

February 2015

Alert No: 19

Safety of patients prescribed clozapine

There has been a death in a London Mental Health Trust of a patient from a bowel condition that arose from a known side effect of clozapine. In this case the patient died from toxic mega-colon. Toxic mega-colon occurs usually as a consequence of an inflammatory bowel disease.

The term megacolon (Ogilvie's syndrome) refers to a dilated colon that can be complicated by severe constipation, ischaemic necrosis and perforated bowel ("necrotising colitis"). It can occur as a side effect of antipsychotics. The primary mechanisms are blockade of acetyl choline muscarinic receptors and serotonin receptors. While chlorpromazine was involved in many of the earlier cases, the drug most likely to be involved now is clozapine.

The patient's condition in this case deteriorated rapidly. Having been observed to appear unwell, their blood pressure and pulse were found to be very low, an ambulance was called and paramedics found oxygen saturations of 72%. They applied oxygen but the patient went into cardiac arrest, and attempts to revive them were unsuccessful.

The Coroner observed that "It is perfectly possible for patients to show no signs of a toxic mega-colon and there are no obvious symptoms. This was not caused by an overdose but by continued use of clozapine, which the patient had been using since 1999."

There have also been incidents of severe harm experienced by patients of this Trust, receiving clozapine, related to bowel heath and constipation.

Clozapine-induced constipation may be associated with serious effects such as intestinal obstruction, bowel perforation and toxic megacolon, and can be fatal. Patients on clozapine are often prescribed additional anti-cholinergic drugs to counteract the side effect of hyper-salivation. This combination increases the risk of constipation and megacolon, as do tricyclic antidepressants.

Clozapine prescribing should be accompanied by regular physical monitoring, appropriate and timely use of laxatives, and early referral of constipated patients--before life-threatening pathologic processes develop.

If a patient on clozapine presents with GI complaints — constipation, distention, vomiting, abdominal pain — consider the possibility that these may be related to the drug. At the very least, these patients have to be followed carefully.

ACTIONS

- The possible side effects of clozapine need to be explained to patients at the start of treatment and repeated at regular intervals during treatment.
- Patients should be encouraged to report any change in bowel habit to their care co-ordinator, doctor or GP
- Clinical staff should enquire routinely about side effects of clozapine including bowel habits and refer patient for review on an urgent basis if there are signs of constipation or obstruction