



Relationship between indiscriminate use of psychotropic drugs and the development of sigmoid volvulus: a systematic review

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Abstract

Introduction: Sigma volvulus is a common cause of intestinal obstruction, especially in vulnerable populations. Psychotropic drugs, widely used for mental disorders, have side effects that can compromise gastrointestinal motility, increasing the risk of sigmoid volvulus. **Objective:** A brief systematic review was developed to list the central clinical studies and case reports on the relationship between the occurrence of sigmoid volvulus in patients using psychotropic drugs.

Methods: The PRISMA Platform systematic review rules were followed. The search was carried out from November 2024 to January 2025 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

Results and Conclusion: 112 articles were found, 25 articles were evaluated in full and 11 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 31 studies that did not meet GRADE and AMSTAR-2. Most studies did not show homogeneity in their results, with $X^2=79.5\%>50\%$. The indiscriminate use of psychotropic drugs represents an underestimated risk factor for the development of sigmoid volvulus. It is crucial to constantly monitor gastrointestinal side effects in patients treated with these drugs and to encourage a comprehensive approach in their clinical management. Reducing anticholinergic load and avoiding serotonergic antagonists will also mitigate hypomotility. Previous

abdominal surgery and cecal diameter >10 cm was found to be predictive factors for failure of colonoscopic detorsion. Constipation due to psychotropic drug use was a significant predictor of recurrence of sigmoid volvulus. Effective management of constipation is crucial to prevent recurrence.

Keywords: Sigmoid volvulus. Psychotropic drugs. Intestinal motility disorders.

Introduction

The incidence of colonic volvulus varies across regions including Africa, South America, Russia, Eastern Europe, the Middle East, India, and Brazil. Colonic volvulus accounts for up to 42% of all bowel obstructions. Furthermore, volvulus accounts for up to 15% of all large bowel obstructions in the United States and Western Europe. Although any mobile segment of the colon can twist on itself, the sigmoid colon is involved in 75% of cases. Sigmoid volvulus generally occurs in a 4:1 ratio of men to women. In Western countries, sigmoid volvulus predominantly affects older men (age >70), while cecal volvulus affects slightly younger women (age ≤60) [1,2].

In this sense, large bowel obstruction is an emergency condition that requires early identification and intervention, with colonic volvulus being the third leading cause worldwide. [3]. Sigmoid volvulus occurs when the sigmoid colon rotates on its axis, causing an acute intestinal obstruction. In this scenario, psychotropic drugs are drugs that affect the central nervous system to treat disorders such as depression,

anxiety, and psychosis. Their adverse effects include gastrointestinal disorders such as severe constipation, reduced intestinal motility, and an imbalance in the gut microbiota. These conditions can predispose to the development of sigmoid volvulus [3,4].

Due to psychiatric problems, the patient is more likely to be treated with sedatives and psychotropic drugs, causing decreased neuromuscular function of the intestine. The basic principles in the treatment of volvulus are to release the volvulus, decide whether a nonoperative or operative procedure should be used, and treat complications. Colonoscopy appears to have become an important method of treatment for volvulus with established indications [5].

Given this, the present study developed a brief systematic review to list the central clinical studies and case reports on the relationship between the occurrence of sigmoid volvulus in patients using psychotropic drugs.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>. Accessed at: 16/01/2025. The AMSTAR 2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: <https://amstar.ca/>. Accessed on: 16/01/2025.

Search Strategy and Search Sources

The literature search process was carried out from November 2024 to January 2025 and developed based on Web of Science, Scopus, Embase, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors were used in health sciences (DeCS/MeSH): "Sigmoid volvulus. Psychotropic drugs. Intestinal motility disorders", and the Boolean "and" was used between the MeSH terms and "or" between the historical findings.

Study Quality and Risk of Bias

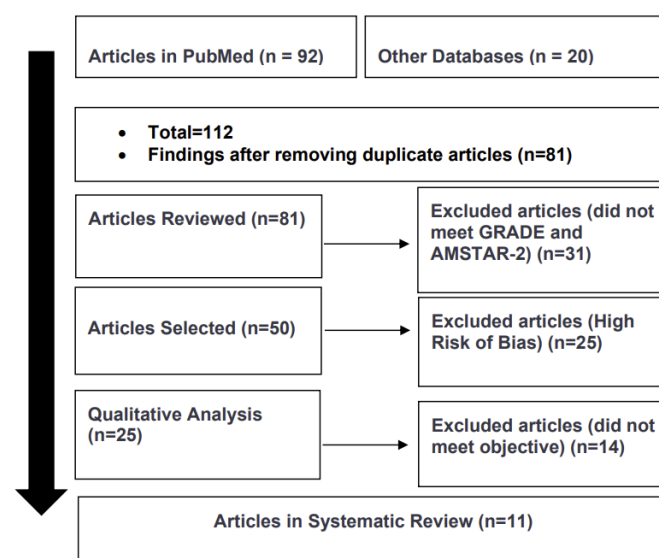
Quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. Low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE

instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's test (d).

