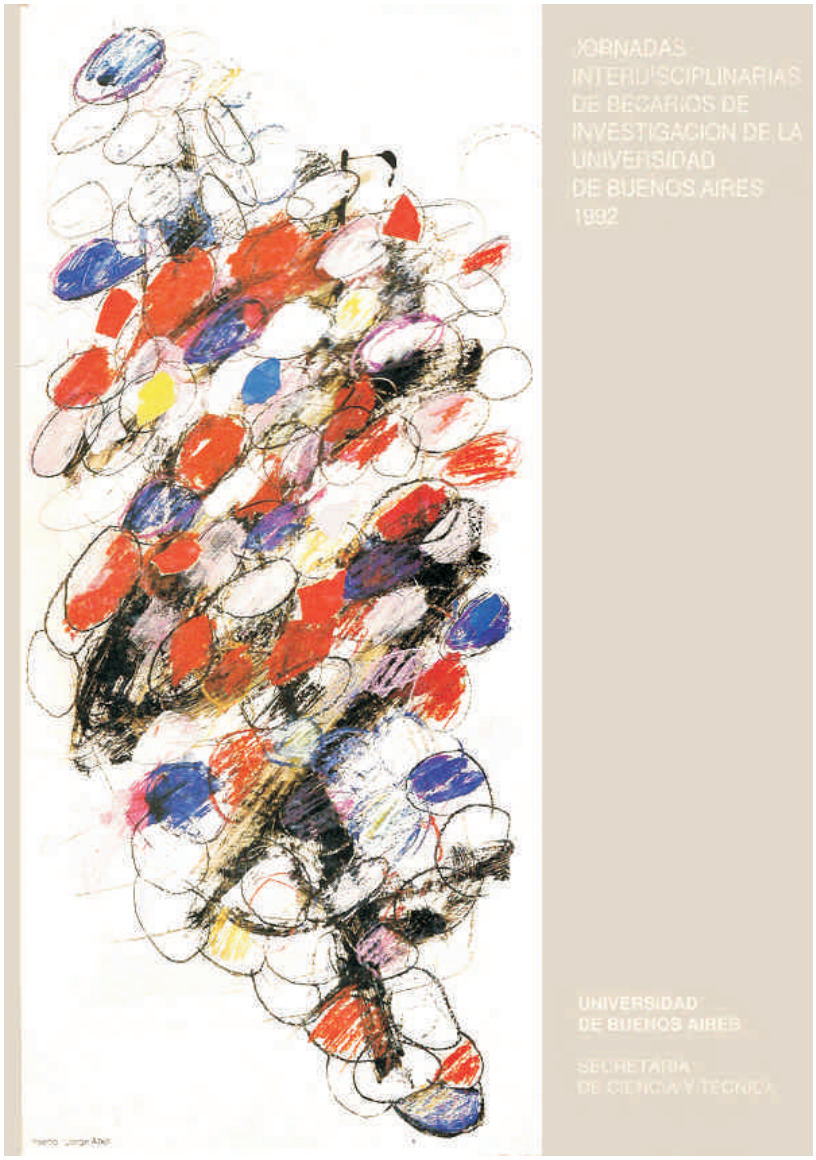

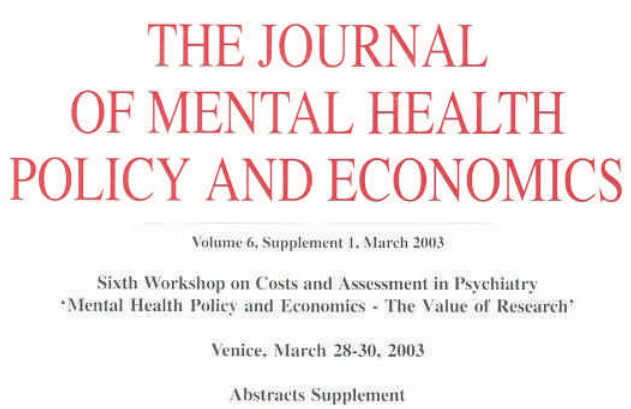
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Findings and Limitations: Our data come from retrospective medical claims data, and we cannot observe reliably the severity of the illness, nor the outcome. In future research we will incorporate findings from an expert panel that will provide outcome estimates for various treatment bundles, thereby permitting the calculation of expected medical outcomes-adjusted price indexes for the treatment of depression.

