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Obesity and schizophrenia: results of a feasibility study with semaglutide to assist weight loss [abstract only]

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EVENAMIDE PHASE 3 PROGRAM: STUDY 023 (ENIGMA-TRS) EVALUATES THE EFFICACY OF ADD-ON GLUTAMATE MODULATION IN PATIENTS WITH DOCUMENTED TREATMENT-RESISTANT SCHIZOPHRENIA

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Introduction: The need for alternative treatment strategies to manage the symptoms and improve the functioning and quality of life of patients with schizophrenia is widely recognized among the scientific community [1]. Although the high number of currently available antipsychotics (AP) may suggest that sufficient treatment options exist, the fact that all of them share a similar mechanism of action poses a limitation. In fact, while DA/5-HT receptor blockade has proved efficacy in ameliorating positive symptoms, this approach alone has not provided evidence of efficacy in treating negative/cognitive symptoms or improving functioning [2]. Moreover, more than half of patients do not gain adequate benefit from antipsychotics, and ~30% develop treatment-resistant schizophrenia (TRS).
Evenamide, a voltage-gated sodium channel blocker devoid of activity at >150 CNS targets, normalizes excessive glutamate release without affecting its basal levels. Experiments in animal models of psychosis and mania have shown benefits associated with evenamide either used as monotherapy or combined with first- or second-generation APs. Preliminary clinical benefits of evenamide as add-on to an AP in TRS patients were demonstrated in a pilot, phase 2, open-label, rater-blinded, 1-year trial [3]. In addition, a phase 2/3, international, randomized, double-blind, placebo-controlled trial in patients with schizophrenia not adequately benefitting from an SGA demonstrated statistically significant and clinically meaningful improvements associated with evenamide add-on treatment for 4 weeks [4].
Aim: Study 023/ENIGMA-TRS (EveNamIde's Glutamate Modulation Ameliorates TRS) will determine the efficacy and safety of evenamide as add-on to therapeutic doses of antipsychotics in patients with documented TRS, according to the TRRIP consensus guidelines [5].
Methods: Study 023 is an international, 1-year, randomized, double-blind, placebo-controlled study with the primary efficacy endpoint at 12 weeks and long-term efficacy endpoints at 26 and 52 weeks. It will be conducted in Europe, Asia, Latin America, and North America. The population will include patients with documented TRS receiving AP treatment but not adequately benefitting from a stable therapeutic dose of an SGA. During the 6-week screening period and throughout the study, adherence to background AP(s) and evenamide will be confirmed through measurements of plasma levels. Psychiatric selection criteria include CGI-S of mildly to severely ill (3-6), BPRS total score ≥45, with a score ≥18 on core symptoms of psychosis, and PANSS total score ≥70. An Independent Eligibility Committee will determine if patients meet protocol selection criteria. Patients improving ≥20% on the BPRS or ≥1 category on the CGI-S during the screening period will be excluded. Efficacy (PANSS, CGI-S/C, Q-LES-Q-SF, GAF, PSP scales) and safety (vital signs, ECG, lab tests, physical/neurological/eye exams, ESRS-A, CDSS, C-SSRS) will be evaluated at regular intervals.
Results: The study has been submitted for regulatory approval in 13 countries and will be initiated by the time of the congress; the up-to-date enrolment status will be presented. Results will determine whether the addition of evenamide to SGAs is associated with benefits in patients with TRS.
Conclusions: Positive results from the global phase 3 program would support add-on glutamate modulation by evenamide as an alternative efficacious strategy for managing unmet needs in TRS.
References
1.Kantrowitz JT, Correll CU, Jain R, Cutler AJ. New Developments in the Treatment of Schizophrenia: An Expert Roundtable. Int J Neuropsychopharmacol 2023. 26(5):322-330. doi: 10.1093/ijnp/pyad011 2.Marder S. Limitations of Dopamine-D2 Antagonists and the Search for Novel Antipsychotic Strategies. Neuropsychopharmacol 1999. 21 (Suppl 2), S117–S121. https://doi.org/10.1016/S0893-133X(99)00105-0 3.Anand R, Turolla A, Chinellato G, Roy A, Hartman RD. Therapeutic Effect of Evenamide, a Glutamate Inhibitor, in Patients With Treatment-Resistant Schizophrenia (TRS): Final, 1-Year Results From a Phase 2, Open-Label, Rater-Blinded, Randomized, International Clinical Trial. Int J Neuropsychopharmacol 2024. 28(1):pyae061. doi: 10.1093/ijnp/pyae061 4.Anand R, Turolla A, Chinellato G, Sansi F, Roy A, Hartman R. Efficacy and safety of evenamide, a glutamate modulator, added to a second-generation antipsychotic in inadequately/poorly responding patients with chronic schizophrenia: Results from a randomized, double-blind, placebo-controlled, phase 3, international clinical trial. Neuropharmacology 2025. 266:110275. doi: 10.1016/j.neuropharm.2024.110275 5.Howes OD, McCutcheon R, Agid O, et al. Treatment-Resistant Schizophrenia: Treatment Response and Resistance in Psychosis (TRRIP) Working Group Consensus Guidelines on Diagnosis and Terminology. Am J Psychiatry 2017. 174(3):216-229. doi: 10.1176/appi.ajp.2016.16050503
Conflict of interest
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OBESITY AND SCHIZOPHRENIA: RESULTS OF A FEASIBILITY STUDY WITH SEMAGLUTIDE TO ASSIST WEIGHT LOSS