Summary of Findings

A total of 112 articles were found and submitted to eligibility analysis, with 11 final studies selected to compose the results of this systematic review. The listed studies were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with $X^2=79.5\%>50\%$. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 25 studies with a high risk of bias and 31 studies that did not meet GRADE and AMSTAR-2.

Figure 1. Flowchart showing the article selection process.

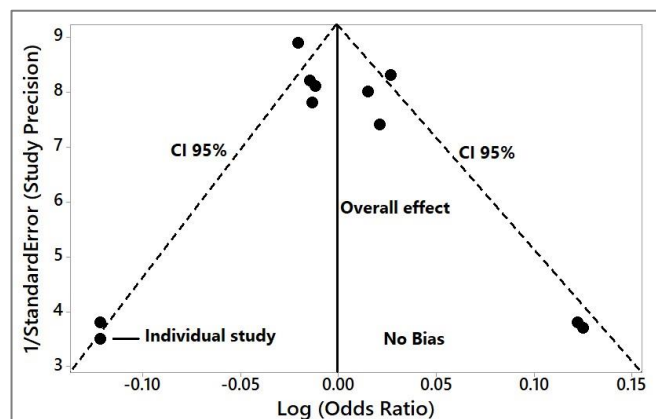


Source: Own Authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample sizes (lower precision) that are shown at the base of the graph and in studies with large sample sizes that are presented at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the studies with small sample sizes that

are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=11 studies).



Source: Own Authorship.

Major Clinical Outcomes

In the setting of sigmoid volvulus under psychotropic drug use, clozapine is prescribed to manage schizophrenia. However, clozapine has hematologic, metabolic, and cardiac side effects. Furthermore, impaired gastrointestinal motility is also common, with an estimated occurrence of 14%. Gastrointestinal hypomotility can lead to paralytic ileus, obstruction, gastrointestinal ischemia, and death [1].

Relatedly, a case report of clozapine-related cecal volvulus was described. A 58-year-old woman with schizoaffective disorder, bipolar type, who had been a resident of a long-term psychiatric unit for chronically ill patients for 6 years, was transferred to an intensive care hospital for evaluation of constipation, abdominal distension, nausea, and bilious vomiting of 3 days' duration. Her psychiatric medications included clozapine 575 mg/d, clonazepam 0.5 mg twice/d as needed, lamotrigine 100 mg/d, and haloperidol 5 mg orally 3 times/d. Diphenhydramine 50 mg orally 4 times/d as needed was recently started for pruritus. She had a history of intermittent constipation but was frequently noncompliant with a recommended bowel regimen consisting of senna/docusate sodium 8.6/50 twice/d and polyethylene glycol daily. She had hypertension of 166/91 mmHg. Her abdomen was distended, soft, and nontender. A comprehensive metabolic panel revealed hypokalemia (2.8 mmol/L) with no other significant abnormalities. Abdominal radiograph revealed marked colonic dilatation containing an air-fluid level occupying the left upper and lower quadrants with preservation of the haustral folds; air-fluid levels were visualized within the loops of the bowel in the pelvis. The initial clinical impression was that of Ogilvie syndrome. Clozapine and diphenhydramine were withheld. The patient was given nothing orally, and potassium was replaced; an

aggressive bowel regimen including polyethylene glycol, senna, and mineral oil enemas was suggested. Subsequent computed tomography (CT) of the abdomen/pelvis with rectal contrast showed progression of the contrast to the splenic flexure/transverse colon and revealed a mesenteric vortex in the right lower quadrant adjacent to a dilated, non-opacified loop of bowel measuring 11 cm and extending into the left hemiabdomen. Cecal volvulus was suspected despite the absence of significant small bowel dilation. Surgical intervention, i.e., exploratory laparotomy, confirmed cecal volvulus and rupture of the intestinal serosa. The transverse colon, descending colon, sigmoid colon, and rectum appeared healthy. A right hemicolectomy with side-to-side stapled anastomosis was performed without complications. Intestinal motility was restored, with significant postoperative progression [6].

In this sense, the anticholinergic, serotonergic, and noradrenergic effects of clozapine are implicated in the production of gastric hypomotility. For patients treated with clozapine who develop abdominal pain and distension, vomiting, and severe constipation, careful investigation of serious causes, e.g., Ogilvie syndrome or cecal volvulus, is necessary to distinguish them [6].