Source of Funding: National Institute of Mental Health, Grant No. RO1MH62028. Additional support for Dr. Busch by the Falk Foundation.

Soho Study (Schizophrenia Outpatient Health Outcomes): Argentinian Results at 3-6 Months

Gargoloff, PR[1], RovnerJ[2], Flores D[3] and Colaborative Group[4]
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[2]Medical advisor (Eli Lilly Interamericana Inc, Argentina)
[3]Medical Director (Eli Lilly Interamericana Inc, Argentina)
[4]J.Abad, H.Battaglia, S.Bertolino, A.Cortijo, E.De Rosa, E.Gris, G. Dorado, M. Gagliardi, R. Galeno, G. García Bonetto, A. Godino, E. Guzzo, M. Halberg, M. Holzer, F. Montaldo Riera, E. Ortíz Frágola, G. Panelo, D.Perinot, G. Petracca, V. Pujía, A.Rodríguez Rech, A. Rotbart, E. Suárez, J. Travella, R. Velasco, J. Vilapriño Duprat, J. Zarra

Background: People suffering from schizophrenia and treated with Olanzapine were evaluated through Randomized Controlled Trials, showing improvement not only on positive, negative, depressive and cognitive symptoms, patient functioning and health-related quality of life, but also a better tolerability profile and long term compliance. Many patients achieve a substantial global relief of their illness, reducing the utilization of the most expensive health care resource such as hospitalization, offsetting consequently the high acquisition cost of this new antipsychotic. Considering additionally the improvement of working and studying capacity achieved with this drug, total cost of these disorders is expected to decrease much more. Thus, this medication could be a good choice for psychiatrists, health policy makers and those who decide how to allocate the budget. Large and broad assessment on health and economic outcomes in natural clinical setting are needed in order to obtain data from the "real world".
Objectives: The primary objective of this study is to evaluate comparative costs and outcomes of outpatients suffering from schizophrenia, treated with Olanzapine versus other antipsychotic. A secondary objective is to understand pharmacological treatment patterns and their relationship with drugs used.
Method: SOHO is a 3-year, prospective, international, non-interventional/observational study of health outcomes associated with antipsychotic medication therapy in outpatients treated for schizophrenia. Its target is to evaluate patients in a natural setting, in which participating psychiatrists decide to initiate or change antipsychotic medication, selecting it at own discretion and implying two cohorts: Olanzapine (Group 1) and Non-Olanzapine antipsychotic (Group 2).The measures, collected at baseline (T1), 3 months (T2), 6 months (T3) and then every 6 months, are: Demographics, Clinical Global Impression and Single items of Schizophrenic symptom clusters, Extrapyramidal and Hyperprolactinemia side effects, Suicide attempts, Sexual dysfunction, items of Work, Living conditions, Violence, EQ5D, Drugs used and Health resources utilization.
Results: Argentina enrolled 362 patients (Mean Age= 37,2y ; 46,6% Female), 37% were under first treatment and in 1/3 of cases the onset of the illness was less than 5 years related to their enrolment time. 30 psychiatrists from different practice setting (public and private practice, academic hospital and social security unit) participated. Antipsychotics utilized were: Chlorpromazine, Haloperidol, Thioridazine, Trifluperaz Risperidone and Ziprasidone. 88 monotheraphy. Reasons for antipsycho were side effects. The previous pres patients in Olanzapine group was Risp Haloperidol. Significant difference in re related with Group 2 was found (T1-T T1-T3: 58.9% vs 39,6%, p=0,005) and T3 (58,9% vs 42,9%, p=0,03). Gro improvement in positive, negative an compared with Group 2 (-1,58 vs -1, p=0,036; -1,15 vs -0,69, p=0,0008).Pa at 3 and 6 months has less sexual dysfu with Risperidone (48,5% vs 71%, p= 0,018) and were prescribed less anti 17,3%, p=0,0003; 5,1% vs 19,3%, p=0, antipsychotics, including Risperidone. found at T3 in weight gain between Ri
Discussion and Implications: Data or and costs in the usual clinical practice p be a contribution for health care provi the selection of most effective and ef outpatients suffering from schizophren needed with this purpose, even more ir the scarcity of resources is a debilitatin of the proper care this population dem

Source of Funding: SOHO study International.

