**Supplementary Table 4. Recent case reports: Life-threatening gastrointestinal hypomotility with clozapine [Supplement to Flanagan and Ronaldson, 2016 (Table 6.1)]**

| **Patient sex, age (yr)** | **Clozapine dose (mg/d)** | **Clozapine duration** | **Clinical features** | **Investigations** | **Treatment** | **Outcome** | **Reference** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| M, 61 | 325 | 5 w | No history of constipation. Sudden collapse. Transfer to ITU. Abdominal distension with hypoactive bowel sounds. Rectal examination: hard impacted stool | Abdominal X-ray: large faecal content in the colon and dilated small bowel suggestive of  bowel obstruction from fecal impaction | Given antibiotics, but rapid decline in clinical status with worsening  hypotension. Deemed too unstable for surgery | Suffered cardiac arrest and died 12 h after presentation | Oke et al. (2015) |
| M, 47 | - | - | Ten yr h/o of constip­ation. On high-fibre diet and laxatives. Abdomen: severe pain  and diffuse tenderness with muscle guarding. Impacted hard faecaloma impossible to extract in the rectal vault. Sudden faeculent vomiting and collapse | CT: dilated colon 11 cm in diameter with faecal impaction. The liver lifted upwards and compressed with subsequent Budd-Chiari syndrome: the  inferior vena cava was compressed and the hepatic veins poorly contrasted | Laparotomy with subtotal colectomy for pancolonic ischemia with double-end ileosigmoidostomy and manual extraction of  the remaining fecaloma | Discharged day 21. Clozapine recommenced. Digestive continuity  restored at 3 months | Osseis et al. (2015) |
| F, 60 | 150 | 10 d | Febrile, tachycardic, hypotensive Abdominal fullness and nausea | Colonoscopy: no evidence of obstruction. CT: paralytic ileus | Clozapine discontinued, and ileus managed clinically | Good response within 24 h. Started on quetiapine | Sarac et al. (2015) |
| F, 58 | 600 | 5 yr | Sudden diffuse abdominal cramping pain accompanied by nausea and retention vomiting. Abdomen distended, no bowel sounds, no signs of peritoneal irritation | X-ray: small bowel loops dilated (air present in the rectal ampulla), confirmed by CT. No obstruction or other complications | Clozapine stopped. Bowel function regained after a week with supportive measures and without solid food | Clozapine reintroduced cautiously (final dose 550 mg/d). Laxatives and lifestyle  modifications instituted | Castillo-García et. (2016) |
| M, 66 | 200 + quetipine |  | Faeculent emesis, abdomen distended but not tender. In severe respiratory distress. | CT: acute respiratory  distress syndrome due to aspiration and impacted stool throughout his colon. | Drugs stopped. Manual disimpaction and enemas. Copious bowel movements and resolution of abdo­minal distension. Clozapine restarted day 11, but day 16 quetiapine restarted. Recurrence of abdo­minal distension and onset of copious foul-smelling hematemesis. Abdominal X-ray showed diffuse small bowel dilation | Severe diffuse ulcer­ation in the oesphagus, stomach and duodenum. Developed septic shock  and died within 24 h of developing symptoms | Osterman et al. (2017) |
| M, 34 | 200 | 13.3 yr | Abdominal pain | Ileus in small intestine | Laxatives | Discharged after 2 d | Ingimarsson et al. (2018) |
| M, 47 | 300 | 15.3 yr | Nausea, vomiting, abdominal pain | CT: bowel obstruction | Laxatives not success­ful. Intubated: aspir­ation pneumonia, also renal failure, hypo­tension. Colon­oscopy unsuccessful. Total resection of necrotic colon and ileostomy | Intraabdominal abscess. ITU 27 days; eventual recovery | Ingimarsson et al. (2018) |
| M, 67 | 200 + olanza­pine 10 mg/d | 17.6 yr | In-patient: paralytic ileus, pneumonia and sepsis |  | Medical ward 40 d. Antibiotics and laxatives | Full recovery | Ingimarsson et al. (2018) |