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Introduction: Weight gain has come to define the life experience of many individuals with schizophrenia and other severe enduring mental illnesses (SMI) (1,2). GLP-1 receptor agonists and other incretin therapies could be of substantial value in addressing the challenge of obesity in people with SMI, given the well-established evidence for their ability to reduce weight in overweight individuals. In this clinical intervention study, we aimed to determine whether weekly treatment with the glucagon-like peptide-1 (GLP-1) agonist, semaglutide, as part of usual care, is feasible and acceptable to individuals in a psychiatric inpatient setting.
Methods: 15 inpatients (11 men / 4 women) in a secure care environment, diagnosed with schizophrenia or schizoaffective disorder and with body mass index (BMI) of ≤30 kg/m^2 were commenced on weekly subcutaneous semaglutide as per standard of care. BMI and glycated haemoglobin (HbA1c) were measured at baseline and monthly follow-up to 6 months, and quality of life (QOL) was surveyed at baseline and 6 months. Analysis was based on intention-to-treat.
Results: Mean age of patients was 37 years (range 23–63). Time since diagnosis varied from 2 to 25 years. Mean initial BMI was 48.7 kg/m^2 for women and 37.2 kg/m^2 for men. Duration of semaglutide treatment ranged from 2–6 months. Five patients discontinued semaglutide before the study end, including two who were discharged and no longer able to receive the intervention, and three who withdrew due to medical concerns.
Individual percentage weight change varied from +1% to -12% (median 5%), and weight reduction was seen in all except two patients. The EQ5D5L QOL visual analogue scale (3) showed a mean improvement of +7.5 (from 60 to 67.5) points. Improvement in QOL was overall significantly greater in those who remained on semaglutide (+9.5) than those who discontinued. All but one patient demonstrated a reduction in HbA1c levels.
Mean HbA1c fell significantly from 41 (range 34–47) mmol/mol to 35.3 (31–45) mmol/mol. Importantly, all patients with baseline HbA1c in the non-diabetic hyperglycaemia range (42-47 mmol/mol) demonstrated a reduction of HbA1c to below 42 mmol/mol by 3 months.
Prior to initiation of semaglutide, mean blood pressure was 127 (range 117–145) mmHg systolic and 82 (62–99) mmHg diastolic. At last assessment, average blood pressure was reduced to 121 (107–136) mmHg systolic and 79 (65–96) mmHg diastolic.
Conclusion: In this feasibility study, weekly semaglutide treatment was associated with reductions in BMI, HbA1c and blood pressure, and significant improvement in self-rated overall QOL, in 13/15 inpatients with obesity and serious mental illness (SMI) at up to 6 months follow-up. Even in patients who discontinued treatment before 6 months, initial benefits of weight reduction and improved QOL were still demonstrated.

Further evaluation, including health economic assessment and longer-term follow up, may support the expanded use of GLP-1 agonists and similar therapies in improving the cardiometabolic profile and longitudinal health outcomes in individuals with SMI.

References

1.Heald AH, Martin JL, Payton T, Khalid L, Anderson SG, Narayanan RP, De Hert M, Yung A, Livingston M. Changes in metabolic parameters in patients with severe mental illness over a 10-year period: A retrospective cohort study. Aust N Z J Psychiatry. 2017 Jan;51(1):75-82. 2.Zhang JP, Gallego JA, Robinson DG, Malhotra AK, Kane JM, Correll CU. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: a systematic review and meta-analysis. Int J Neuropsychopharmacol. 2013 16:1205-18 3.Euroqol. EQ-5D-5L. (Internet). Available from: https://euroqol.org/information-and-support/euroqol-instruments/eq-5d-5l. Accessed 1 April 2025

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PREVALENCE AND APPROPRIATENESS OF ANTIPSYCHOTIC PRESCRIBING IN ITALIAN PRISONERS

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Introduction and aims: In Western societies, it has been reported that the prevalence of mental disorders is up to 7 times higher in prisoners than in the general population [1]. Specifically, results of recent epidemiological research in Italy suggested that although 70% to 75% of Italian inmates shows some kind of psychiatric disorders, severe mental illness (most of them generically defined as "psychosis") represents approximately 4% to 5% of the total cases [2]. Substance use disorder is also a major disabling diagnosis in Italian prisoners. In this respect, it has been reported that more than 35% of the Italian inmates has pathological substance dependence already before the prison admission [3]. Given the high prevalence of mental disorders in prison, antipsychotic (AP) prescription remains widely extended in the common clinical practice. Despite some studies examining the administration of psychotropic drugs in inmates, robust, high-quality prescribing data are not routinely available from prisons (especially for APs), yet this is crucial to manage the safe, cost-effective, and overall clinical use of psychotropic medications. Furthermore, recent crucial issues regard the continuity, equity and appropriateness of prescribing psychotropic medicines (especially APs) for prisoners with mental disorder. In this respect, evidence of discontinuity of psychotropic prescription between the community and jail has been reported. Specifically, some authors observed that during the first week after incarceration, 50% of all psychotropic drugs prescribed by community mental health care centers were discontinued in jail, often without recorded justifications or evidence of clinical review. Differently, other studies raised doubts about an inappropriate overprescription of psychotropic medications in prison (also for APs), sought or illicitly traded for their sedative rather than therapeutic effects. The aim of this research was to investigate prevalence and appropriateness of AP prescription in an Italian prison to expand our understanding on this crucial area of clinical-forensic practice.