Who Uses Self-Help?

P. Goering, J. Dubin, T. Sheldon, J. Oc Centre for Addiction and Mental Heal and Consulting Unit, 33 Russell St., 3 Toronto, ON, M5S 2S1, Canada

Background: Studies of the value of consider the full range of available op mode of service delivery that is view providing services and supports in the co about who is served by these prograr targeted and well-researched options s
Aims: This paper uses information fr community mental health services to a How do diagnosis, functioning and se Survivor Initiative (CSI) and Assertive participants compare? 2) What other s ACT participants using?
Methods: A multi-site study of comm in Ontario offers a unique opportunity Using a longitudinal design, seven eva community mental health care are l common protocol of measurement and the evaluations is examining the effect peer initiatives in four communities in As a reference group, we can compa (n=133) clients of four assertive cor Central East Ontario. Both sets of pr contexts, i.e. small urban and semi-rur of the *Canadian Toolkit for Measur* collected information regarding socio-d financial status; legal system contact an experience and hospital utilisation. The from charts and providers. The *Serv* developed to retrospectively collect in services and supports.
Results: While the groups overlap in several significant differences in bo

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XX Reunión Científica

Programa y Resúmenes

La Plata 12 y 13 de diciembre de 1991

revista de experiencias clínicas y neurociencias

Estudio abierto randomizado sobre el uso de Ranitidina a diferentes dosis para el control del aumento de peso asociado a la administración de Olanzapina

Andrea López-Mato
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Oscar Boullosa
Médico psiquiatra (UBA). Docente de PNIE. Co-director del IPBI

Resumen
El potencial aumento de peso debiera ser tomado en cuenta en pacientes que inician tratamiento con Olanzapina. Si bien la decisión de usar una molécula debe tener en cuenta su eficacia, eficiencia y perfil de efectos de adversos, se admite que el aumento de peso puede eventualmente comprometer la salud del paciente y la adherencia al tratamiento indicado para condiciones psiquiátricas severas. Existen eficaces y terapéuticas intervenciones farmacológicas preventivas para controlar este efecto adverso. En este estudio, la administración concomitante de ranitidina previno o corrigió el aumento de peso en 59.6% de los casos. Los pacientes que siguieron un tratamiento con olanzapina en dosis habituales mostraron los siguientes resultados: olanzapina sin ranitidina, exhibieron un aumento promedio de peso de 3,4 kilogramos, con un rango entre -2.5 y +16 kg. Esto implicó un aumento promedio de IMC de 1.19 para este grupo. Pacientes tratados adicionalmente con Ranitidina en dosis de 300 mg/día, mostraron un aumento promedio de peso 0.9 kilogramos con un rango entre -4 y +10.6 kg , implicando un aumento promedio de IMC de 0,34. En pacientes tratados con ranitidina en dosis de 600 mg/día, la curva de aumento de peso tendió a normalizarse con un decremento de 1,6 kilogramo con un rango entre -15 y +7 kilogramos, implicando una disminución de 0,6 puntos en el IMC. Mientras investigaciones más extensas son necesarias, este estudio estuvo destinado a demostrar que podemos contar con respuestas potencialmente simples y útiles para el tratamiento del aumento de peso asociado al uso de olanzapina. La relación riesgo/beneficio es el paradigma de la práctica de la medicina. En el caso de olanzapina, la balanza claramente se inclina a favor de este último, haciéndola la droga de elección en el tratamiento de la Esquizofrenia y otros desordenes psicóticos.
Palabras clave: Olanzapina – Ranitidina – Aumento de peso – Manejo – IMC.