| M, 54 | 300 | 8.7 yr | Constipation 2 yr | Volvulus. One yr later: acute abdomen. Volvulus and pneumonia | Laxatives and sigmoidoscope. Total colectomy with ileostomy | ITU: respiratory failure. Eventual recovery | Ingimarsson et al. (2018) |
| M, 46 | 700 | - | Presented with mild lower abdominal pain on background of one month history of constipation. Sudden deterioration. | Abdomen mild distention, soft, non-tender. Digital rectal examination revealed loose, non-bloody stools. CT: grossly distended rectum and sigmoid full of faeces. Thickening of the wall of the rectum and sigmoid colon. Marked distention of rest of colon with a combination of fluid and faeces | Treated conservatively but further deterior­ation day 2. CT suggested colon ischaemia. Emergency laparotomy: colon and rectum hugely dilated with unusually thick walls. Total colectomy and formation of end ileostomy. | Required ventilation, haemodialysis and total par­enteral nutrit­ion. Developed lower lobe pneumonia. Discharged on day 109 on risperidone, but remained on haemo­dialysis. | George et al. (2019) |
| M, 24 | 500 | 14 w | Sudden occurrence of colicky pain in abdomen associated with recurrent bilious vomiting and abdominal distension with obstipation. | Abdominal radiograph and contrast enhanced CT of the abdomen showed ceco-colic volvulus with malrotation of gut and oedematous bowel. No evidence of gangrene or perforation | At laparotomy cecum and ascending colon hugely dilated. No evidence of gangrenous changes. Volvulus de-rotated. Right hemicolectomy with ileo-transverse anastomosis | Developed paralytic ileus on day 4 that responded to treatment. Discharged day 7. Started on aripiprazole | Aneja et al. (2020) |
| M, 45 | 1200 | ‘Years’ | H/o chronic constipation. Somnolent and unresponsive. Soft, nontender, mildly distended abdomen with reduced bowel sounds. Day 2 bilious emesis and mildly tender abdomen | CT: large stool burden diffusely in small and large intestines but no obvious transition point for ileus. Histology consistent with acquired hypoganglionosis | Manual therapy to remove stools but repeat CT: markedly dilated colon. Total colectomy with ileostomy | Cautiously restarted on clozapine, but at lower dose than before. No recurrence of toxicity | Gisi et al. (2020) |
| F, 63 | 400 +  olanzap-­  ine 20 mg/d | 10 yr | Nausea, confusion. Hyponatremia, COVID-19 | Ileus | Clozapine stopped 1 week | Clozapine gradually reintroduced when bowel function returned to normal | Dotson et al. (2020) |
| M, 29 | 200 | - | One day h/o vomiting, abdominal pain and distension | CT: no obstruction but dilation from the caecum to the ileum; caecum diameter 87 mm: sepsis due to intestinal ischemia diagnosed (Ogilvie syndrome) | Enema: voluminous stool discharge. Respiratory distress, hypotension, loss of consciousness; intubated | Cardiac arrest x 3; died 13 hours post-admission | Akkaş & Demir (2020) |
| F, 64 | 700 | >3 yr | C/o abdominal pain with diarrhea, vomiting, loss of appetite; gradually developed sedation and confusion. No fever. ED presentation day 14 lethargic with fluctuating confusion, sedation, loss of appetite, abdominal pain. | CT showed light dilated loops with diffuse stercoral retention with numerous faeces formed at the rectal level without actual fecal impaction. Infectious colitis suspected | Clozapine dose reduced to 400 mg/d. Ileus resolved slowly. Given antibiotics | Discharged on clozapine 600 mg/d | Bebawi et al. (2021) |

Abbreviations: BP, blood pressure; CT, computerized tomography; d, day(s); F, female; GI, gastrointestinal; h, hour(s); INR, international normalized ratio; IV, intravenous; m, month(s); M, male; PEG, polyethyleneglycol; w, week(s); yr, year(s).

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