Clozapine induced bowel obstruction

A N U N D E R - E S T I M A T E D S E V E R E S I D E E F F E C T

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Introduction

Anti-depressants and anti-psychotics are frequently used by patients presenting to acute medicine admission units. Their side effect profiles are well documented in psychiatric literature. It is important to appreciate these iatrogenic effects as there is a significant associated morbidity and there have been reported cases of death. Clozapine is an atypical anti-psychotic that is used in treating patients with treatment-resistant schizophrenia and those with severe treatment related cognitive and side effects. Clozapine has marked anti-cholinergic effects and occurs in 14-60% patients.

Psychotropics associated with constipation

Antidepressants

Amitriptyline, Clomipramine, Doxepin, Mianserin, Mirtazapine, Nortriptyline, Venlafaxine.

Antipsychotics

Atypical antipsychotics (e.g. risperidone, olanzapine, quetiapine, clozapine, aripiprazole, ziprasidone).

Risk factors for constipation

- Sedentary lifestyle.
- Low fibre diet.
- Dehydration.
- Psychiatric patients: - Inability to verbalise symptoms.
- Long history of anti-psychotic medication.
- Use of other anti-cholinergic or CYP enzyme inhibitors.
- High doses or serum levels.
- Recent initiation of Clozapine.
- Regular laxatives and enemas prescribed.
- Good progress.
- Good exercise, fluid intake and dietary fibre.
- Increased exercise, fluid intake and dietary fibre.
- Avoid in rectal impaction.
- Use of other anti-cholinergic or CYP enzyme inhibitors.
- Comorbid medical illness.

Case Report

We describe a case of severe constipation leading to bowel obstruction in a schizophrenic patient treated with high doses of Clozapine who previously reported being chronically constipated. Once the patient was stabilized and intestinal perforation ruled out he was treated with regular bowel movements and daily enemas. It is noteworthy that this treatment was based on our personal experience as no local or national guidelines are available currently for the management of severe gastrointestinal adverse effects associated with Clozapine. These guidelines would represent a very useful tool to avoid constipation and other more serious gastrointestinal adverse effects.

In the United Kingdom there have been a few reports of Clozapine’s induced gastrointestinal (GI) hypomotility and occurs in 14-60% patients. The 5-HT3 receptor within the gut is known to be involved with motility. Clozapine has marked anti-cholinergic effects and occurs in 14-60% patients. This by blocking muscarinic (M3) receptors. It is also able to block adrenergic, histaminergic and serotoninergic receptors. The 5-HT3 receptor within the gut known to be involved with motility. Clozapine induced gastrointestinal (GI) hypomotility can be explored by its unique receptor profile. Constipation is a common GI side effect and occurs in 14-60% patients. In the UK there have been a few reports of Clozapine’s severe GI side effects.

Life threatening adverse effects of Clozapine include adynamic ileus, gastric outlet obstruction, ischaemia, severe GI side effects.

There are a number of important points to highlight from this case. Firstly, patients treated with Clozapine are at higher risk of GI complications directly related to their psychiatric treatment. Secondly, there is a lack of awareness about the side effects and the risk of progression to more serious complications. In addition, the early signs of constipation are underestimated.


In 2005, Graylands Hospital, Australia proposed a bulletin specifically dedicated for the management of adverse effects associated with the use of Clozapine, which includes a specific section for constipation. Our case along with many others described in the literature support that constipation is one of the few reported severe anti-psychotic side effects and therefore not adequately treated.