A retrospective clinical study analyzed the medical records of 45 patients with colonic volvulus, 17 with cecal volvulus, and 29 with sigmoid volvulus (1 had both). A total of 66% of the patients were demented, bedridden, or taking constipating medications. Initial nonoperative decompression was achieved in 26 of 29 patients with sigmoid volvulus, but in only three of nine patients in whom it was attempted with cecal volvulus. There were no deaths in the 15 patients with sigmoid volvulus who were selected for successive nonoperative treatment. Two of nine patients died after right hemicolectomy. These data suggest that if elective surgery is performed for sigmoid volvulus, it should be done after one or more recurrences and that nonoperative decompression can be performed safely on successive occasions [7].

Authors Surek et al. (2021) [8] performed a retrospective clinical study to show that colonoscopic detorsion is the first treatment option for uncomplicated sigmoid volvulus after colonoscopic detorsion. There were 21 patients in the unsuccessful colonoscopic detorsion group and 52 patients in the successful colonoscopic detorsion group. The rate of unsuccessful colonoscopic detorsion was 28.76%; this is likely a function of more neuropsychiatric disease, more accompanying sigmoid diverticulum, previous abdominal surgery, abdominal tenderness, symptom onset for more than 48 h, higher mean intra-abdominal pressure (IAP), IAP over 15 mmHg, larger mean cecal diameter, cecal diameter over 10 cm, and higher mean

C-reactive protein values as statistically significant. In multivariate analysis, previous abdominal surgery and cecum diameter >10 cm were found to be predictive factors for colonoscopic detorsion failure ($p = 0.049$, OR = 0.103 and $p = 0.028$, OR = 10.540, respectively).

Furthermore, authors Uda et al. (2024) [9] conducted a retrospective cohort study to identify factors influencing the recurrence of sigmoid volvulus to develop effective preventive strategies. A total of 44 patients diagnosed with sigmoid volvulus were included. Of the 44 patients, 20 had recurrences. Single regression analysis identified constipation, neuropsychiatric disorders, and sigmoid colon overgrowth as significant factors. Logistic regression analysis confirmed constipation due to psychotropic drug use as an important predictor of recurrence (OR: 8.84, 95% CI: 2.05-38.1, $p=0.0034$). The area under the receiver operating characteristic (ROC) curve for the model was 0.804 (95% CI: 0.67-0.938), indicating good predictive accuracy. Effective management of constipation is crucial to prevent recurrence.

In addition, a case of colonic ileus has been described in a patient with schizophrenia under treatment with paliperidone palmitate. Thorough physical examination and rigorous screening for side effects are recommended when antipsychotics are prescribed. Ileus is an important side effect of antipsychotic treatment, with potentially morbid and fatal consequences if early detection fails. Preventive measures should be promoted and appropriate interventions implemented [10]. Also, clinical case reports and retrospective studies documenting patients with sigmoid volvulus under treatment with psychotropic drugs were selected. Information collected included age, comorbidities, type of psychotropic drug used, and clinical outcome. Gastrointestinal side effects of psychotropic drugs [11-14]:

1. Chronic constipation: It is a common effect of antidepressant (amitriptyline, fluoxetine) and antipsychotic drugs (risperidone, haloperidol) due to their anticholinergic action. Chronic constipation may contribute to distension of the sigmoid colon.
2. Intestinal motility disorders: Opioids, occasionally used in psychiatric patients, decrease intestinal motility by acting on μ -opioid receptors in the enteric nervous system.
3. Impact on gut microbiota: Psychotropic-induced changes in intestinal flora may affect stool consistency and colonic motor function.

In a cohort study of 150 patients with sigmoid volvulus, 12% were on antipsychotics or antidepressants. A case of a 65-year-old male with schizophrenia treated with haloperidol who developed sigmoid volvulus after several months of severe

constipation was reported. - Another study identified that patients using opioids had a 30% higher risk of developing intestinal obstructions Discussion Pathophysiological mechanisms [15]:

1. Anticholinergic effect: Psychotropic drugs inhibit muscarinic receptors, decreasing peristaltic contractions and promoting the accumulation of fecal matter in the sigmoid colon.
2. Chronic dilation of the colon: Chronic constipation generates prolonged distension, weakening the intestinal wall and increasing the risk of torsion.
3. Alterations in neurological signaling: Medications that affect serotonin and dopamine may alter colonic motor coordination [16].

Limitations

Although the association between psychotropic drugs and sigmoid volvulus is plausible, prospective studies are required to establish a causal relationship. Furthermore, factors such as diet, age, and comorbidities also influence the onset of this condition.

Conclusion

The indiscriminate use of psychotropic drugs represents an underestimated risk factor for the development of sigmoid volvulus. It is crucial to constantly monitor gastrointestinal side effects in patients treated with these drugs and to encourage a comprehensive approach in their clinical management. Reducing anticholinergic load and avoiding serotonergic antagonists will also mitigate hypomotility. Previous abdominal surgery and cecal diameter >10 cm was found to be predictive factors for failure of colonoscopic detorsion. Constipation due to psychotropic drug use was a significant predictor of recurrence of sigmoid volvulus. Effective management of constipation is crucial to prevent recurrence.

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