P.084 Clinical results of the use of the highest approved dose of monthly paliperidone palmitate: PICTURE sub-analysis study

M. Vega [1,*], S. Arqués [2], R. Vázquez-Noguerol [3], B. Nebot Tarazona [4], B. Herrera [4], M. García Dorado [4]

[1] *University Hospital Ramón y Cajal- Madrid, Psychiatry Unit, Madrid, Spain*
[2] *University Hospital La Fe- Valencia, USM Trinitat, Valencia, Spain*
[3] *Hospital Nicolás Peña- Vigo, Psychiatry Unit, Vigo, Spain*
[4] *Janssen, Medical Affairs Department, Madrid, Spain*

Introduction: Today, the remission of symptoms is considered an achievable goal for many patients with schizophrenia, since the focus in recent years has shifted from this symptomatic remission to a more global functional recovery [1]. The tolerability of antipsychotics is important to increase compliance with treatment and, consequently, to achieve the goals of rehabilitation in people with schizophrenia [2]. To achieve these objectives, it has been seen that there is a percentage of patients who may need, given their more severe clinical status, the use of higher than recommended doses of antipsychotic treatment [3].

Objective: To assess patients' own perceptions regarding functionality and quality of life in a subpopulation of patients diagnosed with schizophrenia and treated with high doses ($\geq$ 150 mg eq) of monthly Paliperidone Palmitate (PP1M) for at least six months. These patients at least 90% of the time have been at high doses ($\geq$150 mg eq) and if there has been any dose below 150 mg eq, this has been 100 mg eq.

Method: Post-hoc analysis of a cross-sectional observational study of a subgroup of patients with schizophrenia treated with PP1M for at least 6 months with maintenance doses $\geq$ 150 mg eq and who had previously received oral antipsychotics. The total sample of the study was of 356 patients, being the subpopulation of this subgroup of patients of 139. Of the total sample of patients included in the study (356) only 23 (6.5% of the total) have been in maintenance with at least one dose$>$ 150 mg eq.

Clinical situation (CGI-SCH, hospitalizations / emergency visits, suicide attempts); disability / functionality (WHODAS); attitude towards treatment (DAI-10); Quality of life (EuroQoL-5D / 5L) and tolerability were evaluated.

Results: One hundred and thirty nine (139) patients were included in this subgroup: mean time since diagnosis 15.0 years (mean age 42.1 years); mean time in treatment with PP1M 26.9 months, 28.8% were in antipsychotic monotherapy and 22.3% have alternated periods of mono and polytherapy where 51.6% have been $>$ 12 months in monotherapy. 16.5% received at least one dose $>$ 150 mg eq (6.5% of the total of 356 patients). The average dose per patient was 152.0 mg eq.

Scores of the scales: CGI-SCH: 3.3; WHODAS: 23.0 (59.7% with mild or no disability); quality index 0.785 (score between 0-1). 80.4% presented a positive attitude towards medication (DAI-10). Significant decrease in hospitalizations and emergency visits vs. the period with oral Antipsychotics (AP) ($p < 0.001$). 81.3% did not have any adverse reaction (AR) at least possibly related to PP1M and of the 29 patients who reported at least 1 (AR), none of them was serious.

Conclusions: In this subpopulation of patients who have needed doses $\geq$ 150mg eq, most are currently clinically stable, with a positive attitude towards treatment, an adequate quality of life and tolerability, which supports the individualized use of the treatment according to the clinical characteristics of each patient.

Disclosure statement: Miguel Vega is the study coordinator of this study, Sergio Arqués and Raúl Vázquez-Noguerol have participated as investigators recruiting patients for the study (all them have received honoraria based on their responsibilities). Begoña Nebot, Berta Herrera and Marta García-Dorado are full employees of Janssen.

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P.085 Cortical dopamine is essential for the hallucinogenic effect of 3,4-methylenedioxypyrovalerone (MDPV) demonstrated by enhanced EEG activity in rats

I.M. Shokry [1,2,*], J.J. Callanan [1], R. Tao [2]

[1] *Ross University School Of Veterinary Medicine, Biomedical Sciences, Basseterre, St. Kitts and Nevis- Federation of*
[2] *Charles E. Schmidt College of Medicine-Florida Atlantic University, Biomedical Science, Boca Raton, USA*

Background: The main psychoactive ingredient in synthetic cathinones ('bath salts') is 3,4-methylenedioxypyrovalerone (MDPV). Abuse of MDPV induces hallucinatory delirium and drug addiction [1]. Symptoms of the hallucinatory delirium are clinically similar to those of positive schizophrenia (PSZ). Positron emission tomography (PET) scan studies revealed that PSZ patients had an increased dopamine (DA) in the subcortical regions [2]. In contrast, the cortical DA is very low in terms of PET-scan density and unaffected in the PSZ patients. Recently, the DA hypothesis for PSZ has been conveniently used as the basis for understanding hallucination caused by psychostimulants, including MDPV [3]. However, MDPV-elicited hallucination is an iatrogenic disorder, which may be different from idiopathic hallucination occurred in PSZ patients. Additionally, little is known about differential effects of MDPV on subcortical and cortical DA transmissions. Thus, whether

the relationship between DA and MDPV-elicited hallucination is similar to that of PSZ remains to be determined.