RANDOMIZED, OPEN LABEL STUDY ON THE USE OF RANITIDINE AT DIFFERENT DOSES FOR THE MANAGEMENT OF WEIGHT GAIN ASSOCIATED WITH OLANZAPINE ADMINISTRATION

Summary
Potential weight gain must be taken into account in the patient's comprehensive treatment approach when initiating antipsychotic treatment with Olanzapine. There are effective preventive and therapeutic pharmacological interventions to control this adverse effect. Not addressing this eventual treatment aspect of Olanzapine treatment may compromise the patient's health and his/her compliance with the pharmacological treatment indicated in serious psychiatric conditions. The decision to use a molecule must be made taking into account its efficacy, efficiency and adverse effect profile. In this study, concomitant administration of Ranitidine prevented or corrected weight gain in 59.6% of cases. Patients followed by 16 weeks had shown the following results: Olanzapine without Ranitidine, exhibited an average weight gain of 3.4 kilograms, ranging between -2.5 and +16 kg. This implies an average increase of 1.19 in BMI for this group. Patients treated additionally with Ranitidine at doses of 300 mg, a 0.9 kilogram weight gain ranging between -4 and +10.6 kg was observed, implying an average BMI change of 0.34. In patients treated with Ranitidine at doses of 600 mg, the weight gain curve trended toward normalization with a 1.6 kilogram decrease, ranging between -15 and +7 kilograms, accounting for a decrease of 0.6 points in BMI. While more extensive studies are required, our interest with this study is to demonstrate that we can count on a potentially simple and useful response for the treatment of weight gain associated with Olanzapine use. The risk/benefit ratio is a paradigm in the practice of medicine. In the case of Olanzapine, the scale clearly tips in favor of the latter, making it the drug of choice in the treatment of schizophrenia and other psychotic disorders.
Key Words: Olanzapine – Ranitidine – Weigth Gain – Management – BMI.

REEMPLAZO DE Mg POR Mn EN REACCIONES PARCIALES DEL CICLO DE LA Ca-ATPasa DEL RETICULO SARCOPLASMICO. D. A. González, D. Takara, J. L. Rovner, G. L. Alonso y J. J. Lacapere (*). Cátedra de Biofísica, Facultad de Odontología, UBA, y (*) Departement de Biophysique, CEN Saclay, Francia.

La Ca-ATPasa del retículo sarcoplásmico (RS) posee al menos dos estados conformacionales diferentes, E_1 y E_2. E_1 es fosforilado por ATP y tiene alta afinidad por Ca^{2+}. E_2 es fosforilado por Pi. La transconformación $E_2 \longrightarrow E_1$ es activada por ATP y Ca^{2+}. El Mg^{2+} es cofactor de las fosforilaciones por ATP y Pi; se une al ciclo catalítico en ciertas etapas. Varios cationes divalentes, especialmente el Mn^{2+}, pueden reemplazar a Mg^{2+} en la activación de la ATPasa y como cofactor en la fosforilación con ATP. Además, el Mn^{2+} tiene la ventaja de que se dispone de un radioisótopo útil (^{54}Mn), y de que es un elemento paramagnético, lo que facilita el estudio de su unión a la ATPasa. Aquí estudiamos el efecto del Mn^{2+} sobre la unión del Ca^{2+} al sitio de alta afinidad, y como cofactor en la fosforilación por Pi.
Se estudió el cambio de fluorescencia que acompaña la transconformación $E_2 \longrightarrow E_1$ por efecto de Ca^{2+} y su modificación por adición de Mn^{2+}, y el efecto del Mn^{2+} sobre la unión de ^{45}Ca a la ATPasa. A pH 5.5, utilizado para minimizar el efecto de Ca contaminante, se observó solo pequeña disminución de la afinidad del sitio de transporte por Ca^{2+}, por efecto de Mn^{2+} hasta 20 mM.
La intervención de Mn^{2+} en la fosforilación por Pi se estudió en tres tipos de experimentos, en ausencia de Ca^{2+}: i. Fosforilación con ^{32}P en función de [Mn]. La fosforilación es algo mayor con Mn^{2+} que con Mg^{2+}. $K_{0.5}$ para ambos cationes es del mismo orden, bajo milimolar, con 20 uM Pi, DMSO y pH 5.5. ii. Medida de unión de ^{54}Mn; es significativamente mayor en presencia (3 nMol/mg Pr) que en ausencia (1 nMol /mg Pr) de 10 mM Pi, utilizando 20 uM Mn, DMSO y pH 5.5. El Mn unido a la ATPasa se disocia facilmente en medio ácido y en presencia de EGTA. iii. Análisis de la variación de la fluoresecencia de la ATPasa cuando se fosforila con Pi en presencia de Mn. Tanto el aumento en la concentración de Mn como el agregado de DMSO aumentan la afinidad de la ATPasa por Pi.

