

Review of Clozapine-Related Intestinal Perforation

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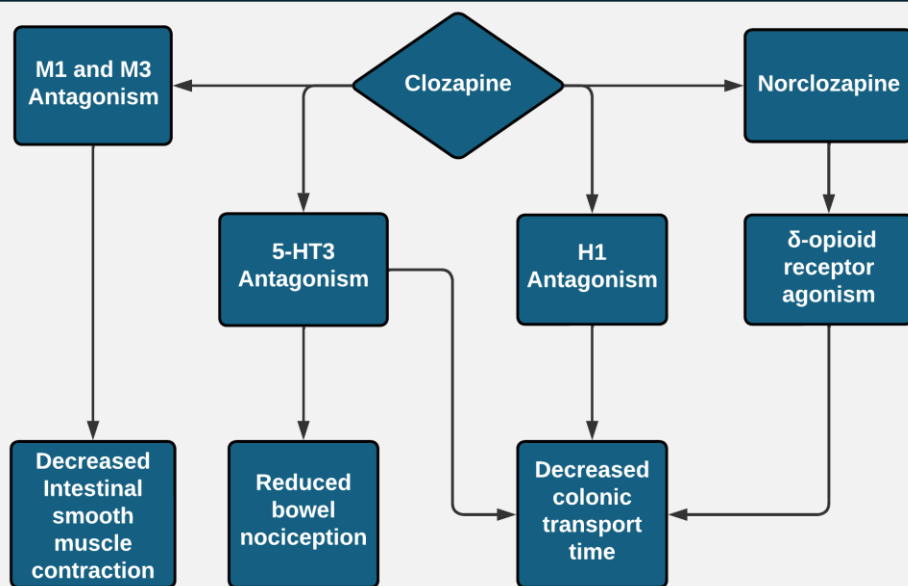
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Background

- Clozapine's severe gastrointestinal complications are less recognized than its hematological and cardiovascular side effects.
- Clozapine-associated constipation affects up to 60% of patients and can lead to ileus, colitis, or perforation requiring surgery.
- We aim to highlight the characteristics associated with intestinal perforation.



Methods

- This literature review used PubMed, Scopus, Embase, Web of Science, and PsycInfo, covering publications from 1992 to 3/14/2024.
- Search terms included "clozapine," "perforation," and "peritonitis."
- Case reports and series describing clozapine treatment and gastrointestinal perforation events were included.

Take Home Message:

Clozapine can cause fatal bowel complications, even at FDA-approved doses, with laxative use, or years later!

AI-generated image using commands: "Create an image showing clozapine-related bowel perforation for scientific purposes."



References

Results

- 239 articles screened; 6 studies reported 9 cases of clozapine-associated intestinal perforation.
- Mean age: 42.6, Male : Female = 3.5
- Schizophrenia was the primary psychiatric diagnosis.
- Clozapine doses: 275-550 mg/day (mean 391.6 mg/day).
- Perforations occurred 1 week to 67 months after starting clozapine (mean 19.1 months).
- 5 cases used laxatives, 1 did not, 3 unreported.
- 4 large bowel, 3 ileocecal, 1 small bowel, 1 unspecified perforation.
- Most cases were rechallenged with clozapine post-stabilization.

Sex:Age	Presenting symptoms	Clozapine dose	Duration of clozapine	End point
Male:23	Vomiting Loss of appetite Abdominal pain	400 mg/day	1 week	Perforation
Male:42	Abdominal pain Distention Anorexia	500 mg/day	Unknown	Multiple small perforations on jejunum and ileum
Male:46	Abdominal discomfort Constipation Vomiting	275 mg/day	15 months	Colon perforation Appendicitis
Male:46	Abdominal pain	275 mg/day	14 months	Perforation
Male:47	Abdominal pain Loss of appetite	550 mg/day	67 months	Perforation
Male:49	Abdominal pain Constipation	400 mg/day	6 weeks	Colon perforation
Male:62	Constipation Distention Vomiting	375 mg/day	19 months	Perforation
Female:24	Abdominal pain	450 mg/day	18 months	Perforation
Female:45	Abdominal pain Rectal bleeding	300 mg/day	"Long term"	Sigmoid colon perforation

Discussion

- Clozapine-induced gastrointestinal side effects are underreported but linked to severe morbidity and mortality.
- Possible mechanisms: anticholinergic, serotonin, and histamine antagonism.
- Schizophrenia may impair pain reporting, complicating early detection.
- Laxative use doesn't eliminate the risk of severe complications.
- Clozapine rechallenge can be considered post-stabilization if needed.
- Early identification, prevention, and management are crucial.

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