

with a wide variety of clinical features such as stereotypic movements, dystonia, etc. There are many treatment approaches but the level of evidence is low. (Vasan et al. StatPearls Pub 2024)

**Objectives:** To draw attention to the clinical presentation of tardive dyskinesia and its treatment.

**Methods:** A detailed case report is documented.

**Results:** A 43-year-old woman, married, housewife, diagnosed with psychotic disorder. Last year, she admitted to our outpatient clinic for the first time. She was receiving Amisulpride 400 mg/g, Zuclopentixol deconoate 200 mg/month, Biperiden 4 mg/g, Propranolol 80 mg/g on admission. Her complaints were slowed movements and difficulty in doing housework. On examination, mouth puckering and periodic head movement were noticeable. She complained of contractions in her legs and numbness in her tongue. Her speech and walking were slow. In cerebellar tests she was clumsy. She stated that her complaints increased sometimes, the contraction in her neck and legs never stopped, but the mouth puckering movement ceased at night. Her AIMS scale point was 11.

It was learned that about 4 years ago she had started to complain of feeling that she was being spied on and hearing bad things. She had been hospitalized and diagnosed with psychotic disorder. Paliperidone and aripiprazole long-acting injections, olanzapine, quetiapine treatments had been tried during hospitalization and outpatient follow-up. She had been continuously switched to another treatment because of her suspicion. Lastly zuclopentixol deconoate had been started and combined with amisulpride. She stated all her complaints of movement appeared shortly after first hospitalization. Biperiden and propranolol were added to treatment, but her complaints didn't improve. During our follow-up she was consulted to neurology. Her current picture was evaluated as tardive dyskinesia. Her treatments were gradually stopped. Clonazepam was started and gradually increased to 2 mg/g and combined with vitamin E and its dosage was increased to 1200 mg/g. After discontinuation of antipsychotics during close follow-ups she had no psychotic complaints. Within 5 months, mouth puckering movement, stereotypic left-turning movement in the neck, numbness in the tongue and contraction in the leg completely resolved. Her speech and walking improved. Last AIMS scale point was 3.

**Conclusions:** Tardive dyskinesia is an iatrogenic movement disorder. Many methods have been proposed for treatment but no definite treatment is known. It's thought that vitamin E may be beneficial with its antioxidant effect and clonazepam may be effective above 2 mg. The case is important in terms of demonstrating the efficacy of the combination of vitamin E and clonazepam. (Cornett et al. *Ochsner journal* (2017):162-174.)

**Disclosure of Interest:** None Declared

## EPV1616

### Exploring cholinergic dysfunctions in schizophrenia as targets for a new generation of antipsychotics- The current level of evidence

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**Introduction:** The dopaminergic hypothesis of schizophrenia has been constantly revised and virtually all the antipsychotics currently available for the treatment of schizophrenia are based on this pathogenetic hypothesis. However, the involvement of cholinergic, glutamate, gamma-amino-butyric acid, serotonin, neurotrophins, and pro-inflammatory cytokines in the onset of psychotic disorders is attracting more and more interest. This interest is fueled by the high rates of treatment resistance in schizophrenia, which reaches 15-40% (Wong et al Transl Psychiatry 2024;50 14) and requires second-line treatment, frequently associated with significant adverse events. Finding new pharmacological agents that can be used either as monotherapy or as add-ons to the ongoing treatment in patients with schizophrenia is essential for improving the chances of functional recovery.

**Objectives:** To review the evidence supporting the modulation of cholinergic neurotransmission as a potential pharmacological target for treating schizophrenia.

**Methods:** Two clinical studies repositories (US National Library of Medicine- clinicaltrials.gov and WHO International Clinical Trials Registry Platform-<https://www.who.int/clinical-trials-registry-platform>) and the PubMed database were explored using "choline\*" and "schizophrenia" or "psychotic disorders" or "schizophrenia spectrum disorders" for studies and reviews focused on cholinergic agents targeting symptoms of schizophrenia.

**Results:** Positive allosteric modulation of the  $\alpha 7$  nicotinic receptors and M1/M4 muscarinic receptor agonism are the two pharmacodynamic mechanisms explored for cholinergic-based antipsychotics. Other possible mechanisms of interest are positive allosteric modulation of the M5 muscarinic receptors, selective M4 positive allosteric modulation, and cholinesterase inhibition. Out of these preclinically explored options, only xanomeline, an M1/M4 muscarinic receptor agonist, has reached phase III of clinical research with significant antipsychotic effects. The currently explored formula is an association of a fixed dose of xanomeline (selective M1/M4 cholinergic agonist) and trospium (a cholinergic antagonist), the last agent being included to decrease the risks of peripheral cholinergic adverse events. Studies investigating cholinesterase inhibitors have not been associated with favorable results, and the tolerability was low. Positive allosteric modulators of the  $\alpha 7$  nicotine receptors are investigated in preclinical studies, but in phase 1b such an agent, i.e., AVL-3288, failed to show efficacy versus placebo.

**Conclusions:** The association of xanomeline, an M1/M4 receptor agonist, and trospium, a peripheral cholinergic antagonist, led to favorable results in phase III trials. Other molecules with cholinergic mechanisms are also explored in schizophrenia, but the results are not yet clinically significant.

**Disclosure of Interest:** None Declared

## EPV1617

### Atypical antipsychotics as add-ons to antidepressants in the major depressive disorder – A risks and benefits analysis

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**Introduction:** Major depressive disorder (MDD) is associated with high rates of incomplete response during treatment, with only