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Speaker Information

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First Announcement

Latin America Regional Neuroscience Conference

March 27-29, 2006
Buenos Aires, Argentina

Lilly

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Program

Day 1 – March 28, 2006 9:00AM-4:00PM

- Schizophrenia Overview
- How Significant Is the Relationship Between Cognition and Outcomes?
- Individualizing Treatment Plans Based on Endocrine Risks
- Goals, Fantasies, and Realities Associated With Treatment Effectiveness
- The Calculus of Treatment Adherence Over the Course of the Illness
- The Crucial Relationship Between Successful Acute Treatment and Outcomes: Fact or Fiction?

Day 2 – March 29, 2006 9:00AM-12:00PM

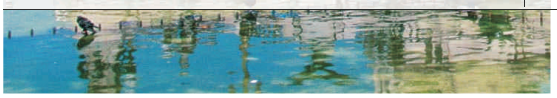
- Bipolar Disorder Overview
- Mixed Bipolar Disorder and Factors That Predict the Best Outcomes
- Has the Natural History of Bipolar Depression Been Altered by Newer Agents?

Meeting Location

Hilton Buenos Aires
Pacifico B
Buenos Aires, Argentina

Meeting Format

March 27	Arrivals
March 28	Scientific Session I
March 29	Scientific Session II



Letter of Invitation

Dear Colleague,

On behalf of Eli Lilly and Company, I would like to extend an invitation to you to be our guest at the upcoming **Latin America Regional Neuroscience Conference**. As a regional thought leader, you have been selected to attend this meeting, which will be held March 27-29, 2006, in Buenos Aires, Argentina.

As you can see from the agenda, this program will deliver an interactive and educational journey through schizophrenia and bipolar disorder. During the course of the program, we will explore new treatment options and patient management strategies that may redefine successful outcomes for those suffering from serious mental illness.

Leading researchers and international experts will begin day one with an overview of schizophrenia, followed by presentations on cognition, EPS, and endocrinology. Treatment effectiveness (as evidenced by CATIE trial outcomes), time to treatment discontinuation, and acute treatment will also be reviewed.

On day two, we will present an overview of bipolar disorder, bipolar depression, and mixed bipolar disorder.

It is with great pleasure that I cordially invite you to attend this conference. We trust that the faculty will deliver an interactive and informative program of the highest scientific standards which will be thought provoking and clinically relevant.

Sincerely,

Martin Dossenbach, MD
Medical Fellow I,
Medical Leader, Neurosciences
Lilly Intercontinental Region and Japan
Lilly Research Laboratories
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Answers That Matter.

CURRICULUM VITAE - JORGE ROVNER

PUBLICACIONES

Long-term antipsychotic monotherapy: clinical outcomes from the 3-year Intercontinental Schizophrenia Outpatients Health Outcomes Study (IC-SOHO)

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ABSTRACT

Objective: The Intercontinental Schizophrenia Outpatients Health Outcomes Study (IC-SOHO) was a pan-regional, 3-year, observational study of participants (pts) with schizophrenia, designed to examine the economic, clinical, and functional outcomes associated with treatment in a 'real-life' context. Here we describe the comparative effectiveness of antipsychotic monotherapies.

