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Influence of haloperidol and clozapine on the cognitive performance in patients with psychotic disorders: possible attributes

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Antipsychotic medications are commonly used in the management of psychotic disorders. Evidences suggest that antipsychotic medications influence the cognitive performances significantly. Cognitive deficit is a core symptom of schizophrenia and other psychotic disorders. Worsening of cognitive performance by antipsychotic medications may have more detrimental effect on the cognitive performances. A recent network meta-analysis by Baldez et al had revealed that worsening of cognitive performance is more evident with use of antipsychotic medications like haloperidol and clozapine.

Haloperidol is a high-potent first-generation antipsychotic medication, which has an increased propensity to cause extrapyramidal side effects. Haloperidol produces parkinsonian side effects by blocking striatal dopamine receptors. Striatal dopamine deficit is associated with impairment of processing speed.² Due to higher risk of extrapyramidal side effects with haloperidol, patients receive central acting anticholinergic medications like trihexyphenidyl, procyclidine, and benztropine. Anticholinergic medication use is associated with impairment in cognitive functions, which is more so in adult to elderly population than the pediatric population.^{3,4} Therefore, the cognitive side effects of haloperidol can be perceived in an exaggerated manner in the research due to the use of concomitant anticholinergic medications.

Similarly, clozapine is often used in patients with resistant schizophrenia.⁵ Patients with treatment-resistant schizophrenia are usually more severe cases in terms of the severity of their psychopathology, duration of illness, poor response to multiple antipsychotic trials (even electroconvulsive therapy), and duration of antipsychotic treatment. All these factors are likely to influence the cognitive performance of the person with psychotic disorder, more adversely. Due to multiple background adverse factors in the patients who receive clozapine, the poor cognitive outcome might be more evident.

Hence, haloperidol and clozapine need to be judged considering the background and contextual variables associated with the use of these medications in patients with psychotic disorders. Maybe studies that compare the cognitive outcomes with respect to variation in the antipsychotic medication use by matching these confounding factors will give insight about the differential influence of antipsychotic medications on the cognitive functioning in patients with psychotic disorders.

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