Methods and procedures: A cross-sectional (census day) design was used among male adults in the Parma Penitentiary Institutes (PPI). Sociodemographic, clinical and prescription data were collected from the PPI electronic clinical database management system. The AP prescribing appropriateness was examined in accordance with the therapeutic indications included in the Italian National Formulary. A descriptive statistical analysis was performed.

Findings and results: A total of 98 (14.1%) of 696 PPI prisoners were taking AP medications. Moreover, 90 (91.8%) of the 98 PPI participants were also taking other psychotropic medications concurrently. Quetiapine and olanzapine were the most common prescribed APs. Antipsychotic medications were most likely to be prescribed for off-label indications (74.4%). Less than one fifth of all AP prescriptions were for psychotic disorders.

Implicationsand conclusions: Antipsychotic medications are widely used in prison, often together with other psychotropic drugs. Considering their common adverse effects, it is crucial to longitudinally monitor their potential risk of metabolic, cardiovascular, and extrapyramidal symptoms and signs, as well as their early risk of mortality. Given the high prevalence of AP off-label prescription, the rationale for AP prescribing should be clearly documented and regularly reviewed within the prison by mental health professionals.

References

[1] 1.Fazel S, Hayes AJ, Bartellas K, et al. Mental health of prisoners: prevalence,adverse outcomes, and interventions. Lancet Psychiatry. 2016;3:871–881. [2] 4.Pelizza L, Zaimovic A, Veneri B, et al. The Parma integrated model forintervention on pathological addictions in an Italian prison: process description and preliminary findings. Acta Biomed. 2021;92:e2021223. [3] Pelizza L, Zambelli U, Rossi E, et al. Mental health interventions in an AQ3 Italian prison: the Parma integrated approach. Int J Prison Health. 2020; Available at: https://doi.org/10.1108/IJPH-07-2020-0046.

Conflict of interest

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CENTRAL NERVOUS SYSTEM ACTING MEDICATIONS USED BY PATIENTS WITH BORDERLINE PERSONALITY DISORDER IN SWEDEN: 2005-2020

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Background and Objectives: No medication is approved for the treatment of borderline personality disorder (BPD). International guidelines recommend psychotherapy as first-line treatment, and to consider medication for comorbid conditions and in the event of acute crises [1, 2]. Previous studies indicate that most individuals diagnosed with BPD use psychotropic medications, often for long durations and in co-medication [3, 4]. BPD symptom severity and medication misuse is elevated in young adulthood [5], but studies of medication use in young-adults with BPD are lacking. This study aimed to investigate patterns of use of central nervous system (CNS) acting medications in individuals diagnosed with BPD in the entire Swedish population, focusing on young adults aged 18-24, around the time of being diagnosed.

Methods: Using Swedish national registers, we conducted a cohort study of individuals with a registered BPD diagnosis from 1997 onward. The use of CNS acting agents, including medications licensed for psychiatric and non-psychiatric conditions, were investigated. Data on dispensed prescriptions between 1st of July 2005 and 30th of June 2020 were utilized. Prevalent use, long-term use, and co-medication were first investigated throughout, regardless of the time and age when first being diagnosed. In young adults, specific years were investigated, primarily focusing on the time around the first established diagnosis (i.e.; the year before, the first-, the second-, and the third year after diagnosis). Additionally, sample years 2006, 2010, 2014, and 2019 were investigated for time trends in use in individuals diagnosed prior to those specific years. Medication use during the year after the first established diagnosis was compared between individuals with BPD and matched individuals diagnosed with depression in specialist care as a reference group.

Results: Most individuals (98.8%) with a registered BPD diagnosis (N=34,430) had used CNS acting medications at some point between 2005 and 2020, and the most commonly used group of medications were anxiolytics, hypnotics and sedatives (94.3%). In 18–24-year-olds, 91.1% had used medication, it peaked for all three measures of use (prevalent use, long-term use and co-medication) in the year following first BPD diagnosis and was then more extensive than for individuals diagnosed with depression. An increase in use over the years (2006-2019) was found in the young adult group with a priorly estabilised BPD diagnosis, particularly for ADHD medication (5.5 times) and Lamotrigine (2.3 times).

Conclusions: Almost all individuals diagnosed with BPD had used CNS acting medication. The time when first being diagnosed with BPD was crucial in relation