Methods: Clinical and functional assessment of outpatients initiating or switching to olanzapine (olz, n=2641), risperidone (ris, n=863), quetiapine (quet=142) or haloperidol (hal, n=189) was made at 0, 3, 6, 12, 18, 24, 30, and 36, months. Kaplan-Meier estimates of time to discontinuation, response, relapse, and remission were calculated while patients remained on their baseline (B) monotherapy. Response=Clinical Global Impressions (CGI) total score decreased by >2 points lower than B, if the B CGI total score was ≥4, or >1 point lower if the B CGI total score=3. Remission=CGI total, positive, negative, and cognition scores ≤2 for 2 consecutive visits > 6 months post baseline and no inpatient admissions.

Results: Patients on olanzapine were more likely (p<.001) to maintain their monotherapy than patients on risperidone, quetiapine, or haloperidol; and were also more likely (p<.001) to respond than risperidone, quetiapine or haloperidol patients, with median response times (months) of: olz 5, ris 6, quet 11, and hal 12. Median times to remission (months) were – olz 25, ris 36, and quet 36; patients on olz were more likely (p<.001) to experience remission than ris or hal patients. For haloperidol, the risk of relapse was 2.8 times that (p<.001) of olanzapine, and 2.1 times that (p=.006) of risperidone.

Conclusion: Antipsychotic monotherapy is a viable treatment strategy for schizophrenia, however there appears to be variable effectiveness across compounds.

OBJECTIVES

- To assess the comparative effectiveness of globally available and registered antipsychotics for treatment of schizophrenia, with a specific emphasis on olanzapine.
- To understand the pharmacological treatment patterns associated with olanzapine and other antipsychotics.

METHODS

Study Design

- Three-year, prospective, observational, open-label study
- Included patients from four continents
- Usual standard-of-care at the discretion of treating team
- Study assessments at baseline, 3, 6 months, and every 6 months up to 36 months

Enrolment

- Male or female outpatients ≥18 years of age
- Initiating or changing antipsychotic medication for treatment of schizophrenia (ICD-10 or DSM-IV)
- Patient consent followed country requirements

Sampling

- Olanzapine patients were systematically over-sampled to achieve two equal cohorts. Patients who:

  1: initiated or changed to olanzapine (alone or in combination)

  2: initiated or changed to non-olanzapine (alone or in combination)

Measures

- Demographics and clinical status:

  Age, gender

  Diagnosis and history

  CGI severity, and single items for severity of symptom clusters

CGI: Clinical Global Impression-Schizophrenia Scale[1]

- Brief assessment instrument - evaluated positive, negative, cognitive, depressive and overall symptoms on the day of assessment on 7-point scale:

  1-Normal, not at all ill; 2-Borderline ill; 3-Mildly ill; 4-Moderately ill; 5-Markedly ill; 6-Severely ill; 7-Among most severely ill.

Definitions

Discontinuation:

- Included discontinuation of the original baseline antipsychotic or the addition of, or switch to, another antipsychotic.
- Patients who were lost to follow-up or had missing drug information were also considered as a discontinuation event.

Response:

- CGI total score decreased to at least 2 points lower than baseline, if baseline CGI total score ≥4.
- CGI total score decreased to at least 1 point lower than baseline, if baseline CGI total score =3.
- Patients with a baseline CGI score of 1, 2, or missing were excluded from the analysis.

Remission:[2]

- CGI total, positive, negative, and cognition score ≤2 for two consecutive visits, and
- at least 6 months postbaseline, and
- had no inpatient admissions during the two visits.

Relapse:

- Only patients who met the criteria for response were eligible for analysis.
- CGI total score reversed back to the severity at baseline or worse.
- CGI total score increased at least 2 points.

Data Analysis

- This report evaluates a subset of patients who were prescribed olanzapine, risperidone, quetiapine or haloperidol monotherapy at enrolment and maintained this treatment for at least 3 months.
- Time from baseline visit until treatment discontinuation, response, and remission were estimated by Kaplan-Meier survival curves.
- Time to relapse was calculated from date of response.
- Patients who did not experience an event were censored at the last evaluable monotherapy visit.
- Where an event occurred between two visits, 1 day prior to the date of the later visit was used.
- Treatment groups were compared using Cox proportional hazards regression models and results reported as hazard ratios with 95% confidence intervals (CI).
- Given the large number of statistical comparisons undertaken, the level required for statistical significance was defined, *a priori*, to be p<.001.