Objective: The goal of this study was to test the hypothesis that cortical DA is necessary for the hallucinogenic effect of MDPV, even though both cortical and subcortical DA is increased.

Methods: Experiments were carried out on male Sprague-Dawley rats. MK-801 and ketamine are known to cause hallucination and schizophrenia-like behavior in rats [4] and thus were used as a reference drug to compare with MDPV. Hallucinogenic effects were assessed with an electroencephalogram (EEG). EEG electrodes were anchored on the surface of scalps (above the dura mater). Activity of DA neurotransmission was estimated using brain microdialysis. Subcortical and cortical DA transmissions were determined in the nucleus accumbens (NAcc) and prefrontal cortex (FCx), respectively. Statistical significance was assessed using the ANOVA test.

Results: The effect of MDPV (0.25, 0.5, 1 and 2 mg/kg, i.p.) was compared to the hallucinogenic drugs MK-801 (0.05, 0.1 and 0.5 mg/kg, i.p.) and ketamine (5, 15 and 25 mg/kg, i.p.). We found that MDPV, similar to MK-801 and ketamine, caused a dose-dependent increase in the EEG synchronization. The synchronization was blocked by the D1R antagonist SCH23390 (0.1 mg/kg, i.p.) and D2R antagonist sulpiride (100 mg/kg, i.p.). Regarding DA levels, increased dopamine caused by MDPV was higher in the NAcc compared to the FCx, although MDPV caused a dose-dependent increase in both regions. Importantly, DA in the NAcc was increased by a low dose of MDPV sufficient to cause addiction, but not hallucination. In contrast, cortical DA was not increased unless the dose was high enough to cause hallucination. MK-801 and ketamine also produced differential effects on subcortical and cortical DA. Specifically, the hallucinogenic drugs MK-801 and ketamine increased DA, mainly in the FCx, but had a little effect on DA in the NAcc.

Conclusion: MDPV exerts a differential effect on subcortical and cortical DA. Although MDPV causes a greater increase in subcortical DA than the cortical, cortical DA may be essential for eliciting the hallucinogenic effect of MDPV.

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P.086 Antipsychotics in adolescents at ultra-high risk of psychosis: Findings from the "Reggio Emilia At-Risk Mental States" project

G. Galli[1,*], L. Pelizza[2], M. Poletti[2], S. Azzali[2], F. Paterlini[2], S. Garlassi[2], I. Scazza[2], L.R. Chiri[3], F. Fontana[2], V. Barbanti Silva[2], R. Favazzo[2], M. Fabiani[2], L. Pensierini[2], L. Cioncolini[2], E. Semrov[2], A. Raballo[4]

[1] *School of Psychiatry- University of Modena and Reggio Emilia, Department of Diagnostics- Clinical and Public Health Medicine, Modena, Italy*
[2] *Reggio Emilia Public Health-Care Service, Reggio Emilia Mental Health Department, Reggio Emilia, Italy*
[3] *Bologna Public Health-Care Service, Bologna Mental Health Department, Bologna, Italy*
[4] *Childhood and Development Research Group- Norwegian University of Science and Technology NTNU, Department of Psychology, Trondheim, Norway*

Introduction. Specialized intervention for young people at Ultra-High Risk (UHR) of psychosis can effectively reduce psychosis conversion rate [1]. In this regards, the European Psychiatric Association (EPA) [2] considers that in adult UHR individuals a staged intervention model should be applied with the least restrictive service approach (i.e. Cognitive-Behavioral Therapy [CBT]) being offered as first choice. Where psychological interventions have proved ineffective, they should be complemented by low dose second-generation antipsychotics if severe and progressive UHR symptomatology is present and with the primary aim to achieve a degree of symptomatic stabilization, required for psychological interventions to be effective. However, the clinical significance and the prognostic value of UHR criteria in adolescents is less clear in comparison with adults [3]. Indeed, the EPA considers that the current evidence for the efficacy of psychological and pharmacological interventions in UHR children and young adolescents is not sufficient to justify primarily preventive interventions [2], but specific psychological interventions should be provided as part of an overall treatment plan. UHR symptoms should be carefully monitored over an extended period, and the treatment plan should be adapted according to their course. Aim of the current study was to investigate the use of antipsychotic medication in an early detection/intervention program for help-seeking adolescents, based on CAARMS (Comprehensive Assessment of At-Risk Mental States) UHR criteria (i.e. the "Reggio Emilia At-Risk Mental States" [ReARMS] project [4]).

Methods. One-hundred-five adolescents (aged 13-18 years) were assessed with the CAARMS, which identified 37 UHR individuals (35.2%). In this group, we calculated antipsychotic prescription rate over a 1-year follow-up period.

Results. Six of the 37 UHR+ adolescents had a follow-up period of $<$ 1 year. After 12 months of follow-up, 2 (6.5%) of the remaining 31 UHR+ individuals had transitioned to full-blown psychosis. One of them had been prescribed antipsychotics during the follow-up period. Antipsychotic medications were prescribed to 9 of the 31 UHR+ adolescents (29%). Three of the 8 UHR+ adolescents who did not convert to psychosis, were still being prescribed antipsychotics at 12 months.