Associations between risk of paralytic ileus and atypical antipsychotic use in mixed dementia

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Abstract:

Dementia affects 35 million people worldwide. Although Alzheimer's Disease (AD) is the most common form of dementia, 25% of patients have vascular dementia (VaD) and a further 20–40% have mixed dementia with VaD and AD. More than 90% of patients with dementia will experience at least one behavioural and psychological symptoms of dementia (BPSD), such as delusions, hallucinations, agitation and aggression during the course of their condition. Both atypical and conventional antipsychotics are used in the management of BPSD. However, prescribing trends heavily favour atypical antipsychotics because of a modest advantage with respect to tolerability and safety.

This article wants to present the side effect of atypic antipsychotics in a old female with mixed dementia with behavioural symptoms who developed progressively accentuated transit disorders in the absence of other detectable causes.

Informations from literature:

Antipsychotic drugs are the drugs most prescribed for behavioural and psychological symptoms, such as aggression or hallucinations, in people with dementia. In some people antipsychotics can eliminate or reduce the intensity of certain symptoms. It is generally accepted that atypical antipsychotics have an important but restricted role in the short-term.

The mechanism of medication-induced gastrointestinal hypomotility is primarily caused by muscarinic cholinergic antagonism. This effect may cause constipation and paralytic ileus, which may lead to fatal complications. Different antipsychotics have different anticholinergic potencies, which should be taken into consideration during medication selection.

One systematic review study recently found history of abdominal surgery, longer duration of psychiatric disorders, and older age to be risk factors of relapse of ileus. Overall, patients treated with antipsychotics had a 1.9 times higher risk to develop constipation compared to non-users. In severe cases, constipation may progress to ileus and bowel ischemia with multiple fatalities related to sepsis and bowel perforation. Therefore, we should pay more

attention to antipsychotic-related constipation and further complications, such as ileus, to prevent possible fatalities.
Quetiapine was also prone to cause anticholinergic side effects. In the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, quetiapine was found to have significantly more anticholinergic side effects in phase 1, phase 2, and phase 3 trials. Anticholinergic adverse effects had been found in 27% of the patients treated with quetiapine, and the most common complaints were dry mouth, urinary hesitancy and constipation.
Motor side effects are less pronounced with the group of atypical or second-generation antipsychotics. Other side effects that have received attention in the literature are metabolic abnormalities, cardiovascular risk, prolactin elevation, sexual dysfunction, Q_{tc-} prolongation, myocarditis, cataract. Different groups have published guidelines to screen and monitor patients for cardio-metabolic side effects.
A side effect that has received little attention is constipation. Constipation was described with typical antipsychotics mainly in association with the use of anticholinergic agents. But also some of the newer agents have intrinsic anticholinergic activity and can induce constipation.

Case study:
A 93-year-old patient, known to have neurocognitive disease- mixed dementia for 4 years when she was admitted to our clinic, (in treatment with Memantine, Mirtazapine, Quetiapine), stented Myocardial Infarction -2004 and deep vein thrombosis of the right leg-2021 (treated with Apixaban) shows abdominal flatulence and diffuse abdominal pain with intestinal transit present for faecal matter and gas. Biological assessment and abdominal CT were performed to detect the cause. Since the patient's condition no longer allowed treatment in our residence, she was transferred to the surgery department.
During hospitalization, recto Proctoscopy and ultrasound were performed, which ruled out an oncological cause. Imaging, clinical and biological data led to the diagnosis of intestinal paralysis secondary to medication. After removing Quetiapine from the regimen, stopping oral feeding and evacuation enemas, the patient's condition began to improve slowly.
Due to her advanced age and cardiovascular pathologies, the surgical treatment is delayed, the patient needing mashed food in the form of purees and laxatives in an increased dose with daily transit monitoring.
Behavioural disorders did not appear after the withdrawal of the antipsychotic (we mentioned that the dose of Quetiapine administered to the patient was 25 mg/day). He had mild episodes of agitation that were combated with Valerian and Passiflora supplements.
Biological: iron deficiency anaemia, inflammatory syndrome, hypoproteinemia, normal oncological markers, Cl creatinine=36ml/min/1.73m2.
Proctoscopy: without obstructive elements, faecal matter in large quantities 5 cm from the external anal opening.
Abdominal radiography: mixed intestinal content, distension of the colic loops with a tendency to images on the flanks, opacified costodiaphragmatic sinuses.
Native abdominal CT (renal cronic disease): an important distension of the descending, sigmoid colon and rectal ampulla with increased air and stercoral content is noted
Treatment: Lactulose, Memantine, injectable iron supplements, vitamins, Apixaban

Conclusions:

Constipation associated with antipsychotic treatment is frequent in patients with dementia. It can be severe when early detection fails. It leads to long-term prescription of pharmacological interventions. Clinical staff should be aware of this association and actively screen, monitor and provide early treatment. Preventive action with advice on diet, hydration and adjustment of physical activity levels should be promoted.

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