RESULTS

Figure 1. Patient Disposition

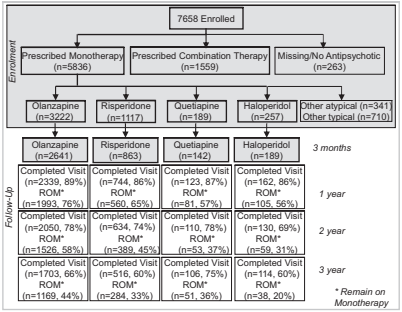


Table 1. Baseline Characteristics

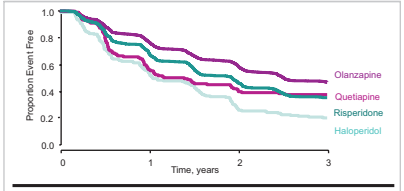
Characteristic	Olanzapine (n=2641)	Risperidone (n=863)	Quetiapine (n=142)	Haloperidol (n=189)	P value*
Gender, % women	45.2	48.1	54.6	47.1	0.0949
Mean age, years (SD)	34.8 (12.2)	36.0 (12.3)	35.6 (12.2)	35.1 (11.4)	0.1005
Mean duration illness, years (SD)	8.6 (9.7)	9.2 (10.1)	9.6 (10.8)	9.4 (9.6)	0.2266
First time use of antipsychotic, %	18.1	18.1	11.3	19.0	0.2319
Involved in relationship, %	35.8	38.0	45.1	26.9	0.0060
Involved in social activities, %	59.2	60.7	63.6	49.7	0.0327
Employment (paid or unpaid), %	23.2	23.3	23.4	16.4	0.1967
Living independently, %	32.9	33.3	40.4	27.1	0.0913
Overall CGI, mean (SD)	4.35 (1.07)	4.33 (1.09)	4.22 (1.06)	4.30 (1.07)	0.0134
Positive CGI, mean (SD)	3.90 (1.41)	3.82 (1.47)	3.85 (1.40)	4.15 (1.31)	0.0576
Negative CGI, mean (SD)	3.97 (1.33)	4.07 (1.42)	3.88 (1.25)	3.79 (1.37)	0.0607
Depressive CGI, mean (SD)	3.37 (0.03)	3.54 (0.12)	3.24 (0.05)	2.89 (0.10)	<.0001
Cognitive CGI, mean (SD)	3.69 (1.37)	3.67 (1.32)	3.63 (1.36)	3.62 (1.33)	0.6169

CGI: Clinical Global Impression-Schizophrenia scale

* Groups compared using analysis of variance or Wald chi-square test.

Figure 2. Time to Drug Discontinuation:

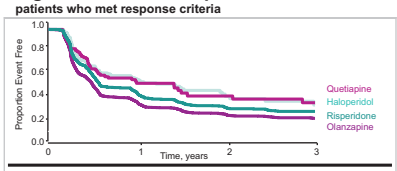
patients who discontinued their baseline monotherapy



	Olanzapine	Risperidone	Quetiapine	Haloperidol
Discontinued	1476 (56%)	581 (67%)	91 (64%)	151 (80%)
Kaplan-Meier median, years (CI)	2.5 (2.5, 2.6)	1.9 (1.6, 2.0)	1.3 (1.0, 2.0)	1.1 (0.9, 1.5)
Hazard ratio vs olanzapine	-	**1.4 (1.3,1.6) p<.001**	**1.5 (1.2, 1.8) p<.001**	**2.2 (1.8, 2.6) p<.001**
Hazard ratio vs risperidone	-	-	1.1 (0.8, 1.3) p=.678	**1.6 (1.3, 1.9) p<.001**
Hazard ratio vs quetiapine	-	-	-	1.5 (1.1, 1.9) p=.005

Figure 3. Time to Response:

