Body mass index and metabolic changes following antipsychotic drug treatment of first-episode psychosis: influences of childhood trauma and tobacco smoking [abstract only]

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absorption models for each formulation best described the data. Absorption of the Ari 2MRTU formulation was modeled by a parallel zero-order and lagged first-order process that accounted for an identified double peak in plasma concentrations of aripiprazole post-administration of Ari 2MRTU. All disposition parameters were shared between the formulations except Vc/F (oral and AOM formulations, 93.4 L; Ari 2MRTU formulation, 2035 L); the different Vc/F value for the Ari 2MRTU formulation was attributed to the terminal half-life being absorption driven. Sex was a significant covariate on the absorption of the Ari 2MRTU formulation (90.7% higher absorption rate constant and 56.0% lower fraction of first-order absorption in males versus females); however, simulated $C_{avg,ss}$ values were identical in both sexes, indicating no clinically relevant effect. As expected, simulated aripiprazole concentrations were higher in poor versus extensive metabolizers of CYP2D6; the effect of CYP2D6 metabolizer status was thus retained as a covariate from the prior model.

Conclusion: The final popPK model was considered fit for purpose, adequately describing aripiprazole PK following administration of Ari 2MRTU 960. The model also established estimates for key popPK parameters and identified sources of variability in drug exposure. The model will be used to perform simulations to support dosing of Ari 2MRTU 960 across multiple realistic clinical scenarios.

References

[1] T. Kishimoto, K Hagi, S Kurokawa, et al, Long-acting injectable versus oral antipsychotics for the maintenance treatment of schizophrenia: a systematic review and comparative meta-analysis of randomised, cohort, and pre–post studies, Lancet Psychiatry 8 (2021) 387404. https://doi.org/10.1016/s2215-0366(21)00039-0. [2] Y Wang, X Wang, M Harlin, et al, An alternative start regimen with aripiprazole once-monthly in patients with schizophrenia: population pharmacokinetic analysis of a single-day, two-injection start with gluteal and/or deltoid intramuscular injection, Curr. Med. Res. Opin. 37 (2021) 1961–1972.

Conflict of interest:

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BODY MASS INDEX AND METABOLIC CHANGES FOLLOWING ANTIPSYCHOTIC DRUG TREATMENT OF FIRST-EPISODE PSYCHOSIS: INFLUENCES OF CHILDHOOD TRAUMA AND TOBACCO SMOKING

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Background: Antipsychotic treatment may induce weight gain, a risk factor for metabolic disturbances [1]. Childhood trauma and tobacco smoking are also risk factors for both metabolic and psychiatric pathology. However, data on long-term metabolic effects associated with antipsychotics (AP) are scarce.

Objective: To evaluate up to one-year changes in body mass index (BMI) and related metabolic abnormalities in psychotic patients receiving AP, and determine if childhood trauma or tobacco smoking are associated with these changes.

Methods: We included 82 first-episode psychosis patients (FEPp) aged 16-64 years treated with AP at baseline and followed up for 12 months, excepting 17 followed up at 3 months. All measurements were performed in the Ribeirão Preto Early Intervention in Psychosis Programme [2], including fasting glucose, total cholesterol, triglycerides, HDL-c and LDL-c. Childhood trauma was evaluated using Childhood Trauma Questionnaire [3]. Composite International Diagnostic Interview tobacco section classified the frequency of tobacco smoking considering the regular cigarette use in the past 12 months. Data were analysed by ANOVA with follow-up group as a cofactor, followed by post-hoc Bonferroni tests.

Results: Forty-nine FEPp were men (59.8%), 47 were white (57.3%), and the average age was 32.5±14.4 years. At 6-month follow-up, 51.2% had a confirmed diagnosis of schizophrenia, 32.9% bipolar and 13.0% depressive disorder. Patients exhibited a significant increase in BMI (baseline: 25.2±6.4 kg/m2; follow-up: 27.4±7.1 kg/m2, $p<0.001$). The percentage of obese (BMI $\geq$ 30 kg/m2) subjects among FEPp rose from 15.9 to 29.3% after follow-up. The percentage of those meeting criteria for overweight (BMI $\geq$ 25, <30kg/m2) also increased, from 31.7% to 32.9%. At baseline, 64.6% received haloperidol and 35.4% second-generation AP. After follow-up, 26.8% received haloperidol, and 73.2% of patients second-generation AP, grouped based on the AP propensity for weight gain (low: haloperidol; high: quetiapine, risperidone, olanzapine and clozapine). Forty-one (50.0%) FEPp gained clinically significant (≥7%) weight, but no significant differences were observed between high- and low groups ($p=0.139$). Sex, ethnicity and age had no significant influence on BMI changes. The mean difference in BMI during the follow-up did not significantly differ between the AP groups (low: 2.0±3.6 kg/m2; high: 2.3±2.4 kg/m2, $p=0.600$). Of metabolic measurements, glucose ($p=0.007$), cholesterol ($p=0.002$), triglycerides ($p=0.008$) and LDL-c ($p<0.001$) significantly increased at follow-up. The low and high groups showed no significant differences in metabolic measures. Eighteen (22.0%) FEPp had experienced trauma. History of emotional or physical abuse was significantly associated with elevated glucose ($p=0.037$; $p=0.012$, respectively). Moreover, physical neglect was correlated with LDL-c ($r=0.240$, $p=0.046$). However, no childhood maltreatment (global and subtypes) was significantly related to BMI or other metabolic markers. The current smoking frequency was 37.8%. High blood pressure was associated with tobacco smoking ($p=0.032$). FEPp with physical childhood abuse had a higher smoking rate than non-smokers FEPp ($p=0.042$). Other childhood maltreatment subtypes or metabolic markers did not show significant differences in relation to tobacco smoking.

Conclusions: The first year of AP treatment has significant effects on BMI and metabolic markers, and experience of childhood maltreatment may contribute as a risk factor for increased metabolic profile in psychosis.

References

[1] Cooper, J.S., et al., 2016. BAP guidelines on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment. J Psychopharmacol 30(8), 717-48.

[2] Corrêa-Oliveira, G.E., et al, 2022. Early intervention in psychosis in emerging countries: Findings from a first-episode psychosis programme in the Ribeirão Preto catchment area, southeastern Brazil. Early Interv Psychiatry 16(7), 800-807.

[3] Grassi-Oliveira, R., et al., 2006. Translation and content validation of the Childhood Trauma Questionnaire into Portuguese language. Rev Saude Publica 40(2), 249-55.

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RISK FACTORS AND CLINICAL OUTCOMES AMONG HOMELESS WOMEN WITH SCHIZOPHRENIA: A SYSTEMATIC REVIEW

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Introduction: Several factors have been identified as potential contributors of mental health service underusage in people suffering from schizophrenia and related disorders [1]. Travel distance to care provision and restricted service hours are recognized deterrents. Personality features, perception of adverse treatment effects and cognitive deficiencies are additional patient related-factors [1]. In homeless patients with schizophrenia, the functional impact of mental