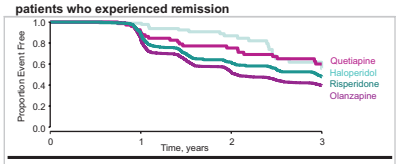
patients who met response criteria



	Olanzapine	Risperidone	Quetiapine	Haloperidol
Responded	1945 (74%)	530 (61%)	62 (44%)	85 (45%)
Kaplan-Meier median, years (CI)	0.44 (0.42, 0.46)	0.53 (0.50, 0.56)	0.94 (0.53, 1.46)	0.97 0.55, 1.48)
Hazard ratio vs olanzapine	-	**0.76 (0.69, 0.83) p<.001**	**0.57 (0.44, 0.74) p<.001**	**0.54 (0.43, 0.67) p<.001**
Hazard ratio vs risperidone	-	-	0.76 (0.58, 0.98) p=.038	0.71 (0.57, 0.90) p=.004
Hazard ratio vs quetiapine	-	-	-	0.95 (0.68, 1.31) p=.736

Figure 4. Time to Remission:

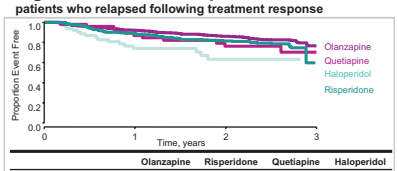
patients who experienced remission



	Olanzapine	Risperidone	Quetiapine	Haloperidol
Remitted	960 (36%)	24 (17%)	218 (25%)	18 (10%)
Kaplan-Meier median, years (CI)	2.1 (2.0, 2.4)	3.0 (2.5, 3.1)	3.0 (2.9, ⇨)	>3.0
Hazard ratio vs olanzapine	-	**0.78 (0.67, 0.90) p<.001**	0.56 (0.37, 0.85) p=.006	**0.35 (0.22, 0.56) p<.001**
Hazard ratio vs risperidone	-	-	0.72 (0.47, 1.11) p=.136	0.45 (0.28, 0.73) p=.001
Hazard ratio vs quetiapine	-	-	-	0.63 (0.34, 1.16) p=.139

Figure 5. Time to Relapse:

patients who relapsed following treatment response



	Olanzapine	Risperidone	Quetiapine	Haloperidol
Relapsed	227 (12%)	11 (18%)	73 (14%)	17 (20%)
Kaplan-Meier median, years	>3.0	>3.0	>3.0	>2.5
Hazard ratio vs olanzapine	-	1.4 (1.0,1.8) p=.022	1.6 (0.8, 2.8) p=.156	**2.8 (1.7, 4.7) p<.001**
Hazard ratio vs risperidone	-	-	1.1 (0.6, 2.1) p=.159	2.1 (1.2, 3.5) p=.006
Hazard ratio vs quetiapine	-	-	-	1.8 (0.9, 3.9) p=.117

KEY FINDINGS

- Patients switched to/initiated on olanzapine were significantly more likely (p<.001) to:
  - maintain their baseline monotherapy than patients on risperidone, quetiapine, or haloperidol
  - respond to their baseline monotherapy than patients on risperidone, quetiapine, or haloperidol
  - experience symptom remission than patients on risperidone or haloperidol.
- Patients on olanzapine monotherapy were 2.8 times less likely (p<.001) to experience symptom relapse than patients on haloperidol monotherapy.
- Patients on risperidone were significantly more likely (p<.001) to maintain their baseline monotherapy than patients on haloperidol.

CONCLUSIONS

- The IC-SOHO study provides important insight into the clinical and functional outcomes associated with long-term antipsychotic treatment in less-studied outpatient communities across the world in a naturalistic setting.

REFERENCES

[1] Haro JM, Kamath SA, Ochoa S, Novick D, Rele K, Fargas A, et al. The Clinical Global Impression-Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. Acta Psychiatr Scand Suppl. 2003;416:16-23.

[2] Andreasen NC, Carpenter Jr WT, Kane JM, Lasser RA, Marder SR, Weinberger DR. Am J Psychiatry. 2005;162: 441-9.

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